Inhibition of iron absorption by polyphenols as an anti-cancer mechanism

L. MASCITELLI1 and M.R. GOLDSTEIN2

From the 1Comando Brigata Alpina ‘Julia’, Medical Service, Udine, Italy and 2Fountain Medical Court, 9410 Fountain Medical Court, Suite A-200 Bonita Springs, FL 34135, USA

Address correspondence to Dr L. Mascitelli, Comando Brigata Alpina ‘Julia’, Medical Service, 8 Via S. Agostino, Udine 33100, Italy. email: lumasci@libero.it

It is well known that cancer might be considered in part to be a preventable disease, highly susceptible to modulation by dietary factors. Polyphenol compounds, which are abundant in fruits, vegetables, seeds and drinks, have been shown to play a potential role as chemopreventive agents.1 The mechanisms underlying this beneficial effect are not fully understood. Assessing the real impact of such constituents on human health is difficult, as in many cases the exact composition of foods and the bioavailability of active molecules are not known. However, there is evidence that polyphenol compounds can prevent the DNA damage caused by free radicals or carcinogenic agents. The mechanisms can be direct radical scavenging, chelating divalent cations involved in Fenton reaction and modulating enzymes related to oxidative stress.1 We suggest that some of the involved mechanisms might be related to inhibition of iron absorption by polyphenols present in the diet.

Iron is an essential nutrient in humans and both iron deficiency and iron excess can result in deviation from the optimal health. Although the absolute amount of iron extracted from the diet is small, its absorption is highly regulated in humans since there is no physiologic pathway for active iron excretion. Haem and non-haem iron enter intestinal mucosal cells by two independent pathways, haem iron being more efficiently absorbed (25–30%) from the diet than non-haem iron (5–15%).2 Although non-haem iron is not absorbed as well as haem iron, it is an important source because haem iron comprises only about 15% of total iron in the typical western diet.3 Beyond its chemical form, the availability of iron for absorption is determined by the presence of enhancers and inhibitors in the meal. Among the latter, polyphenols represent important compounds.

The phenolic compounds are released from food or beverages during digestion, and can combine with iron in the intestinal lumen making it unavailable for absorption. The polyphenols are such powerful inhibitors of non-haem iron that substantial changes in the amount of iron absorbed are more likely to occur if the timing of consumption is altered, rather than the quantity.2 For example, a serving of yod kratin (leaves of the lead tree, Leucaena glauca, a vegetable with a high content of polyphenols and widely consumed in Thailand) reduced iron absorption from a composite meal of rice, fish and vegetables by almost 90%.4 Among elderly participants in the Framingham Heart Study, each cup of coffee (236 ml) consumed in a week was associated with 1% lower serum ferritin, a good measurement of body iron stores.5 Interestingly, all major types of food polyphenols can strongly inhibit dietary non-haem iron absorption, and a dose-dependent inhibitory effect of polyphenol compounds on iron absorption has been demonstrated. In particular, it has been reported that any beverage providing 20–50 mg total polyphenols reduce iron absorption from a bread meal by 50–70%, whereas beverages containing 100–400 mg total polyphenols reduce iron absorption by 60–90%.6 It was noticed that a single serving of instant coffee contains 120 mg of polyphenols.6

© The Author 2010. Published by Oxford University Press on behalf of the Association of Physicians. All rights reserved. For Permissions, please email: journals.permissions@oup.com
Because this study used a simple bread meal, extrapolation of the results to more complex meals might be difficult. However, it should be noted that sufficiently prolonged use of polyphenol compounds has been found to cause iron depletion or iron deficiency in populations with marginal iron stores. Furthermore, the consumption of polyphenol-containing beverages has been suggested as a useful strategy to reduce iron absorption in patients with iron overload disorders.

The effect of regular tea-drinking during meals on accumulation of storage iron was evaluated in patients with genetic haemochromatosis, and the inhibitory effect of black tea on intestinal iron absorption was confirmed. Body iron stores were evaluated quantitatively by exhaustive phlebotomy, the assessment of body iron status being haemoglobin, saturation of serum iron binding capacity and serum ferritin. A significant reduction in iron absorption was observed when the test meal was accompanied by drinks of tea instead of water. In the tea-drinking group, the increase in storage iron was reduced by about one-third compared with that of the control group.

An effect of iron loss in reducing cancer risk has been confirmed in the Iron (Fe) and Atherosclerosis STudy (FeAST) with subjects randomized to reduction in iron stores or observation. The FeAST study is the first randomized trial of the effects of reduction of stored iron on cancer mortality. In the iron reduction group, mean serum ferritin declined from 122.5 ng/ml to 79.7 ng/ml, a 35% decrease. This reduction is within normal reference ranges for serum ferritin, and although it does not equate to iron depletion, it is noteworthy that in the FeAST trial it is of the same order of magnitude of the decrease of storage iron as reported with the regular consumption of a polyphenol-rich tea with meals in the population with genetic haemochromatosis.

In the FeAST study, during 4.5 years of follow-up, the risk of new malignancy was significantly lower in the iron reduction group than in controls. Among patients with new cancers, those with iron reduction had highly significant lower cancer-specific and all-cause mortality. The FeAST trial results suggest that reduction of stored iron may have a broad anti-tumour effect. These findings are plausible in view of the mounting evidence on the role of iron in cancer.

Iron reduction may have multiple anti-cancer actions, which might include depriving neoplastic cells of a key required nutrient, thereby producing an anti-angiogenic effect from reduction of ferritin, inhibition of the formation of 8-hydroxydeoxyguanosine and influencing cell cycle regulation at multiple sites. Finally, tumour suppressor genes may have specific vulnerability to the iron-catalyzed Fenton reaction.

It is therefore plausible that increased intake of polyphenol compounds may, among other beneficial effects, maintain a relatively low iron status and, as a result, reduce the risk of cancer. It is important in future studies of polyphenols action to include assessments of the effects of the intervention on iron status.

**Conflict of interest:** None declared.

**References**


