Cholesterol Metabolism Is Affected by Calcium Phosphate Supplementation in Humans

Bianka Ditscheid, Sylvia Keller, and Gerhard Jahreis

Friedrich Schiller University, Institute of Nutrition, Department of Nutritional Physiology, D-07743 Jena, Germany

ABSTRACT  Dietary calcium and phosphate precipitate in the small intestine to form insoluble amorphous calcium phosphate (ACP). The ability of ACP to bind and inactivate luminal bile acids might have an effect on cholesterol metabolism. To test this hypothesis, a placebo-controlled, double-blind, crossover study with pentacalcium hydroxy-triphosphate supplementation (CaP; 1.0 g elemental calcium) was conducted in 31 young healthy volunteers. The CaP was incorporated into bread. Serum cholesterol concentrations were lower after 4 wk of supplementation than after 4 wk of placebo (4.36 vs. 4.60 mmol/L; P = 0.008). Serum LDL cholesterol and the ratio of LDL:HDL cholesterol also tended to be lower after CaP supplementation than after placebo (−5.6%, P = 0.083 and −5.4%, P < 0.062, respectively). The participants’ fat and cholesterol intakes and fecal fat excretion did not differ in the 2 periods. Although the analysis of fecal samples showed no difference in the excretion of total neutral sterols (sum of cholesterol and its transformation products), the excretion of cholesterol itself increased (9.64 vs. 5.80 μmol/g dry matter; P = 0.025; n = 25), whereas the excretion of the metabolite coprostanol decreased (18.5 vs. 21.0 μmol/g dry matter; P = 0.025; n = 25) in the CaP period. Bile acid excretion increased during the CaP period compared with the placebo period (25.4 vs. 22.9 μmol/g dry matter; P = 0.003). The observed beneficial effects on cholesterol metabolism are not the result of an increased excretion of cholesterol, but might be explained by an increased bile acid excretion and a subsequent regeneration of bile acids from endogenous cholesterol in the liver. J. Nutr. 135: 1678–1682, 2005.

KEY WORDS: • cholesterol • calcium phosphate • fecal sterols • bile acids • human

In animal models (1,2) as well as human studies (3,4), an elevated plasma cholesterol level was found to be associated with impaired endothelial function. Furthermore, there is a proportional increase in the risk of coronary heart disease with rising serum cholesterol levels (5,6). A recently published observational study showed an inverse relation between calcium intake and the plasma lipoprotein-lipid profile (7). However, intervention studies have not produced consistent results (8–12).

Thus, there is a demand for further investigations in the context of dietary calcium intake and serum lipid and lipoprotein concentrations. Saponification due to ionic binding of Ca++ to fatty acids is one mechanism that might explain the effects of calcium supplementation. However, there might be another mechanism via calcium phosphate as supplement. Calcium phosphates are insoluble (in water) at a neutral pH. During digestion they are solubilized in the stomach (acidic milieu). Starting at pH 5.6 up to pH 7.0, calcium phosphate precipitates (13). Thus, calcium phosphates are regenerated in the small intestine as insoluble amorphous calcium phosphates (ACP) (14). The ability of this amorphous compound to bind and precipitate bile acids has been described repeatedly in in vitro (13,15) and in vivo (16) studies; therefore, it might contribute to a risk reduction in colon carcinogenesis. This bile acid binding might in itself, or via a coprecipitation of cholesterol, affect cholesterol metabolism. The purpose of this study was to investigate the effects of a dietary supplementation with a particular calcium phosphate compound, pentacalcium hydroxy-triphosphate, on serum lipids and lipoproteins and to clarify the underlying mechanisms.

SUBJECTS AND METHODS

Subjects and study design. Healthy, omnivorous men and women were recruited for participation in this study. Subjects with diseases of the gastrointestinal tract and pregnant women were excluded. The participants were carefully informed, both verbally and in writing, of the purpose, the course, and possible risks of the study before giving their written consent to participate. The study protocol was approved by the Ethical Committee of the Friedrich Schiller University of Jena.

