Proceedings of the Nutrition Society (2010), **69 (OCE6)**, E473 doi:10.1017/S0029665110003368

Summer Meeting, 28 June–1 July 2010, Nutrition and health: cell to community

Effects of genetic polymorphism in soyabean isoflavone absorption and metabolism

L. A. Wakeling and D. Ford

Human Nutrition Research Centre and Institute for Cell and Molecular Biosciences, Newcastle University, Newcastle Upon Tyne NE2 4HH, UK

Soyabean isoflavones may confer a number of health benefits, including reduced risk of CVD and cancer. In unfermented plant sources, isoflavones occur as β-glucosides. Absorption from the intestine requires cleavage by intestinal enzymes with β-glucosidase activity (lactase phlorizin hydrolase (LPH) and cytosolic β-glucosidase (CBG)). Intestinal and hepatic UDP-glucuronosyl transferases (UGTs) including UGT1A1 are involved in phase-II conjugation.

There is large inter-individual variation in isoflavone bioavailability which cannot be explained fully by studies investigating soya matrix, microbial action, gender or age alone and so it is likely that polymorphisms within the enzymes involved in absorption and metabolism can account for this variation. Non-synonymous coding SNP in *LPH* and *CBG* may contribute to variability in isoflavone absorption. An insertion polymorphism ($(TA)_7$) in the promoter region of *UGT1A1* may also alter isoflavone bioavailability.

The Soya Isoflavone Metabolism Study (SIMS) was designed to establish if genotype influences the metabolism of a single, bolus, oral dose of soyabean isoflavone β-glucosides. Healthy pre-menopausal females (n 100) aged 18–50 years were genotyped for the polymorphisms in *LPH* (G666A), *CBG* (T1417A) and *UGT1A1* (*UGT1A1**28 A$(TA)_7$TAA) using an assay based on the analysis of real-time PCR hybridisation probe melting temperature. Thirty women were selected according to genotype to participate in the second stage of SIMS. A fasting blood sample was taken 3 h after isoflavone administration and all urine collected over 24 h. Samples were analysed by RP-HPLC for isoflavones and their glucuronides. Participants completed 3-d food diaries to assess normal daily isoflavone intake.

The minor allele, A, in the LPH polymorphism was associated with a reduction in percentage of total and individual isoflavone as sulphates in the plasma at 3 h [$P<0.022$ for genistein, $P<0.022$ for daidzein, $P<0.043$ for total isoflavones by Mann–Whitney test (two-tailed)]. The UGT1A1*28 polymorphism was associated with an increase in the percentage of total and individual isoflavone as sulphates in urine over 24 h ($P<0.001$ for glycitein, $P<0.015$ for total isoflavones by univariate ANOVA), supporting the hypothesis that the reduced UGT1A1 activity associated with this genotype leads to reduced levels of glucuronidation, and as a consequence increased sulphation, assuming a level of competition between the two conjugation pathways. The total isoflavone excreted in urine appeared to be influenced by habitual dietary isoflavone intake indicated by a positive correlation ($r^2 = P<0.006$) between isoflavone consumption over the 3-d period recorded and isoflavone excretion in urine (but not in plasma).

In conclusion, the results of this study indicate that inter-individual genetic variation in LPH and UGT1A1 influence isoflavone absorption and metabolism. Genetic background may, therefore, influence the degree to which specific individuals may benefit from the consumption of isoflavones. It is important to consider the potential impact of such genetic variability on isoflavone bioavailability when designing future intervention studies.