Dietary conjugated linoleic acid mixture affects the activity of intestinal acyl coenzyme A: cholesterol acyltransferase in hamsters

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The present study was designed to study the mechanisms by which dietary conjugated linoleic acids (CLA) decrease serum cholesterol. Hamsters were fed a semi-synthetic diet containing 1 g cholesterol/kg diet with or without supplementation with 20 g linoleic acid (LA) and 20 g CLA/kg diet. After 8 weeks, serum fasting total cholesterol (TC) and triacylglycerol (TG) were significantly lower in the LA-supplemented and CLA-supplemented groups compared with those of the control (CTL) hamsters. In contrast to LA, CLA significantly lowered hepatic cholesterol but it increased the level of adipose tissue cholesterol, suggesting that the hypocholesterolaemic mechanism of CLA is different from that of LA. CLA decreased the activity of intestinal acyl CoA:cholesterol acyltransferase (ACAT) whereas LA had no effect on this enzyme. Consequently, CLA supplementation increased the faecal excretion of total neutral sterols, but it had no or little effect on the faecal acidic sterols. If the ACAT is associated with cholesterol absorption, the part of mechanisms by which CLA decreases serum cholesterol may involve down-regulation of intestinal ACAT activity.

Cholesterol: Conjugated linoleic acids: Linoleic acid: Triacylglycerol

Conjugated linoleic acids (CLA) refers to a group of positional and geometric isomers of linoleic acid (LA). In contrast to those in LA, the double bonds in CLA are conjugated, instead of being in the typical methylene interrupted configuration. CLA is predominantly found in meat and dairy products (Ha et al. 1989; Chin et al. 1992). Low concentrations of CLA also occur in the lipids of human blood, tissue and milk (Cawood et al. 1983; Iversen et al. 1985). CLA can also be prepared chemically by biohydrogenation (Kepler & Tove, 1967; Hughes et al. 1982) and by alkali isomerization of LA (Nichols et al. 1951).

High plasma cholesterol has been ranked as one of the greatest risk factors in development of CHD (Neaton et al. 1984; Grundy, 1986). Supplementation with CLA could significantly lower serum total cholesterol (TC), LDL-cholesterol and triacylglycerol (TG) in rabbits (Lee et al. 1994) and hamsters (Nicolosi et al. 1997). Thus, the risk factors for atherosclerosis including the LDL-cholesterol: HDL-cholesterol ratio and the TC:HDL-cholesterol ratio were significantly reduced. However, the hypocholesterolaemic mechanism involved remains poorly understood. We have previously chosen Golden Syrian hamsters (Mesocricetus auratus) to study the potency of green tea catechins (Chan et al. 1999). Golden Syrian hamsters have been increasingly used as a model to estimate the efficacy of hypocholesterolaemic agents in human subjects (Sugiyama et al. 1995). Unlike rats, in which most of the serum cholesterol is in HDL, the major cholesterol carrier in hamsters is LDL as in man (Nistor et al. 1987; Lehmann et al. 1993). There are many similarities between hamsters and man in their intrinsically low rate of hepatic cholesterologenesis, in their response to different diet and drugs, and in the manner in which they handle biliary sterol secretion (Nistor et al. 1987). The present study was designed to test our hypothesis that dietary CLA decreases serum cholesterol, probably by its inhibition on cholesterol absorption, using hamsters as an animal model.

Abbreviations: ACAT, acyl CoA:cholesterol acyltransferase; CLA, conjugated linoleic acids; HMG, 3-hydroxy-3-methylglutaryl; LA, linoleic acid; TC, total cholesterol; TG, triacylglycerol.
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which is believed to play an important role in esterification
intestinal acyl CoA:cholesterol acyltransferase (ACAT),
The hamsters were then killed without overnight fasting
similarly maintained on one of the three diets for 8 weeks.