Volunteers (n = 31; 16 women, 15 men), aged 25 ± 2 y (range: 21–29 y), with a BMI of 21.7 ± 2.4 kg/m² (range: 17.3–28.1 kg/m²) participated in this study. All 31 participants completed the study. The supplement, pentacalcium hydroxy-triphosphate [Ca₅(PO₄)₃OH]; cfβ], an odorless and tasteless white microfine powder was added to a commercial whole-meal bread baking mixture (3% of dry matter) and the bread was prepared according to the instructions on the packaging. The daily portion of 140 g of this bread provided an additional intake of 1060 mg calcium and 490 mg phosphorus compared with the unsupplemented placebo bread.

1 To whom correspondence should be addressed.
E-mail: Gerhard.Jahreis@uni-jena.de.
TABLE 1
Nutrient intakes during the defined diet in the 2 study periods

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>CaP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry matter, g/d</td>
<td>186 ± 86</td>
<td>180 ± 80</td>
</tr>
<tr>
<td>Calcium, mg/d</td>
<td>1193 ± 295</td>
<td>1193 ± 295</td>
</tr>
<tr>
<td>Phosphorus, mg/d</td>
<td>1528 ± 288</td>
<td>1998 ± 291*</td>
</tr>
<tr>
<td>Protein, mg/d</td>
<td>85.9 ± 16.3</td>
<td>85.5 ± 16.5</td>
</tr>
<tr>
<td>Fat, g/d</td>
<td>83 ± 23</td>
<td>83 ± 23</td>
</tr>
<tr>
<td>Fatty acids, % of total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated</td>
<td>51.4 ± 2.6</td>
<td>51.5 ± 2.7</td>
</tr>
<tr>
<td>trans</td>
<td>2.3 ± 0.2</td>
<td>2.3 ± 0.2</td>
</tr>
<tr>
<td>Monounsaturated</td>
<td>34.8 ± 1.5</td>
<td>34.9 ± 1.5</td>
</tr>
<tr>
<td>Polysaturated</td>
<td>11.0 ± 1.3</td>
<td>10.8 ± 1.3</td>
</tr>
<tr>
<td>Cholesterol, mg/d</td>
<td>309 ± 72</td>
<td>311 ± 74</td>
</tr>
<tr>
<td>Fiber, g/d</td>
<td>36.7 ± 6.3</td>
<td>34.9 ± 6.8</td>
</tr>
<tr>
<td>Energy, kJ/d</td>
<td>9019 ± 1764</td>
<td>8964 ± 1786</td>
</tr>
</tbody>
</table>

1 Values are means ± SD, n = 31. *Different from placebo, P < 0.05.

The study was designed as a placebo-controlled, double-blind, crossover trial. The participants were randomly divided into the 2 supplementation regimens, receiving first the calcium phosphate (CaP) bread and then the placebo bread (n = 12) or vice versa (n = 18). The supplementation regimen did not influence the results. Each period (CaP, placebo) lasted 4 wk. In wk 4 of each period, participants consumed a defined diet that was designed by the study center. According to the recommendations of the German Nutrition Society, the defined diet was designed as a mixed diet containing a wide range of different food components. The diet was preweighed and participants were instructed not to eat any food other than the diet provided. U neca food was weighed once again and the food intake was calculated. The diet was the same in wk 4 of the CaP and the placebo period. The defined diet was necessary to exclude the effect of individual nutritional habits (e.g., fat intake, cholesterol intake). The nutrient intakes were calculated from the analysis of the food components and the weighed amounts of ingested food. While consuming the defined diet, subjects collected feces quantitatively for 5 d (d 3–7 in wk 4 of each period). At the same time, a 24-h urine collection was performed for each period. Blood samples were drawn from fasting subjects on d 6 of wk 4 of both periods.

Serum biochemistry. After enzymatic preparation, serum total cholesterol and HDL cholesterol as well as triacylglycerol were measured by photometry on the autoanalyzer Synchron® LX 20 (Beckman Coulter). LDL cholesterol was calculated using Friedewald’s formula. Serum calcium concentration was analyzed using the isoperibolic bomb calorimeter PARR 1261 (PARR Instrument).

