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Distribution of 24-h urinary equol excretion as an indicator of the physiological range in healthy Japanese equol excretors

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ABSTRACT

Equol is produced from daidzein, a soy isoflavone, through metabolism by intestinal bacteria, and benefits health. This cross-sectional study aimed to investigate its physiological range, using 24 h urinary equol excretion as an indicator, in Japanese people who consume soybeans in their usual diet. The 24 h urine of 1345 subjects (545 men and 800 women) was collected, and equol, daidzein, and genistein concentrations were measured. Subjects with detectable equol in their urine (⩾0.27 nmol/ml) were considered equol excretors. Among men, 36.3% were equol excretors; among women, 40.8%. The rate of equol excretors and urinary equol excretion differed significantly by age, but not by gender. In all equol excretors, the range of 24 h urinary equol excretion was 0.4–318.0 μmol/day; the median was 12.5 μmol/day; and the 95th percentile was 119.2 μmol/day. This range appears to be the physiological range of equol excretion in Japanese people who consume soy food regularly.

1. Introduction

Soybeans, a traditional food in Asian countries, are consumed more in Asia than in Western countries (Kim & Kwon, 2001; Messina, 2010; Messina, Nagata, & Wu, 2006). High soy consumption may be linked to better health outcomes in Asia. Previous studies have shown that the incidence of breast and prostate cancers is much lower in the Asian population than in the Western population, which might suggest that soy intake is related to a reduced risk for certain cancers (Oseni, Patel, Pyle, & Jordan, 2008; Wu, Yu, Tseng, & Pike, 2008). Soy isoflavones (daidzein, genistein and glycitein) are commonly referred to as phytoestrogens, but because they preferentially bind to and transactivate estrogen receptor beta in comparison to estrogen receptor alpha, they are also classified as selective estrogen receptor modulators (Sonoda et al., 2004). Soy isoflavones have been reported to have positive influences on breast and prostate health (Blake, Hansen, Simmons, & Lephart, 2013; Morton, Arisaka, Miyake, Morgan, & Evans, 2002; Yamamoto, Sobue, Kobayashi, Sasaki, & Tsugane, 2003), although there are still concerns about their estrogenic effects (Ju et al., 2001; Ju, Fultz, Allred, Doerge, & Helferich, 2006).

Equol is a daidzein metabolite produced by intestinal bacteria (Setchell, Brown, & Lydeking-Olsen, 2002; Yuan, Wang, & Liu, 2007). Equol has been proposed to have health benefits

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Abbreviations: HPLC, high-performance liquid chromatography; SD, standard deviation
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superior to those of its parent isoflavone (Setchell et al., 2002), and it may affect hormone-related cancers in a similar manner as soy isoflavones (Atkinson et al., 2003, 2008; Ingram, Sanders, Kolybaba, & Lopez, 1997; Kurahashi, Iwasaki, Inoue, Sasazuki, & Tsugane, 2008; Nettleton et al., 2005; Tanaka et al., 2009). However, isoflavone (daidzein and genistein) and equol have weak estrogenic activity, and there are concerns about possible estrogen-related cancers caused by overdose. In a previous study (Oyama et al., 2012), it was reported that daily doses of 10–30 mg S-equol delivered via a new fermented soy-based supplement did not affect serum sex or thyroid hormone levels, the uterine endometrium, vaginal smears, or breast density (mammography). However, the periods of soy consumption in these studies were relatively short (12–24 weeks), so the effects of an overdose or consumption for a prolonged period of time remain unknown. First, it is necessary that we have an accurate understanding of the physiological range of equol in healthy Japanese people who consume soy food regularly for information about safety of equol. It has been reported that the prevalence of equol excretors is approximately 30% in Western populations (Bolca et al., 2007; Fuhrman et al., 2008; Gardana, Canzi, & Simonetti, 2009; Song et al., 2006; Törmälä et al., 2008; Verheus et al., 2008) and is approximately 50% in Asian populations (Arai et al., 2000; Guo et al., 2010; Morton et al., 2002; Song et al., 2006). The daily diet (milk and egg yolk) provides only a small amount of equol (Kuhnle et al., 2008; Ward et al., 2010), except for stinky tofu, which is a special and popular fermented soy food traditionally consumed in China and Taiwan (Abiru, Kumemura, Ueno, Uchiyama, & Masaki, 2008; Jou, Tsai, Tu, & Wu, 2013). Frankenfeld (2011) reported that equol concentrations (geometric mean concentration of detectable equol: 0.049 nmol/mg creatinine) in low soy-consuming populations (daidzein intake: 0.36 ± 0.073 mg/day) may reflect the intake of equol from mammalian milk sources rather than the endogenous production of equol from microbial metabolism of daidzein. However, in high soy-consuming populations, including the Japanese, equol concentrations might be strongly influenced by the production of equol from daidzein by intestinal bacteria. The isoflavone and equol levels in spot urine and serum specimens were highly influenced by the sampling time for the reasons of their absorption and metabolism. The isoflavones (daidzein and genistein) in soy exist in glycoside forms (daidzin and genistin) and are hydrolyzed to absorbable aglycones and transformed into metabolites, such as equol, by intestinal bacteria. Therefore, the 24 h urinary

Table 1 – Range of 24 h urinary isoflavonoid excretion in Japanese men and women.

Isoflavonoid		Total (age, 20–73 years)	Men (age, 20–64 years)	Women (age, 20–73 years)
Equol				
n[a]		1345	545	800
Excretors	(%)	39.0	36.3	40.8
Mean[b]	(μmol/day)	11.3	11.1	11.4
SD	(μmol/day)	29.8	30.3	29.5
Minimum	(μmol/day)	0.0	0.0	0.0
Maximum	(μmol/day)	318.0	314.2	318.0
10th percentile	(μmol/day)	0.0	0.0	0.0
50th percentile	(μmol/day)	0.0	0.0	0.0
95th percentile	(μmol/day)	61.9	61.9	60.6
Daidzein				
n[a]		1332	533	799
Excretors	(%)	98.3	97.6	98.7
Mean[b]	(μmol/day)	37.8	44.7[***]	33.3
SD	(μmol/day)	60.4	71.4	51.4
Minimum	(μmol/day)	0.0	0.0	0.0
Maximum	(μmol/day)	530.0	530.0	503.2
10th percentile	(μmol/day)	3.1	2.8	3.3
50th percentile	(μmol/day)	16.2	18.8	15.1
95th percentile	(μmol/day)	149.0	175.7	138.1
Genistein				
n[a]		1337	539	798
Excretors	(%)	98.7	97.4	98.9
Mean[b]	(μmol/day)	19.5	24.0[***]	16.5
SD	(μmol/day)	38.8	47.2	31.6
Minimum	(μmol/day)	0.0	0.0	0.0
Maximum	(μmol/day)	474.6	474.6	412.7
10th percentile	(μmol/day)	1.4	1.6	1.3
50th percentile	(μmol/day)	7.8	9.8	6.9
95th percentile	(μmol/day)	78.3	96.2	65.6

[a] Data determined incapable of judgment by analysis were excluded.
[b] Values below the lower limit of detection by HPLC (equol, 0.27 nmol/ml; daidzein, 0.05 nmol/ml; genistein, 0.09 nmol/ml) were assigned a value of 0.0 μmol/day.
[***] $P < 0.001$ vs. women (Student's *t* test).