The animals were housed (two hamsters per cage) in an
animal room at 23°C for 14 h. The blood was collected via the
abdominal aorta. After clotting, the blood was centrifuged
discarded. Food intake was measured daily and body
diet was given to the animals daily, and uneaten food was

Thirty-six male Syrian Golden hamsters (125±140 g;
The hypercholesterolaemic diet described by Sanders &
conramstarch, sucrose, AIN-76 mineral mix, AIN-76A
vitamin mix, dL-methionine and cholesterol as shown in
Table 1. The ingredients were purchased from Harlan
Teklad (Madison, WI, USA) except for lard, which was
obtained from the local market, and dL-methionine and
cholesterol, which were purchased from Sigma (St Louis,
MO, USA). To achieve the high hypolipidaemic activity,
CLA (purity 890 g/kg, Tonalin™, Natural Lipids Ltd, AS,
Hovdebygda, Norway) and LA (Sigma) were added to the
diet at a level of 20 g/kg diet. The diets (1 kg) were then
mixed with 250 ml gelatin solution (40 g/l). Once the
gelatin had set, the food was cut into cubed portions of
about 20 g and stored frozen at −20°C.

Thirty-six male Syrian Golden hamsters (125–140 g; The
Chinese University of Hong Kong, Shatin, Hong Kong)
were randomly divided into three groups (n 12 per group) with approximately equal mean group bodyweights. The animals were housed (two hamsters per cage) in an animal room at 23°C with a 12 h light–dark cycle. The hamsters were fed one of the three diets for 8 weeks. Fresh
diet was given to the animals daily, and uneaten food was
discarded. Food intake was measured daily and body
weight was recorded twice per week. The protocol was
reviewed and approved by the Committee of Animal
Ethics, The Chinese University of Hong Kong. The 4 d total faecal output was collected during feeding. All
hamsters were killed at the end of experiment after food
depivation for 14 h. The blood was collected via the
abdominal aorta. After clotting, the blood was centrifuged
at 1300 g for 15 min, and serum was then collected. The liver, peri-renal adipose tissue, kidney, heart, brain and
muscle (Adductor longus) were also retained.

At the same time, another thirty hamsters were divided randomly into three groups (n 10 per group) and were
similarly maintained on one of the three diets for 8 weeks. The hamsters were then killed without overnight fasting
(full stomach). The objective was to enhance the activity of
intestinal acyl CoA:cholesterol acyltransferase (ACAT),
which is believed to play an important role in esterification
before absorption of dietary cholesterol. To be consistent,
the first 10 cm of intestine from the stomach was discarded,
and the next 30 cm was taken for the intestinal ACAT
assay (Helgerud et al. 1981; Murakami et al. 1995). All the
tissues were stored at −78°C.

**Analysis of conjugated linoleic acids in the diet**

The pure CLA mixture (890 g/kg, 3 kg) was obtained as a
gift from Natural Lipids Ltd, AS. The CLA from diet was
converted to the corresponding fatty acid methyl esters with
methanolic hydrogen chloride under N2 at 90°C for 45 min. The CLA–fatty acid methyl esters were separated and
quantified using capillary GLC method previously
described by us (Chen et al. 1997) and Ag2+ HPLC method
described by Sehat et al. (1998). In the GLC method, the
CLA–methyl esters were separated in a flexible silica capillary column (SP 2560, 100 m x 0.25 mm internal
diameter; Supelco, Inc., Bellefonte, PA, USA) in a HP 5890 Series II GLC equipped with a flame-ionization
detector (Hewlett-Packard, Palo Alto, CA, USA). In the
Ag2+ HPLC method, the analysis was performed on a Ag2+
impregnated column (4-6 mm internal diameter x 250 mm; Chrompack, Bridgewater, NJ, USA) with an Alltech Model
525 HPLC equipped with a ternary pump delivery system
and a u.v. detector (Alltech, Deerfield, IL, USA). The fatty
acid composition of the three diets is shown in Table 2.

**Determination of blood cholesterol**

Enzymatic kits were purchased from Sigma to measure
serum TG (catalogue number 336-20) and TC (catalogue
number 352-20). HDL-cholesterol was isolated by pre-
cipitation of the apolipoprotein B-containing lipoproteins
using sodium phosphotungstate–magnesium chloride using
the commercial Sigma kit (catalogue number 352-4) as
described by Lee et al. (1994) and Nicolosi et al. (1997).

**Table 1. Composition of experimental diets**

<table>
<thead>
<tr>
<th>Content</th>
<th>CTL (g/kg)</th>
<th>LA (g/kg)</th>
<th>CLA (g/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornstarch</td>
<td>488</td>
<td>478</td>
<td>478</td>
</tr>
<tr>
<td>Casein</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Lard</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Sucrose</td>
<td>150</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>Mineral mix</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Vitamin mix</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>dL-Methionine</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>-</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>Conjugated linoleic acids</td>
<td>-</td>
<td>-</td>
<td>20</td>
</tr>
</tbody>
</table>

CTL, control diet; LA, linoleic acid-supplemented diet; CLA, conjugated linoleic acids-supplemented diet.