Fecal biochemistry. The separate fecal samples were immediately frozen at −20°C. Finally, all samples from 1 subject and 1 period were defrosted and homogenized using a commercial blender. Aliquots were lyophilized and stored at −20°C until analysis.

Fecal neutral sterols and bile acids were analyzed as described previously (17). Briefly, aliquots of lyophilized feces were put into test tubes containing internal neutral sterol standard (5α-cholestan-3-one after measuring the solvent extraction was performed. The sterols were resolved in decane and injected into the GC-MS (GC17-QP5000, Shimadzu). For the analysis of primary and secondary bile acids, the residue of the sterol extraction was saponified with NaOH. The samples were then acidified to pH 1 with HCL and extracted with diethyl ether. The extracts were combined in a tube containing internal bile acid standard (hydroxycholic acid). The solvent of the combined extracts was evaporated and the residue was methylated and silylated. After evaporation, the residue was dissolved in decane, shaken, and centrifuged. The clear solution was injected into the GC-MS.

Fecal fat was measured as ether extract after acid hydrolysis by conventional Soxhlet extraction on a SOXHERM 2000 automatic (Gerhardt). Fecal minerals were determined using ICP-OES (Liberty Series II, Varian Analytical Instruments). Before analysis, the samples were ashed for 5 h at 525°C. The ash was dissolved in HCl (25%) and diluted with distilled water.

Further variables. The excretion of calcium in urine was measured using the same method as for the analysis of serum calcium concentration.

The fat content of foods was measured after acid hydrolysis by conventional Soxhlet extraction on a SOXHERM 2000 automatic. For the analysis of percentages of fatty acids, the fat was extracted by the method of Folch et al. (18), with slight modifications (use of trichloromethane instead of dichloromethane). Fatty acids were methylated with tetramethyglycium. FAMEs were separated by TLC and measured using GC-FID (GC-17A, Shimadzu). The cholesterol content of foods was determined by photometry using an enzymatic test kit (Cholesterol, 10 139 050 035, Boehringer Mannheim/R-Biopharm AG). Total dietary fiber in foods was determined by an enzymatic-gravimetric method (Total dietary fiber, 1.12979, BIOQUANT®, Merck KGaA). Protein content in foods was calculated as analyzed diet nitrogen × 6.25. The physiological energy intake was calculated from the physical energy of foods, which was determined using the isoperibolic bomb calorimeter PARR 1261 (PARR Instrument).

Statistics. Data were analyzed using the statistical software package SPSS for Windows Vs. 11.5. The effect of the supplementation was tested using the GLM (General Linear Model)-procedure of repeated measurements. Differences were considered significant at P < 0.05. Associations were tested using Pearson’s linear correlations. Values are reported as means ± SD.

RESULTS

Nutrient intake. The defined diet was necessary to exclude differences in nutrient intake during the time of sample collection (feces, blood, urine). The calculated nutrient intake shows that the CaP and the placebo periods did not differ except for calcium and phosphorus (Table 1). The calcium intake was 1.01 g higher, whereas the phosphorus intake was 0.47 g higher in the CaP period compared with the placebo period, thus reflecting the supplementation of calcium phosphate.

Calcium status. Although calcium absorption from the supplemented calcium phosphate was presumed to be very low, data concerning calcium excretion were recorded. Most of the supplemented calcium was excreted in feces (Table 2). Serum calcium levels did not change (2.34 ± 0.06 mmol/L in the CaP period and 2.34 ± 0.09 mmol/L in the CaP period). Renal calcium excretion increased significantly in the CaP period (Table 2). In addition, daily renal calcium excretion was correlated with calcium intake (r = 0.402, P = 0.001).

