Bioavailability, metabolism and potential health protective effects of dietary flavonoids - DTU Orbit (09/11/2017)

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Dietary flavonoids constitute an important group of potential health protective compounds from fruits, vegetables, and plant-based products such as tea and wine. The beneficial effects of a diet high in flavonoids on the risk of coronary heart disease (CHD) have been shown in several epidemiological studies but the evidence is inconclusive. One major obstacle for epidemiological studies investigating associations between flavonoid intake and risk of CHD is the estimation of flavonoid intake. There is a vast variety of flavonoids in commonly eaten food products but only limited knowledge of their content. In addition, variation in individual metabolic genotype and microflora may greatly affect the actual flavonoid exposure. The preventive effects of flavonoids on CHD are mainly ascribed to their anti-inflammatory and antioxidant activities. Several mechanisms of anti-inflammatory and antioxidant function of flavonoids have been shown in vitro; yet, only few have been confirmed in vivo. Knowledge of the bioavailability and metabolism of flavonoids is together with information from in vitro studies important steps towards identifying the compounds that are most likely to have biological activity. The present thesis was initiated with two objectives. One objective was to investigate the bioavailability and metabolism of the dietary important flavonoids hesperetin and naringenin from commercial, hesperidin-fortified, and enzymatically treated orange juice. The other objective was to explore the association between exposure to dietary flavonoids and the risk of acute coronary syndrome (ACS) in a nested case-control study. The bioavailability and metabolism of hesperetin and naringenin was investigated by analysing urine and plasma from 16 subjects after consumption of three treatments of orange juice: commercial orange juice with a natural concentration of hesperetin and naringenin rhamnoglucosides, 3-times hesperidin (hesperetin-7-O-rhamnoglucoside) fortified orange juice and orange juice enzymatically treated to yield hesperetin and naringenin-7-O-glucosides. The effect of enzymatic treatment on bioavailability was statistically significant compared to commercial orange juice and showed 3 and 4 fold increases in bioavailability of hesperetin and naringenin, respectively. A total of eight hesperetin and naringenin phase II conjugates excreted in urine was identified by comparison with synthetic standards, NMR spectroscopy and differential pH spectrophotometry. Quantification was performed on six of the eight conjugates based on calibration curves with the identical conjugates. There was no difference in the profile of the excreted conjugates according to treatment. The results demonstrated the more effective absorption of hesperetin and naringenin from the small intestine when consumed as glucosides compared to absorption in the colon VII after microbial degradation of the rhamnoglucosides. In addition it was shown that the conjugate profile was neither affected by the absorption site nor by a 3-fold change in dose. The urinary excretion of ten dietary flavonoids was analysed after enzymatic hydrolysis by LC-MS and associated to the risk of ACS in a nested case-control study with 393 case-noncase pairs. The 393 case-noncase pairs were identified in the Danish Diet, Cancer and Health cohort comprising biological samples and food frequency questionnaires (FFQs) from 57 053 cohort members. Higher urinary excretion of kaempferol was statistically significant associated with a consistent 44-60 % lower risk of ACS. The lower risk associated with urinary kaempferol excretion was probably attributable to tea consumption. There were no monotonic dose-response relations between higher excretion of any of the flavonoids and lower risk of ACS. This was the first time that flavonoid excretion was measured in spot-urine samples and associated to risk of ACS in a nested case-control study. The results indicate that the study was too limited in size to account for the variation associated with quantifying flavonoids in spot-urine samples. However, the non-monotonic, but statistically significant, association between higher kaempferol excretion and lower risk of ACS indicate that the lack of associations were not due to lack of potential cardio-protective effects of flavonoids. This should be investigated in a larger study.

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