* For details of preparation of the diets see p. 936.

**Table 2. Fatty acid composition of diets**

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>CTL (g/kg)</th>
<th>LA (g/kg)</th>
<th>CLA (g/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myristic</td>
<td>2.05</td>
<td>1.93</td>
<td>1.96</td>
</tr>
<tr>
<td>Palmitic</td>
<td>26.65</td>
<td>25.99</td>
<td>26.31</td>
</tr>
<tr>
<td>Palmitoleic</td>
<td>1.91</td>
<td>1.90</td>
<td>1.87</td>
</tr>
<tr>
<td>Stearic</td>
<td>15.77</td>
<td>15.93</td>
<td>16.14</td>
</tr>
<tr>
<td>Oleic</td>
<td>31.94</td>
<td>32.46</td>
<td>33.00</td>
</tr>
<tr>
<td>Vaccenic</td>
<td>1.86</td>
<td>1.85</td>
<td>1.87</td>
</tr>
<tr>
<td>Linoleic</td>
<td>9.82</td>
<td>9.37</td>
<td>10.01</td>
</tr>
<tr>
<td>Arachidic</td>
<td>0.23</td>
<td>0.24</td>
<td>0.25</td>
</tr>
<tr>
<td>Linolenic</td>
<td>0.46</td>
<td>0.48</td>
<td>0.47</td>
</tr>
<tr>
<td>Others</td>
<td>4.3</td>
<td>4.84</td>
<td>5.11</td>
</tr>
<tr>
<td>Total CLA</td>
<td>-</td>
<td>-</td>
<td>17.97</td>
</tr>
<tr>
<td>(c10, c10)-CLA</td>
<td>-</td>
<td>-</td>
<td>0.92</td>
</tr>
<tr>
<td>(c9, t11)-CLA</td>
<td>-</td>
<td>-</td>
<td>0.98</td>
</tr>
<tr>
<td>(c11)-CLA</td>
<td>-</td>
<td>-</td>
<td>7.92</td>
</tr>
<tr>
<td>(t11, c12)-CLA</td>
<td>-</td>
<td>-</td>
<td>7.82</td>
</tr>
<tr>
<td>(c9, c11)-CLA</td>
<td>-</td>
<td>-</td>
<td>0.16</td>
</tr>
<tr>
<td>(c10, c12)-CLA</td>
<td>-</td>
<td>-</td>
<td>0.17</td>
</tr>
</tbody>
</table>

CTL, control diet; LA, linoleic acid-supplemented diet; CLA, conjugated linoleic acids-supplemented diet; t, trans; c, cis.

* For details of analytic procedures see p. 936.
**Determination of tissue cholesterol**

TC was determined as previously described by Chan et al. (1999). In brief, the total lipids were extracted, and the lipid extracts were then saponified. The non-saponified substances including cholesterol were converted to their trimethylsilyl-ether derivatives and subjected to the GLC analysis in a fused silica capillary column (SAC™, 30 m x 0.25 mm, internal diameter; Supelco, Inc.) using a Shimadzu GC-14 B GLC equipped with a flame ionization detector (Shimadzu, Tokyo, Japan).

**Determination of faecal neutral and acidic sterols**

Faecal neutral and acidic sterols were determined as previously described by Chan et al. (1999). In brief, the faecal samples were saponified. The total neutral sterols were extracted using cyclohexane and were then converted to their corresponding trimethylsilyl-ether derivatives for GLC analysis. The remaining aqueous layer was treated with 10 M-NaOH and 3 M-HCl followed by twice-repeated extraction with diethyl ether. The acidic sterols were similarly converted to their trimethylsilyl-ether derivatives and subjected to GLC analysis.

**Assays of 3-hydroxy-3-methylglutaryl-CoA reductase**

Liver microsomes were isolated according to Erickson et al. (1977). The activity of liver 3-hydroxy-3-methylglutaryl (HMG)-CoA reductase was measured as previously described by Shapiro et al. (1969) and modified by Heller & Strewsbury (1976).