Serum lipids and lipoproteins. Serum total cholesterol concentration decreased due to CaP supplementation with

TABLE 2
Effect of calcium phosphate supplementation on excretion of dry matter, calcium, phosphorus, and fat in young healthy normolipidemic men and women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>CaP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal dry matter, g/d</td>
<td>25.7 ± 4.5</td>
<td>26.3 ± 4.8</td>
</tr>
<tr>
<td>Fecal calcium excretion, mmol/d</td>
<td>20.6 ± 5.9</td>
<td>44.6 ± 11.6*</td>
</tr>
<tr>
<td>Renal calcium excretion, mmol/d</td>
<td>3.14 ± 1.45</td>
<td>3.84 ± 1.40*</td>
</tr>
<tr>
<td>Fecal phosphorus, mmol/d</td>
<td>17.9 ± 5.49</td>
<td>31.3 ± 9.98*</td>
</tr>
<tr>
<td>Fecal fat, g/d</td>
<td>3.9 ± 1.4</td>
<td>4.3 ± 1.1</td>
</tr>
</tbody>
</table>

1 Values are means ± SD, n = 31. *Different from placebo, P < 0.001.
cholesterol converters, low cholesterol converters had an al-
cause of the large margin of deviation. Compared with high
compounds cholesterol and coprostanol did not change be-
grated into the statistical analysis, the excretion of the major
neutral sterol excretion between the periods. When the par-
the whole study population and after exclusion of low con-
verters). Thus, the data were analyzed using the values of
their feces contrasted with the normal profile; this was repre-
sented by high cholesterol and low coprostanol excretion (low
converters). Indeed, the observed reductions in serum cholesterol and
LDL:HDL cholesterol also tended to decrease (5.6 and 5.4%,
respectively). Thus, a larger sample size might underline these
effects. Similar cholesterol-lowering effects were found in 2
erlier crossover studies that tested the effect of calcium sup-
plementation in moderately hyperlipidemic subjects (9,10).
Certainly, the observed reductions in serum cholesterol and
LDL cholesterol (~5–6%) in normolipidemic subjects are
small compared with those resulting from the administration of
statins or other compounds that have to be absorbed. But in

4.60 ± 1.01 mmol/L in the placebo period and 4.36 ± 0.89
mmol/L in the CaP period (P = 0.008). LDL-cholesterol
concentration tended to be lower in the CaP period
(2.37 ± 0.80 mmol/L) than in the placebo period (2.51 ± 0.91
mmol/L; P = 0.083). The ratio of LDL cholesterol:HDL cho-
lesterol tended to decrease after CaP supplementation
(1.59 ± 0.68 vs. 1.68 ± 0.74; P = 0.062).

**Fecal excretion.** Due to calcium phosphate supplementa-
tion, daily fecal phosphorus excretion increased significantly
(31.3 ± 9.98 mmol/d) in the CaP period vs. 17.9 ± 5.49
mmol/d (P < 0.001). Fecal fat excretion did not differ in the 2 periods (P = 0.149; Table 2).

Fecal excretion of neutral sterols was affected by CaP sup-
plementation (**Table 3**). There were a few participants (n = 6)
within the study population whose neutral sterol profile in
their feces contrasted with the normal profile; this was repre-
sented by high cholesterol and low coprostanol excretion (low
converters). Thus, the data were analyzed using the values of
the whole study population and after exclusion of low con-
verters. After analysis, the fecal samples did not differ in total
neutral sterol excretion between the periods. When the par-
participants with a low conversion rate of cholesterol were inte-
grated into the statistical analysis, the excretion of the major
compounds cholesterol and coprostanol did not change be-
cause of the large margin of deviation. Compared with high
cholesterol converters, low cholesterol converters had an al-
terated pattern of neutral sterols in their feces represented by
high cholesterol excretion (23.6 ± 22.1 µmol/g dry matter in
the CaP period vs. 28.9 ± 3.13 µmol/g dry matter in the
placebo period) and a very low excretion of the microbial
transformation product coprostanol (1.88 ± 2.38 vs. 3.96 ± 4.05
µmol/g dry matter, respectively). As a cutoff level for
classification as low converters, a cholesterol concentration was
defined. After exclusion of low converters, a significant increase in
cholesterol excretion was observed, whereas coprostanol excretion
decreased significantly. Fecal excretion of neutral sterols and serum total cholesterol
concentration were not correlated.

