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FILE: ▪ Green Tea (*Camellia sinensis*)
▪ Iron Absorption
▪ Epigallocatechin gallate (EGCG)

HC –070251-285

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RE: Effect of Epigallocatechin Gallate (EGCG) from Tea on Nonheme-iron Absorption in Healthy Women with Low Iron Levels

Ulmann U, Haller, Bakker GCM, Brink EJ, Weber P. Epigallocatechin gallate (EGCG) (TEAVIGO™) does not impair nonhaem-iron absorption in man. *Phytomed.* 2005;12:410-415.

Green tea (*Camellia sinensis*) has been used traditionally for its health benefits in traditional Chinese medicine and throughout the Asia-Pacific area. The catechin constituents are considered to be responsible for most of the therapeutic benefits of this beverage. The primary catechin in green tea is the flavonol (-)-epigallocatechin gallate (EGCG) — a polyphenol molecule with a flavonoid structure.

Research has demonstrated that many beverages that contain polyphenols (such as coffee [*Caffea* spp.], herb teas and green tea) inhibit nonheme-iron absorption. Tea polyphenols have been shown to form insoluble complexes in the intestinal lumen. The galloyl groups specifically bind iron, and the EGCG molecule has two such groups. Since green tea is known to inhibit iron absorption, and EGCG (with two galloyl groups) is its main constituent, it is expected that EGCG will inhibit iron absorption to a degree.

The intention of this trial was to quantify the maximum inhibitory effect of 2 different doses of EGCG on nonheme-iron absorption using a double stable isotope technique. Nonheme iron is the type of iron found primarily in plants foods. Animal products, especially meat, fish and poultry, contain about 40-50% nonheme iron. The other 50-60% is heme iron in the form of hemoglobin and myoglobin.[1] To ensure a high level of iron absorption and "maximize the sensitivity of the study," the subjects were required to have low iron stores (serum ferritin ≤ [equal to or less than] 26 mcg/l), but not be anemic (Hemoglobin ≥ [equal to or greater than] 6.7mmol/l). Thirty healthy women (18-49 years old) [Note: While the title of the article says "man", the only participants in the study were women.] participated in this randomized, double-blind, placebo-controlled, 3 periods cross-over study (TNO, Nutrition and Food Research, Department of Nutritional Physiology in

Ziest, Netherlands). Each treatment period was 8 days. EGCG was administered once each day in the morning with a standardized breakfast (94% pure crystalline EGCG [TEAVIGO™], Roche Vitamins Ltd; Basel, Switzerland.). During the first 3 days of each treatment period, the subjects received a special low iron diet containing 5.6-.9 mg iron/day "to deplete the temporary iron stores in the gastrointestinal mucosa cells." During the last 5 days of the study period, the subjects continued this protocol, and in addition, received supplementation with iron isotopes. ^{57}Fe isotope was given orally, and ^{58}Fe isotope was given intravenously (Chemgas, Boulogne, France).

In order to detect any inhibition of iron absorption, the oral isotope solution was administered concomitantly with the EGCG. The dose of iron was calibrated so that the total amount of iron supplied by the low-iron diet and the isotopes would equal 18 mg/d. The EGCG treatments were given in the form of hard-gelatin capsules containing either 150 or 300 mg EGCG, or placebo. Each 8-day treatment period was followed by a 14-day washout period.

The impact of the 3 treatment plans on intestinal iron absorption was evaluated through assessment of "true fractional iron absorption, measured as the incorporation of physiological doses of stable iron isotopes into red blood cells 14 days after isotope administration." Three variables were used in order to calculate the absorption of true nonheme-iron: the dose of isotopes that was administered, the basal erythrocyte (red blood cell) iron isotope ratios, and the iron isotope ratios 14 days following the last administration of isotopes in that treatment period. This last measurement served as the baseline ratio for the subsequent iron absorption test. Researchers used the formula described by Barret et al. (1999) to calculate the absorption of iron.[2]

The study data clearly demonstrates the effect of EGCG intake on mean fractional nonheme-iron absorption. Absorption was highest with the placebo treatment. Mean fractional iron absorption was reduced by 5.7% versus placebo by consumption of 150 mg EGCG ($P=0.453$), and by 10.5% versus placebo by consumption of 300 mg EGCG ($P=0.0002$). Statistical analysis demonstrated a linear relationship between increasing doses of EGCG and reduced fractional iron absorption ($P=0.0002$). However, the relative reduction in nonheme-iron absorption was 14% for 150 mg EGCG (not statistically significant) and 27% for 300 mg EGCG intake ($P\leq0.05$). Since the reduction of nonheme-iron absorption was statistically insignificant, the authors state that EGCG does not "impair" nonheme-iron absorption.

This level of inhibition in nonheme-iron absorption found in this study is similar to the reported effects of green tea extract with a much lower level of polyphenols. This observation is an indication that different polyphenols vary considerably in their effect on iron absorption. On the other hand, EGCG reduced fractional nonheme-iron absorption much less than the amounts reported in the literature for black tea and other herbs, such as peppermint (*Mentha* x *piperita*) and pennyroyal (*Mentha pulegium*). Furthermore, the authors hypothesize that in real life EGCG will not be consumed at the same time as the principle sources of dietary iron, that the consumers will not have such low iron stores, and that most dietary supplements will contain lower doses of EGCG than those used in the

study. Therefore, they conclude that such supplements will not "be expected to have any health relevant effects on iron absorption in subjects with normal iron stores."

There are two lines of reasoning that could be considered in opposition to this conclusion:

1) There are several population groups in which iron intake is frequently inadequate. These include adolescents and women of childbearing age, whether or not they are pregnant. [3]
2) A quick look at green tea supplement currently on the market reveals that many products are available that contain up to 250 mg EGCG per tablet or capsule. Suggested use for these products ranges from 1-4 capsules per day.

Thus, from a clinical perspective it seems feasible that iron status could be affected by high green tea/EGCG consumption in certain individuals.

–Cathleen Rapp, ND

References

[1]Gropper S, Smith J, Groff J. *Advanced Nutrition and Human Metabolism*. Belmont, CA: Thomson Wadsworth; 2005.
[2]Barrett JF, Whittaker PG, Williams JG, Lind T. Absorption of nonhaem iron in normal women measured by the incorporation of two stable isotopes into erythrocytes. *Clin Sci.* 1992;83:213-219.
[3]Gropper S, Smith J, Groff J. *Advanced Nutrition and Human Metabolism*. Belmont, CA: Thomson Wadsworth; 2005.

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