**Acyl CoA:cholesterol acyltransferase assay**

The mucosa microsome was prepared according to the method previously described by Murakami et al. (1995). The ACAT activity was determined essentially using the method developed by Helgerud et al. (1981) with some modifications. Each assay contained 200 μg microsomal protein and 200 μg fatty acid-free bovine serum albumin in 190 μl potassium phosphate buffer (0.1 M, pH 7.4) containing 1 mM-EDTA. The mixture was incubated at 37°C for 6 min and the reaction was then initiated by adding 5 nmol [1-14C]oleoyl-CoA (NEN™, MA, USA) followed by incubation at 37°C for 6 min. The reaction was stopped by adding 5 ml chloroform–methanol (2:1, v/v) and 1 ml 0.04 M-HCl. To the mixture, 10 μl [3H]cholesterol oleate was then added as an internal standard. After the mixture was vortexed and centrifuged, the organic layer was taken and dried under N2 gas. The sample was then dissolved in 50 μl chloroform containing 0.1 mg cholesterol oleate and spotted on a TLC plate (20 x 20 cm plate precoated with 250 μm silica gel 60A; Macherey-Nagel, Duren, Germany). The different lipid classes were separated in hexane–diethyl ether–acetic acid (80:20:1, by vol.) and then exposed to I vapour. The band containing cholesteryl oleate was scraped off into scintillation vials, and the radioactivity was counted.

### Table 3. Changes in food intake, body-weight gain, and individual organ weights*

<table>
<thead>
<tr>
<th></th>
<th>CTL</th>
<th>LA</th>
<th>CLA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>120.8</td>
<td>121.3</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>7.0</td>
<td>6.0</td>
<td>2.6</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>167.6</td>
<td>167.5</td>
<td>16.7</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>12.3</td>
<td>12.3</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>14.0</td>
<td>2.4</td>
<td>13.9</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>2.4</td>
<td>2.4</td>
<td>2.6</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td>7.57</td>
<td>0.73</td>
<td>7.74</td>
</tr>
<tr>
<td><strong>Peri-renal adipose tissue</strong></td>
<td>2.19</td>
<td>0.82</td>
<td>2.23</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td>0.67</td>
<td>0.04</td>
<td>0.71</td>
</tr>
<tr>
<td><strong>Heart</strong></td>
<td>0.54</td>
<td>0.03</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Brain</strong></td>
<td>0.97</td>
<td>0.11</td>
<td>0.95</td>
</tr>
</tbody>
</table>

*For details of diets see Table 1, and for procedures see p. 936.

**Statistics**

Data are expressed as mean values and standard deviations. ANOVA was used where applicable for statistical evaluation of significant differences among the control, the LA- and CLA-supplemented groups using Sigmasstat (Jandel Scientific Software, San Rafael, CA, USA). Differences were considered significant when P < 0.05.

### Table 4. Effect of dietary conjugated linoleic acids as a mixture and linoleic acid on serum, liver and adipose tissue lipids*

<table>
<thead>
<tr>
<th></th>
<th>CTL Mean</th>
<th>LA Mean</th>
<th>CLA Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean SD</strong></td>
<td>20.8° ± 0.11</td>
<td>2.16° ± 0.04</td>
<td>0.14° ± 0.14</td>
</tr>
<tr>
<td><strong>Mean SD</strong></td>
<td>2.08° ± 0.16</td>
<td>1.06° ± 0.04</td>
<td>0.08° ± 0.04</td>
</tr>
<tr>
<td><strong>Mean SD</strong></td>
<td>3.29° ± 0.53</td>
<td>2.26° ± 0.53</td>
<td>0.55° ± 0.53</td>
</tr>
<tr>
<td><strong>Liver (mg/g)</strong></td>
<td>2.0° ± 3.0</td>
<td>2.6° ± 5.0</td>
<td>8.0° ± 2.0</td>
</tr>
<tr>
<td><strong>Perirenal adipose tissue (mg/g)</strong></td>
<td>1.1° ± 0.1</td>
<td>2.1° ± 0.2</td>
<td>1.6° ± 0.2</td>
</tr>
<tr>
<td><strong>Adductor longus (mg/g)</strong></td>
<td>0.38° ± 0.02</td>
<td>0.34° ± 0.03</td>
<td>0.35° ± 0.02</td>
</tr>
</tbody>
</table>

*For details of diets see Table 1, and for procedures see p. 936.
faster serum TG was markedly decreased by 34% and
21% respectively, in hamsters fed 20 g CLA and 20 g LA/
kg diet in comparison with that in the control group
\((P < 0.01, \text{Table 4})\). However, no difference was observed in
serum HDL-cholesterol among the three groups (Table 4).