Total bile acid excretion in feces increased in the CaP-
supplemented period (25.4 ± 6.98 µmol/g dry matter) com-
pared with the placebo period (22.9 ± 5.45 µmol/g dry matter; P = 0.003, **Fig. 1**). This can be ascribed to the increase in
secondary bile acid excretion (24.1 ± 6.97 vs. 21.5 ± 5.58
µmol/g dry matter; P = 0.002). Excretion of primary bile acids
did not differ in the 2 periods.

**TABLE 3**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>CaP</th>
<th>Placebo</th>
<th>CaP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>10.6 ± 12.4</td>
<td>11.6 ± 11.2</td>
<td>5.80 ± 2.48</td>
<td>9.64 ± 8.26*</td>
</tr>
<tr>
<td>Coprostanol</td>
<td>18.0 ± 12.8</td>
<td>17.4 ± 13.2</td>
<td>21.0 ± 12.1</td>
<td>18.5 ± 10.3*</td>
</tr>
<tr>
<td>Coprostanone</td>
<td>3.53 ± 2.85</td>
<td>3.28 ± 2.27</td>
<td>3.93 ± 2.77</td>
<td>3.61 ± 2.13</td>
</tr>
<tr>
<td>Cholestanol</td>
<td>0.87 ± 0.15</td>
<td>0.80 ± 0.15*</td>
<td>0.87 ± 0.16</td>
<td>0.78 ± 0.13*</td>
</tr>
<tr>
<td>Cholesterolone</td>
<td>0.11 ± 0.04</td>
<td>0.10 ± 0.04</td>
<td>0.11 ± 0.06</td>
<td>0.11 ± 0.04</td>
</tr>
<tr>
<td>Cholestenone</td>
<td>0.77 ± 0.36</td>
<td>0.87 ± 0.41*</td>
<td>0.74 ± 0.31</td>
<td>0.81 ± 0.32*</td>
</tr>
<tr>
<td>Total neutral sterols</td>
<td>33.9 ± 13.5</td>
<td>34.0 ± 17.6</td>
<td>32.5 ± 13.6</td>
<td>33.4 ± 14.9*</td>
</tr>
</tbody>
</table>

*Values are means ± SD. *Different from placebo, P < 0.05.

**DISCUSSION**

In this investigation into the effect of pentacalcium hydroxy-triphosphate on cholesterol metabolism, a significant
reduction in serum cholesterol levels (~5.2%) occurred in
normolipidemic subjects through a doubling of dietary calcium intake (2204 vs. 1193 mg/d) and the addition of pentacalcium hydroxy-triphosphate as a supplement.

Pentacalcium hydroxy-triphosphate seems to be an appro-
appropriate calcium compound to lower serum cholesterol levels. Although the sample size was relatively small in the present
study (31 normolipidemics), LDL cholesterol and the ratio of
LDL:HDL cholesterol also tended to decrease (5.6 and 5.4%,
respectively). Thus, a larger sample size might underline these
effects. Similar cholesterol-lowering effects were found in 2
erlier crossover studies that tested the effect of calcium sup-
plementation in moderately hyperlipidemic subjects (9,10).
Certainly, the observed reductions in serum cholesterol and
LDL cholesterol (~5–6%) in normolipidemic subjects are
small compared with those resulting from the administration of
statins or other compounds that have to be absorbed. But in

![FIGURE 1](https://academic.oup.com/jn/article-abstract/135/7/1678/4663905)
contrast to these, there are fewer systemic adverse effects (19). However, elevated cholesterol levels might be more susceptible to intervention with lipid-lowering agents than cholesterol concentrations in the normal range. Future studies investigating the serum cholesterol–lowering ability of this calcium phosphate compound in moderately hypercholesterolemic persons are warranted.

