Proceedings of the Nutrition Society (2011), **70 (OCE6)**, E356 doi:10.1017/S0029665111004411

Winter Meeting, 6–7 December 2011, 70th Anniversary: Body weight regulation – food, gut and brain signalling

Effect of quercetin on non-haem iron transport in human intestinal Caco-2 cells

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Non-haem iron bioavailability is regulated by a number of dietary components including, polyphenols which are thought to act through chelation of iron. The low solubility of iron/polyphenol complexes is regarded as the primary reason for reduced bioavailabilty. However, recent studies by our group and others suggest that the effects of polyphenols of iron absorption are complex and may involve not only control of iron solubility but also include nutrigenomic effects on iron transporter expression [1,2,3].

In this present study we investigated the influence of quercetin, the most abundant flavonol in the diet on iron bioavailability by measuring transepithelial iron transport using radioactive ^{55}Fe. The chronic effects of quercetin were assessed in fully differentiated Caco-2 (intestinal) cells exposed for 24 h to quercetin (0, 10 μM, and 100 μM). In addition, the acute effects of polyphenols on iron bioavailability were also investigated. In these studies quercetin was added along with ^{55}Fe at the start of the experimental period. Iron uptake was measured as the cellular accumulation of ^{55}Fe over a 20 min time course. Efflux of iron from the cells into the basolateral medium was measured after 120 min. Data are mean ± S.E.M. of 5 observations in each group. Statistical analysis was carried out using One-way ANOVA.

In the acute setting, the initial rate of iron uptake across the apical membrane of Caco-2 cells was significantly increased by the addition of quercetin (control, 5.7 ± 0.9; 10 μM quercetin, 11.0 ± 1.6; 100 μM quercetin 16.7 ± 3.8 nmol/mg protein/20 min; $P < 0.03$). In contrast, iron transport across the basolateral membrane was significantly decreased (control, 5.2 ± 1.6; 10 μM quercetin, 2.8 ± 0.6; 100 μM quercetin 0.12 ± 0.03 nmol/mg protein/120 min; $P < 0.03$). These data are in agreement with the reported effects of grape-seed polyphenols on iron transport [3]and indicate that polyphenols may potentiate iron uptake across the apical membrane but act intracellularly to inhibit iron efflux via ferroportin. The mechanisms involved remain unresolved.

Chronic exposure to quercetin for 24 h had no significant effect on iron uptake ($P = 0.1$), but iron efflux into the basolateral medium was significantly decreased (control, 1.0 ± 0.3; 10 μM quercetin, 0.7 ± 0.1; 100 μM quercetin 0.08 ± 0.03 nmol/mg protein/120 min; $P < 0.002$). These findings are consistent with our previous observation that quercetin significantly decreases the expression of the basolateral iron transporter ferroportin and its partner ferroxidase hephaestin [2].

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3. Kim EY, Ham SK, Shigenaga MK & Han O (2008) *J Nut.* **138**, 1647–51.