**Effect of conjugated linoleic acids supplementation on
hepatic cholesterol and triacylglycerol**

As compared with that of the control and LA-supplemented
group, the hepatic cholesterol level was significantly lower
in CLA-supplemented hamsters (Table 4). However, all
three groups had the similar level of hepatic TG.

**Effect of conjugated linoleic acids supplementation on
levels of cholesterol in other tissues**

Unlike that of liver, the adipose tissue cholesterol level in
the CLA-supplemented group was markedly increased by
45% as compared with the control group \((P < 0.01, \text{Table 4})\).
Significantly lower muscle cholesterol levels in the CLA- and
LA-supplemented groups were also observed as compared with that of the control (Table 4). However, no
differences in the cholesterol level of brain, heart and
kidney were observed (data not shown).

**Effect of conjugated linoleic acids supplementation on
hepatic 3-hydroxy-3-methylglutaryl-CoA reductase and
intestinal acyl CoA:cholesterol acyltransferase**

No differences in hepatic HMG-CoA reductase were
observed among the three groups. The HMG-CoA
reductase activity for the control, LA and CLA groups
was 20.3, 20.4 and 20.7 pmol/min per mg protein
respectively. However, the intestinal ACAT activity of
CLA-supplemented group was reduced by 58% \((P < 0.05)\)
as compared with that of control and LA-supplemented
hamsters (Fig. 1). There was no difference in the intestinal
ACAT activity between the control and LA-supplemented
groups.

**Effect of conjugated linoleic acids supplementation on
faecal neutral and acidic sterols**

The neutral sterols refer to the sum of cholesterol, coprosterol, coprostanone, dihydrocholesterol, campesterol,
β-sitosterol and stigmastenol. The total faecal neutral sterols
were significantly elevated in the CLA-supplemented
groups as compared with the control and LA-supplemented
groups (Fig. 2). The acidic sterols measured include
lithocholic, deoxycholic, cholic acid and ursodeoxycholic
acid (Chan et al. 1999). CLA supplementation did not
affect the faecal excretion of acidic sterols as compared with the control and LA-supplemented groups throughout the
study period except at day 36 and 44 (Fig. 3).

**Discussion**

The present study confirmed that dietary CLA as a mixture
possessed a favourable effect on serum lipids by signifi-
cantly reducing fasting serum TC and TG with no effect on
HDL-cholesterol. Thus, the TC:HDL-cholesterol ratio was
significantly decreased. The result is in agreement with that
of other studies using rabbits (Lee et al. 1994), mice
(Munday et al. 1999) and hamsters (Nicolosi et al. 1997)
as animal models. However, the present result is in disagree-
ment with that reported by de Deckere et al. (1999), who
found that CLA mixture decreased TC at week 4 but it had
no significant effect on TC at week 8 in hamsters fed a diet
containing 0.1 g cholesterol/kg.

The mechanisms by which dietary CLA lowered serum
TC remains poorly understood. It is known that a diet
higher in LA is associated with lower serum TC compared
with a diet higher in saturated fatty acids. It is possible that
CLA acts partially like LA. First, CLA, like LA, may
occupy more space within lipoprotein particles, resulting in
fewer cholesterol ester molecules residing in the core of
LDL particles (Spritz & Mishkel, 1969), provided that CLA
isomers significantly accumulate in LDL particle. Second,
CLA, like LA, may reduce number of LDL particles by
inhibition of hepatic synthesis of apolipoprotein B-contain-
ing lipoproteins (Vegas et al. 1982). In fact, it was recently
found that trans-10, cis-12-CLA isomer could significantly
reduce in vitro apolipoprotein B secretion in HepG2 cells
(Yotsumoto et al. 1999). Third, dietary CLA like LA may
increase the LDL receptor activity and thus enhance the
fractional clearance rate of LDL in circulation (Grundy &

It was also noticed that the mechanism for the
cholesterol-lowering effect of dietary CLA, on the other
hand, might be different from that of dietary LA. First,
dietary CLA decreased not only serum TC, but also liver
cholesterol (Table 4) in comparison with LA, which had no
effect on hepatic cholesterol level. Second, dietary CLA led
to a higher level of adipose tissue cholesterol whereas
dietary LA did not influence the level of adipose tissue
cholesterol as compared with the control hamsters. We
have no explanation for the cholesterol-raising effect of