To clarify the mechanism underlying the lipid-lowering effect of CaP supplementation, we also measured fecal excretion of cholesterol, its metabolites, and bile acids as well as the total fat excretion (ether extract). Fat intake and fat excretion in feces did not differ between the 2 intervention periods nor did the normalization of fat intake to 100 g/d affect fat excretion (data not shown). Thus, the effect of CaP supplementation on serum cholesterol in the present study cannot be explained by an effect on fat excretion as described by others (10,20,21). Reasons for the lack of an effect on fecal fat excretion might be the following: supplementation of 1 g calcium as calcium phosphate (at least that specific calcium phosphate) might not exert any additional effects on fecal fat excretion compared with a calcium intake at the recommended level (see placebo period). In contrast, a large difference in the calcium intake between the study periods (~1800 mg) (10) or very low calcium levels in the control period (410 and 500 mg, respectively) (10,21) might have an effect on fecal fat excretion. Furthermore, compared with the study of Shahkhali et al. (20), who supplemented calcium carbonate, the fat intake in the present study was rather small, and a high-fat diet might be more susceptible to the formation of insoluble calcium-fatty acid soaps.

Calcium supplements that have been commonly used, such as calcium carbonate (9,11,12,20), calcium citrate (22), and calcium citrate malate (10), provide a relatively high bioavailability of calcium. In contrast, the bioavailability of calcium from CaP is relatively low due to its ability to form insoluble amorphous complexes, i.e., after solubilization of calcium phosphate in the acidic environment of the stomach, calcium and phosphate precipitate by forming insoluble ACP when entering the duodenum (pH 5.5–8.0) (13). Data from the present study indicate that the supplemented calcium phosphate was only marginally absorbed. The excreted amounts of calcium and phosphate in feces had a molar ratio of 44.6:31.3, which is the precondition for the formation of ACP (14). The ability of insoluble calcium phosphate to bind and precipitate bile acids in the intestine has been described repeatedly in vitro (13,15) and in vivo (16). It is supposed that the negatively charged carboxylic group of the unconjugated bile acid binds to the positively charged calcium ions on the surface of ACP. Further bile acids may be bound via hydrophobic aggregation (16). Bound components are withdrawn from the enterohepatic circulation and excreted with feces. We hypothesized that cholesterol might also be included in hydrophobic aggregates and eliminated in the same manner. Approximately 250–500 mg dietary cholesterol and 600–1000 mg biliary cholesterol pass through the human intestine every day. Cholesterol is subject to enterohepatic circulation. The remaining cholesterol enters the large intestine and the majority of it might be metabolized through anaerobe gram-positive bacteria (23). The main transformation product of cholesterol is coprostanol, which is generated alternatively through a direct reduction of cholesterol (24) or indirectly via cholestenone and coprostanone; the latter was shown to be the preferred pathway (25). Nevertheless, there are a small number of people who convert little cholesterol to coprostanol, resulting in a high cholesterol and a relatively low coprostanol excretion (26). These so-called “low converters” were excluded from the statistical analysis of our study results. The constant excretion of total neutral sterols (sum of cholesterol and its bacterial transformation products) in feces points to the fact that there is no inclusion of cholesterol and bacterial cholesterol metabolites in ACP complexes. However, significant changes in the profile of excreted cholesterol metabolites were measured (Table 3). The changing profile of bacterial cholesterol metabolites in feces might be explained by an effect of calcium phosphate supplementation on bacterial colonization of the colon. For example, an increased number of ileal and fecal lactobacilli were found in calcium phosphate–supplemented rats (27,28). A change in the microflora would lead to a modified enzyme activity in the intestine, which in turn might cause a change in the cholesterol metabolite distribution of feces. However, the evidence for a similar effect in humans has not yet been found.

