Flavonoids alter P-gp expression in intestinal epithelial cells in vitro and in vivo.

Abstract:
Flavonoids are secondary plant metabolites included in our diet but are also provided in a growing number of supplements. They are suggested to interact with intestinal transport systems including phospho-glycoprotein (P-gp) which mediates the efflux of a variety of xenobiotics back into the gut lumen. In human intestinal Caco-2 cells, we tested the effects of 14 different flavonoids on P-gp expression in vitro. Protein expression levels were quantified by Western blotting, flow cytometry, and real-time PCR. Except apigenin, all flavonoids at concentrations of 10 microM increased P-gp expression in Western blotting experiments when cells were exposed to the compounds over 4 wk. Flavone was one of the most effective P-gp inducers in Caco-2 cells and its effects were, therefore, also assessed for changes in P-gp in vivo in the gastrointestinal tract of C57BL/6 mice. P-gp expression was significantly increased by flavone (400 mg/kg body weight x day over 4 wk) in the small intestine but not in the colon which displayed intrinsically the highest expression level. In conclusion, the increase in P-gp expression caused by flavonoids in intestinal epithelial cells in vitro and also in vivo may serve as an adaptation and defense mechanism limiting the entry of lipophilic xenobiotics into the organism.