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**Fig. 1.** Effects of conjugated linoleic acids (CLA) and linoleic acid
(LA) on intestinal acyl CoA:cholesterol acyltransferase (ACAT)
activity in hamsters. CTL, control; a, control; b, linoleic acid-
supplemented; A, conjugated linoleic acids-supplemented group. For
details of the diets see Table 1, and for procedures see p. 936.
Values are means for ten hamsters per group with standard
deviations represented by vertical bars. Mean values with unlike
superscript letters were significantly different \((P < 0.05)\).
CLA in adipose tissue at the present time. However, CLA supplementation appeared to reduce the adipose tissue fat pads although it was not significant when compared with the control and LA-supplemented groups (Table 3). Similar observations were also made in the studies of Belury & Kempa-Steczko (1997), DeLany et al. (1999) and Park et al. (1999). It is possible that CLA may reduce the fat deposition and increase lipolysis in adipocytes coupled with enhanced fatty acid oxidation in both muscle cells and adipocytes as described previously in mice by Park et al. (1997). Therefore, the level of cholesterol per unit mass increased as the total adipose tissue weight and TG was decreased. The present results clearly suggest that CLA may cause ‘redistribution’ of cholesterol between serum and tissues with a lower level of hepatic cholesterol but a higher level of adipose tissue cholesterol.

One of the other possible mechanisms by which dietary CLA decreased serum cholesterol was explored in the present study. Dietary CLA was associated with increased faecal excretion of neutral sterols. Some of neutral sterols are the products of bacterial modification of cholesterol in large intestine (Kellog, 1974). To the best of our knowledge, the effect of dietary CLA on the faecal excretion of sterols has not previously been reported. Whereas ACAT functions mainly to esterify cholesterol and store it as cholesteryl ester, it may be involved in the intestinal absorption of cholesterol (Heider et al. 1983; Largs et al. 1989). There is evidence that the majority of dietary

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**Fig. 2.** Effects of conjugated linoleic acids (CLA) and linoleic acid (LA) on faecal output of total neutral sterols in hamsters. For details of the diets see Table 1, and for procedures see p. 936. Values are means for 10–12 hamsters per group with standard deviations represented by vertical bars. □, control; ▪, linoleic acid-supplemented; □, conjugated linoleic acids-supplemented group. Mean values were significantly different from those of the control group: *P < 0.05; **P < 0.01.

**Fig. 3.** Effects of conjugated linoleic acids (CLA) and linoleic acid (LA) on faecal output of total acidic sterols in hamsters. For details of the diets see Table 1, and for procedures see p. 936. Values are means for 10–12 hamsters per group with standard deviations represented by vertical bars. □, control; ▪, linoleic acid-supplemented; □, conjugated linoleic acids-supplemented group. Mean values were significantly different from those of the control group: *P < 0.05; **P < 0.01.
cholesterol is esterified before it is assembled in the chylomicron and secreted into the lymphatic system (Wrenn et al. 1995). We hypothesize that dietary CLA may interfere with the absorption of cholesterol by inhibiting the ACAT activity. In fact, the present study clearly showed that the intestinal ACAT was down-regulated by CLA supplementation. This was in agreement with the observation that dietary CLA increased only the faecal excretion of neutral sterols, but it had no or little effect on faecal acidic sterols (Figs 2 and 3). It is known that a high-cholesterol and -lard diet would produce an increase in both liver cholesterol and TG of hamsters (Sessions & Salter, 1994). Thus, if CLA inhibits cholesterol absorption, CLA supplementation will lead to a decrease in both serum TC and TG, and hepatic cholesterol. In addition, dietary supplementation exhibited neutral effect on HMG-CoA reductase. The reduction in serum cholesterol by dietary supplementation is therefore not associated with the inhibition of hepatic HMG-CoA reductase activity, but is most likely to be mediated, at least in part, by its inhibitory effect on cholesterol absorption via the down-regulation of intestinal ACAT activity.

It remains unclear whether dietary CLA reduces serum lipids in man. To the best of our knowledge, there has been no study to date that examines the hypolipidaemic activity of dietary CLA in human subjects. There were, however, only four animal studies to date which examined the regulation of intestinal ACAT activity.

Inhibitory effect on cholesterol absorption via the down-regulation of intestinal ACAT activity.

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References


