Does diet play a role in the interindividual variability of isoflavone excretion?

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Studies have shown large interindividual variations in the metabolism and excretion of soybean isoflavones. It is thought that differences in the population of colonic bacteria involved in the hydrolysis and reduction of glycosidic isoflavones and diet-related differences in colonic bacteria, may contribute to the variation in isoflavone metabolism and excretion. The aim of the study was to determine the interindividual variation in isoflavone excretion and to establish if any component of the diet was a predictor of this variation.

Twenty five healthy women with stable body weight and habitual diet (age: 18-46 y; BMI: 17-32 kg/m^2) were participants in one of two studies conducted over 4 months. In study 1, 14 subjects consumed either an isoflavone tablet (86 mg/d: 52mg of biochanin A, 8mg of genistein, 18mg of formononetin, 8mg of daidzein) derived from red clover or placebo for two months and crossed-over for the final two months. In study 2, 11 subjects consumed the placebo for the 1st month and the isoflavone supplement for the remaining three months. Subject compliance was confirmed by tablet count. Three 24-hour urine samples were collected during the placebo treatment and the 2nd month of isoflavone treatment for analysis of isoflavones by HPLC. Three-day weighed food records were analysed for average macronutrient intake. The relationship between macronutrient intake and isoflavone excretion was examined by a multiple regression model.

Isoflavone supplementation resulted in a 14-fold increase in total urinary isoflavones compared to placebo ($p<0.0001$). The interindividual variation of total isoflavones excreted during the treatment period was 4-fold. There was a strong positive correlation between excretion of daidzein and genistein ($r=0.63$, $P=0.0006$), as well as daidzein and formononetin ($r=0.65$, $P=0.0002$). However macronutrient intake calculated as g/d or % of energy was not associated with isoflavone excretion.

Urinary isoflavone	Placebo supplement			Isoflavone supplement		
□mol/24hr	Mean ± SD	Range	%[1]	Mean ± SD	Range	%[1]
Dihydrodaidzein	0.4 ± 1.1	ND - 5.0	16	5.0 ± 6.2[α]	ND - 18.7	64
Dihydrogenistein	0.2 ± 0.8	ND - 4.0	4	4.0 ± 11.3	ND - 39.8	12
Daidzein	3. 1 ± 2.7	ND - 9.3	52	22.2 ± 11.0[♦]	3.6 - 45.4	100
Equol	0.1 ± 0.7	ND - 3.8	4	4.3 ± 9.1[♣]	ND - 29.6	24
Genistein	0.8 ± 1.3	ND - 5.0	30	7.7 ± 7.6[♦]	0.9 - 17.5	100
O-desmethylangolensin	0.04 ± 0.20	ND - 1.0	4	10.0 ± 7.5[♦]	ND - 32.3	96
Formononetin	ND	ND	0	13.8 ± 7.4[♦]	2.1 - 31.1	100
Biochanin A	ND	ND	0	5.6 ± 2.9[♦]	0.8 - 10.1	100
Total Isoflavones	4.7 ± 5.0	ND - 19.3	N/A	72.7 ± 29.2[♦]	24.0 -127.7	N/A

[1] Prevalence of excretion. Significantly different from placebo [α]P=0.0007, [♣]P=0.03, [♦]P<0.0001.

Our study showed that supplementation of red clover isoflavones, which includes the precursors biochanin A and formononetin, resulted in high interindividual variation of urinary isoflavone metabolites (particularly dihydrogenistein and equol) and that the variation was not explained by choice of habitual diet. Given the differing biological activities of the individual isoflavones, our results have implications for the use of urinary isoflavone levels as biomarkers of isoflavone intake and/or biological activity.