These results indicate that the decrease in serum cholesterol is not due to a binding of cholesterol to ACP in the intestine. A more plausible mechanism is an increased excretion of bile acids (10,29) as a consequence of the binding of these bile acids to ACP. In fact, bile acid excretion during CaP supplementation was 11% higher than during the placebo period. This increase was due exclusively to an increase in fecal secondary bile acids, whereas the fecal excretion of primary bile acids remained constant. The binding of bile acids to ACP might lead to bile acid deprivation in the liver. Thus, bile acids had to be regenerated from cholesterol, leading to a decrease in serum LDL and serum total cholesterol concentrations.

The formation of ACP, which is indicated by the molar ratio of excreted calcium and phosphate in feces and by the increased fecal bile acid excretion, might also be responsible for the lack of an effect of calcium phosphate supplementation on fecal fat excretion. If calcium is used up by the formation of ACP, it would not be available for the formation of calcium-fatty acid soaps. Only a few human studies exist that investigated the effect of calcium supplementation on both fecal fat and fecal bile acid excretion (10,30). Although Denke et al. (10), who supplemented calcium as citrate malate, reported a significantly higher fecal excretion of saturated fat after calcium supplementation, no change in fecal bile acid excretion occurred. This might be explained by the lack of a sufficient amount of phosphate necessary for the formation of ACP: with an adequate phosphorus intake and increased amounts of calcium, some ACP might be formed but could be insufficient to induce any detectable increase in fecal bile acid excretion. Increased Ca^{2+} in the small intestine supports the fatty acid excretion via calcium-fatty acid soaps. Comparing the intake of regular milk products (30 mmol/L calcium) with placebo milk products (3 mmol/L calcium), Govers et al. (30) found significantly increased fecal fat and bile acid excretion. However, the daily fat intake calculated from the energy intake (13.5 vs. 13.1 MJ/d) and the percentage of fat (36.3 vs. 34.5 energy %) were higher in the calcium period than in the placebo period. Wellberg et al. (31) found a significant correlation between calcium intake and the percentage of fecal excretion of total fat as related to fat intake (r = 0.44, P = 0.03). Thus, the increased fat intake during the calcium period in the study by Govers et al. (30) might also be responsible for the higher fecal fat excretion. However, that study was designed to investigate the colon cancer protective effect of milk calcium and not to examine the effects of calcium supplementation on serum lipids and lipoproteins. In further studies on this relation, special attention should be paid to the nutritional intakes of phosphate and fat and the fecal excretion of calcium, phosphate, fat, and bile acids.
In addition to the beneficial effects of pentacalcium hydroxy-triphosphate supplementation observed in normolipidemic subjects, safety aspects also have to be considered. Despite the significant increase in renal calcium excretion, the supplementation in this study was well tolerated and seemed to be safe in general. The increased renal calcium excretion was far below the critical level (7.5 mmol/d for men and 6.2 mmol/d for women according to the definition for hypercalciuria), with regard to the formation of urinary stones. Data from prospective studies indicated a decreased risk of kidney stone formation with a higher intake of dietary calcium in older men (32) and younger women (33); supplemental calcium was not associated with the risk of stone formation (33). Because calcium from pentacalcium hydroxy-triphosphate is slightly absorbed, it might also contribute to the prevention of bone loss. The supplementation of tricalciumphosphate, another insoluble calcium compound, together with cholecalciferol was shown to reduce the risk of hip fractures by 43% and the total number of nonvertebral fractures by 32% in elderly women (34). Thus, pentacalcium hydroxy-triphosphate could be favorable for postmenopausal women as a supplement with combined effects (serum cholesterol lowering and decreased bone fracture risk).

In conclusion, the present study showed for the first time a beneficial effect of pentacalcium hydroxy-triphosphate supplementation on serum lipids in healthy volunteers. Because the lifetime risk of coronary heart disease increases sharply with higher total cholesterol concentrations at all ages (5), pentacalcium hydroxy-triphosphate as a compound in functional food might contribute in the long term to a risk reduction for coronary heart diseases. However, the importance of pentacalcium hydroxy-triphosphate supplementation in moderately hypercholesterolemic subjects has not yet been investigated. Given the beneficial effects observed in the present study, such an investigation is imperative.

LITERATURE CITED


