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# The Effect of Calcium on Blood Lipids

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**The first demonstration of a potential relationship between calcium intake and a variable reflecting the risk of cardiovascular disease (CVD) was reported by McCarron et al.[1] who found a negative association between the daily intake of this mineral and blood pressure. However, this reported association has not generated an immediate interest to explore this finding. The scientific community has waited for almost two decades before significant research was made regarding the link between calcium intake and the risk of metabolic diseases and CVD. The cornerstone of this emerging research topic has probably been the paper by Zemel et al.[2] who published the first evidence documenting a potential role for calcium in variations of body fatness and lipid metabolism. Since the publication of this article, numerous studies have been conducted to investigate the issue, which has been an object of great scientific interest. This paper summarizes the key ideas related to this research with a particular emphasis on the effect of calcium intake on blood lipids.**

## Calcium and fat balance

Fat balance, which is the equilibrium between fat oxidation and fat intake, is highly correlated to energy intake under free-living conditions[3]. Its variations depend on cumulative changes in fat oxidation, fecal fat loss, and spontaneous fat intake. Interestingly, recent data suggest that calcium intake has the potential to influence these three components of fat balance.

The relationship between calcium intake and fat oxidation has been documented by Melanson et al.[4] who reported a significant positive correlation between these two variables. In a subsequent study, these investigators demonstrated the potential stimulating effect of calcium on fat "burning" in a context of food restriction[5].

The first study documenting an enhancing effect of calcium supplementation on fecal fat loss was recently performed in animals[6]. This has been further confirmed in humans by Jacobsen et al.[7] who showed that calcium supplementation may accentuate fecal energy loss as fat by about 50-100 kcal per day.

The most intriguing effect of calcium on fat balance pertains to the possibility of an effect on appetite control. In this regard, it seems that Tordoff[8] was the first investigator to raise the hypothesis of a calcium specific appetite. According to this argument, calcium appetite is the motivation to seek out or choose calcium-containing items, which might be compared to the appetite for macronutrients, which also involve a reservoir. This is concordant with the results of a recently reported study, which showed that rats submitted to a low calcium diet for six weeks developed a preference for a $CaCl_2$ solution[9]. We perceived this observation as consistent with our clinical experience with the use of Caltrate® with Vitamin D to supplement the diet of obese female low calcium consumers with 1,200 mg of calcium + 400 IU of vitamin D/ day. Indeed, in the very low calcium consumers treated with a placebo, there was no significant change in body weight over a 15-week supervised diet restriction. On the other hand, the Caltrate with Vitamin D supplementation prevented this resistance to lose weight by allowing a spontaneous decrease in *ad libitum* fat intake that was highly correlated with body weight and fat loss[10].

In summary, these results suggest that in a context of calcium deficiency, as it is likely to occur in obese low calcium consumers, calcium supplementation can favour a negative fat and energy balance. This effect might be expressed via every component of the fat balance equation. In addition, this suggests that an adequate calcium intake might be prudent in reducing the chances of being overweight.

## Calcium intake and body composition

The above referenced paper of Zemel et al.[2] described two studies leading to the conclusion that an adequate calcium/dairy intake is necessary to maintain an optimal body weight. First, the analysis of the NHANES III data showed that the likelihood to be classified in the upper quartile of body fatness in the study population was more than six times greater in the subjects who were categorized as very low calcium/dairy consumers. This observation was reinforced by an intervention study performed in African-American subjects in whom the effect of a yogurt supplementation on body fat was tested over one year. The results demonstrated that yogurt supplementation induced a mean fat loss of about 5 kg over this period of intervention.

We took advantage of the data of the Quebec Family Study to also investigate the possibility of a relationship between usual calcium/dairy intake on body fatness. This analysis revealed that women who reported a daily calcium intake below 600 mg/d were characterized by a significantly greater percent body fat compared to subjects reporting intake levels greater than this threshold value[11]. Furthermore, the follow-up over six years of subjects of this study who either decreased or increased their consumption of skimmed milk or partly skimmed milk led to a concordant conclusion. Indeed, percent body fat decreased in subjects reporting increased milk consumption whereas the opposite trend was found in individuals decreasing their milk intake over time[12].

