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**Reply to R Draijer and GS Duchateau**

Dear Editor:

Draijer and Duchateau (1) suggest that our observation that green tea (GT) supplementation for 12 wk does not have a significant effect on fat absorption, energy expenditure, and body composition (2) deviates from our earlier results. In this study, our subjects consumed either GT placebo capsules (>0.56 g epigallocatechin gallate/d plus 0.28–0.45 g caffeine/d) or placebo capsules. We used capsules made of hydroxypropyl methylcellulose with cellulose as filler, whereas in some previous studies gelatin capsules were used (3, 4). Draijer and Duchateau mentioned that the bioavailability of GT catechins might be influenced by a hydroxypropyl methylcellulose capsule shell and cellulose as filler, because dissolution may be hampered in the fasted state as well as the fed state, with up to one-half of the material still undissolved after 2 h. We appreciate their interest in our work and that The Journal of Nutrition provides a forum for debate on such issues.

Our observation (2) does not contradict our previous acute or long-term studies on the effects of GT, because in most studies in which a positive effect was found with the use of gelatin capsules, the acute effects of GT were measured (3, 5). In agreement with our study on the long-term effect of GT on fat absorption and energy expenditure, in several previous long-term studies, we did not find a significant effect from GT over the long-term, even though we did use capsule shells made of gelatin in these studies and cellulose was not used as filler (4, 6). We only found a positive effect from GT over the long-term in a study on the effect of GT on body weight maintenance (7).

To test the bioactivity of the actual GT capsules used in our present long-term study, we preclinically tested the effects of these capsules on GT-induced thermogenesis. This resulted in an increase of 8.5% over 3.5 h compared with the basal metabolic rate ($P < 0.001$) (2). This effect was similar to our earlier observation with the use of gelatin capsules (3).

Apart from the possible confounder cellulose, the research on GT catechins implies several confounders. For instance, we discovered that the effects of GT during weight maintenance after weight loss are dependent on protein intake and on habitual caffeine intake (6–8). Furthermore, different alleles of the functional catechol-O-methyltransferase (COMT) Val108/158Met polymorphism appear to play a role in interindividual variability for energy expenditure and fat oxidation after GT treatment (5).

**Habitual Caffeine Consumption**

In a study on the effects of GT on body weight maintenance, we found that after significant body weight loss with the use of a very low-energy diet, body weight regain was not significantly different between the GT and the placebo condition (30.5 ± 61.8% and 19.7 ± 56.9%, respectively) (6). In this study, lack of significance was due to habitual caffeine consumption, because in the GT condition we found that habitually high caffeine consumption was associated with a higher weight regain compared with habitually low caffeine consumption (39 ± 17% and 16 ± 11%, respectively; $P < 0.05$). This was confirmed in a follow-up study in which a GT/caffeine mixture was given during the weight maintenance phase after body weight loss. We found that in low habitual consumers of caffeine, this GT/caffeine mixture still reduced body weight, waist circumference, respiratory quotient, and body fat and increased energy expenditure during weight maintenance ($P < 0.01$). In high habitual consumers of caffeine, the GT/caffeine mixture did not have effects on these variables during weight maintenance (8). In another study in which a low-energy diet was combined with supplementation with a GT/caffeine mixture, we reported no significant effects on weight loss and body composition. In this study, the habitual caffeine intake may also have been too high (4).

**Combination of a GT/Caffeine Mixture and Protein Intake**

As mentioned previously, protein intake can also be a confounder. In a previous study, milk protein appeared to inhibit the effect of GT catechins on diet-induced thermogenesis (3). This was confirmed in a long-term study in which a GT/caffeine mixture along with a high-protein diet improved weight maintenance independently via increased energy expenditure and fat oxidation ($P < 0.05$), although a possible synergistic effect failed to appear (7).

**COMT Polymorphism**

A mechanism behind the effects of GT catechins is the ability to increase energy expenditure and fat oxidation via inhibition of COMT by catechins (5, 9). However, this does not always appear...
unanimously because of large interindividual variability. This may be explained by different alleles of the functional COMT Val108/158Met polymorphism that are associated with COMT enzyme activity: the high-activity COMT<sup>44</sup> allele (Val/Val genotype), and the low-activity COMT<sup>44</sup> allele (Met/Met genotype). Subjects carrying the COMT<sup>44</sup> allele appeared to increase energy expenditure and fat oxidation upon ingestion of GT catechins compared with placebo [incremental area under the curve (iAUC) for energy expenditure: 62.2 and 35.4 kJ/3.5 h for GT and placebo, respectively, P < 0.01; fat oxidation: 18.3 and 15.3 g/d for GT and placebo, respectively, P < 0.001], whereas COMT<sup>44</sup> allele carriers reacted similarly with GT and placebo ingestion (iAUC for energy expenditure: 60.3 and 51.7 kJ/3.5 h for GT and placebo, respectively, not significant; fat oxidation: 17.3 and 17.0 g/d for GT and placebo, respectively, not significant) (5).

Several of these limiting factors of the effects of GT catechin caffeine mixtures appeared again in a meta-analysis. This analysis showed that catechins or mixtures with catechins and caffeine have a small positive effect on weight loss and weight maintenance (standardized mean difference: −1.31 kg; 95% CI: −2.05, −0.57 kg; P < 0.001). The results suggest that habitual caffeine intake and ethnicity may be moderators, because they may influence the effect of catechins (10).

Taken together, we do find positive results from GT catechins in long-term weight maintenance studies after weight loss induced by a very low–energy diet if coingestion of protein is avoided and if habitual caffeine consumption is low (6–8, 10). The main metabolic targets responsible for these effects are energy expenditure and fat oxidation (5, 9), especially in subjects carrying the COMT<sup>44</sup> allele. Irrespective of the nature of the capsules, we find positive results for energy expenditure in short-term experiments (2, 3). Therefore, we are convinced that the lack of positive results in the present study is not caused by lack of bioavailability of the GT/caffeine mixture, but, rather, is mainly caused by the procedure of long-term treatment in energy balance instead of in negative energy balance, in which a GT/caffeine mixture may prevent body-weight regain. Nevertheless, we agree with Draijer and Duchateau that selection and testing of delivery vehicles such as capsules is important, and we will add this to our preclinical testing approach.

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References

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