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Flavonoid-rich berry-extract treatment influences expression of genes in the copper-uptake pathway in human intestinal Caco-2 cells

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Berries are a rich dietary source of bioactive polyphenols, including flavonoids, such as anthocyanins[1]. Dietary flavonoids are known to chelate Cu^{2+} and are known to alter the uptake of metal ions in human intestinal Caco-2 cells[2,3]. However, little is known about the effects of dietary polyphenols on the expression of genes involved in the Cu-uptake pathway in the human intestine. The present study investigated the influence of a flavonoid-rich berry-extract on the expression of the following genes which co-ordinate the intestinal uptake of Cu: the cell surface metalloreductase (DCYTB); the Cu importers, divalent metal ion transporter (DMT1) and Cu transporter 1 (CTR1); the intracellular Cu chaperone (HAH1) and metallothionein (MT); the Cu transporting ATPases (ATP7A and ATP7B)[4].

Human intestinal Caco-2 cells, cultured for 19 d, were treated for 16 h with a flavonoid-rich berry-extract (OptiBerry; InterHealth Nutraceuticals, Benicia, CA, USA) at a final concentration of 0.125 % (w/v). RNA was isolated for quantitative RT–PCR. All gene expression data were normalised to 18S and GAPDH as housekeeping genes and presented as mean normalised expression ratios ±SEM. Statistical significance was determined by Student's *t* test with significance indicated at $P \leq 0.05$ (n 12).

Following treatment with the berry extract there were significant decreases in DMT1 (0.73 ± 0.08, $P<0.04$), CTR1 (0.67 ± 0.06, $P<0.01$), HAH1 (0.82 ± 0.06, $P<0.03$) and ATP7B (0.72 ± 0.05, $P<0.001$) mRNA expression (Fig. 1). The mRNA expression of the other genes did not change significantly in response to the berry-extract treatment.

These results indicate that berry flavonoids influence the expression of components of the Cu-uptake pathway. Studies are in progress to investigate the biological relevance of the observed effects in relation to berry consumption and the bioavailability of dietary Cu.

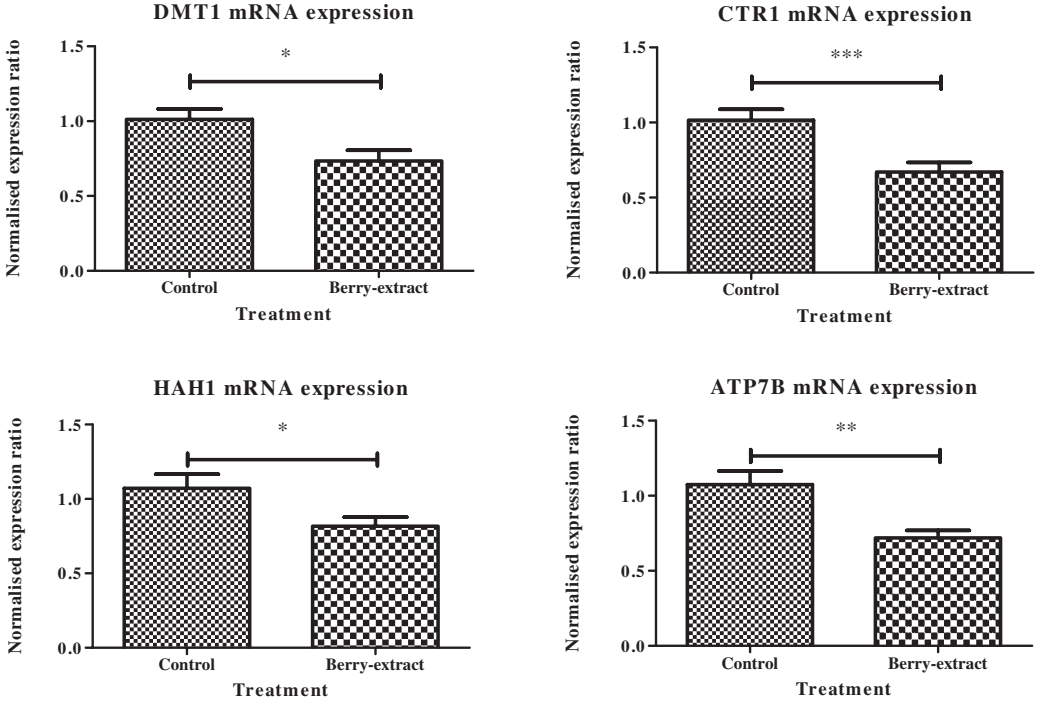

Fig. 1. Effects of berry-extract treatment on the mRNA expression of DMT1, CTR1, HAH1 and ATP7B involved in the Cu-uptake pathway in intestinal Caco-2 cells. Data expressed as mean (SEM), n 12; *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$.

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