Although many other population studies also support the idea that adequate calcium intake might be a prerequisite to body weight stability, it is clear that such an idea lacked the support of clinical trials to provide a more rigorous design of this concept. The first trial that has been performed on this issue was reported by Zemel et al.[13] several years ago. This study consisted of a diet management of obesity in obese low calcium consumers who were categorized in three experimental groups. The first one was subjected to a diet aiming to a daily energy deficit of 500 kcal/day with a placebo. The second group was exposed to the same diet with a calcium supplementation of 1,200-1,300 mg per day whereas the third one was also subjected to the restrictive diet and calcium supplementation, with the exception that the calcium supplement was provided via milk intake. As expected, a significant body weight and fat loss was observed in the three groups. However, the weight/fat loss was accentuated by calcium supplementation and was even greater with milk supplementation. This suggests that calcium supplementation is more likely to promote fat loss in low calcium consumers.

## Calcium intake and blood lipids

The ability of calcium supplementation to induce a negative energy/fat balance in low calcium consumers potentially represents an interesting clinical outcome since a negative energy balance and the related fat loss generally result in an improvement of the plasma lipid/lipoprotein profile. Beyond this observation, it is not unrealistic to raise the question pertaining to the possibility that calcium might influence the lipid/lipoprotein profile independently of variations in body fat and fat distribution. Several years ago, we addressed this question using the data of the Quebec Family Study. As reported by Jacqmain et al.[11], a significant negative correlation was observed in both men and women between the concentrations of total cholesterol or LDL-cholesterol and reported daily calcium intake.

Furthermore, this association, suggesting a protective role of calcium intake against dyslipidemia, remained statistically significant after adjustments for total body fat and waist circumference. This first step of investigation was then perceived as sufficiently promising to justify the initiation of a clinical trial allowing investigation of this issue with more methodological robustness.

We thus undertook a double-blind clinical study[14] in whom 63 obese low calcium consumer women were randomly assigned to one of the two following groups: one group consuming two Caltrate with Vitamin D tablets per day (supplementation of 1,200 mg elemental calcium and 400 IU vitamin D per day) and the other group consuming a placebo. Moreover, both groups were subjected to a 700 kcal per day energy restriction over the 15-week weight loss intervention program. The results showed that initial daily calcium intake was positively correlated with plasma HDL-cholesterol ($r = 0.41$, $p<0.01$). This cross-sectional observation was in total accordance with the outcome of the study. Indeed, as presented in Table 1, a significant time-treatment interaction effect was observed for all the plasma lipid/lipoprotein variables that were investigated. Specifically, the expected reducing effect of weight loss on plasma HDL-cholesterol was attenuated by the calcium + vitamin D supplementation. The table also shows that the reducing effect of the weight loss program was accentuated to a significant extent by the supplementation for the concentrations of plasma triacylglycerol, total cholesterol and LDL-cholesterol. Furthermore, the expected decrease in the ratios LDL/HDL cholesterol and total cholesterol/HDL cholesterol was also more pronounced in response to the supplementation. In this regard, it is also important to emphasize that the latter effect remained statistically significant even after statistical adjustments for changes in fat mass and waist circumference. These results thus provide a robust experimental demonstration of the beneficial effects of calcium + vitamin D supplementation on the lipid/lipoprotein profile of obese low calcium consumers.

## Conclusion

The observations presented in this paper support the idea that calcium intake should be considered as a nutritional variable that can exert a significant impact on fat and energy balance. Such an effect might target every component of the energy balance equation and has the potential to be related to significant variations in body fatness. Beyond this beneficial effect, recent results obtained in our laboratory, be them obtained in the context of cross-sectional population study or in a well standardized clinical trial, demonstrate that calcium intake can also influence the plasma lipid/lipoprotein profile independently of the effect that could be attributable to fluctuations in body fat mass and fat distribution. From a clinical standpoint, this also implies that calcium supplementation should be perceived as an essential tool to optimize the outcome of a weight loss program in obese low calcium consumers.

**Table 1.** Mean changes in plasma lipid/lipoprotein profile in two groups of obese women subjected to an energy-restricted weight loss intervention

| | Caltrate with Vitamin D group | Placebo group |
|---|---|---|
| HDL-cholesterol | - 0.03 | - 0.12* |
| Total cholesterol / HDL | - 0.38 | 0.08*** |
| LDL-cholesterol | - 0.41 | - 0.18* |
| LDL / HDL | - 0.32 | 0.008*** |
| Total cholesterol | - 0.50 | - 0.25* |
| Triacylglycerol | - 0.14 | 0.1* |

Values are in mmol/L

Significant time x treatment interaction reflecting a significant difference between changes in the two groups, * $p = 0.08$; ** $p < 0.05$; *** $p < 0.01$

Adapted from reference 14

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