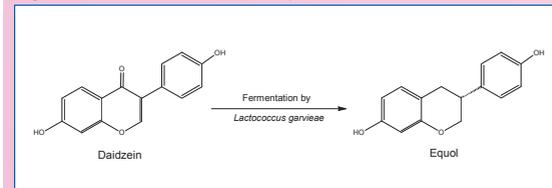


Equol

- Equol exists in S- and R- isomers.
- S-equol is the naturally occurring form produced in the body.
- S-equol is considered to be the isomer that is believed to have benefits.

Figure 1. Daidzein Metabolism to Equol



Equol vs. Non-Equol Producers

- Approximately 50% of Japanese are equol producers while in the U.S. and Europe only 30% can produce equol in response to a soy challenge test.
- Japanese women ages 40-65 yrs were tested for equol production. There were 145 equol producers and 166 non-producers. Serum uric acid concentrations were 4.4 and 4.6 mg/dL, respectively (P=0.02). Serum triglycerides were 87 and 107 mg/dL, respectively (P=0.003).
- In a recent study in China about 23% were equol producers. After a 3-day challenge with soy isoflavones added to the diet, 55% were equol producers.
- Of the 553 subjects tested, 185 were pre-menopausal women and 84 were post-menopausal women. Within the pre-menopausal group 52 (28%) were equol producers and their serum uric acid was 3.5 mg/dL vs 4.2 mg/dL for the non-producers (P=0.019). Within the post-menopausal group 11 (13%) were equol producers and their serum uric acid was 4.0 mg/dL compared to 4.9 mg/dL for non-producers (P=0.017).

Introduction

- Equol is a metabolite of daidzein, a soy isoflavone. It is a non-steroidal estrogen and major intestinal derived bacterial metabolite of daidzein one of the principle isoflavones found in soybeans and most soy foods.
- Natural S-equol has been developed as a nutraceutical ingredient via a patented process using soy germ fermented with *Lactococcus garviae*.
- S-equol has been shown to have affinity for the ER receptor-β. It is thought to be beneficial for prevention or treatment of estrogen dependent conditions such as menopause.
- Natural S-equol has been studied for its benefits for relief of menopausal symptoms in Japanese perimenopausal and postmenopausal women.

Abstract

Soy bean isoflavones have a structure similar to estrogen and are sometimes referred to as phytoestrogens. It is thought that soy isoflavones may reduce the symptoms of hormone-dependent disorders such as menopause. Equol is an active metabolite of the soy isoflavone daidzein. The ability to convert daidzein to equol depends on the presence of certain intestinal microflora. Approximately half of the Japanese population produce equol. In non-Asian populations in North America and Europe only 20 to 30% of the population produces equol after consuming isoflavone-containing soy foods or dietary supplements. Equol production and absorption (as determined by measuring urinary equol output) may change with soy content of diet. In a study of 584 men and women living in the Chinese cities of Beijing, Shanghai and Guangzhou, 23.4% were equol producers. After three days of adding soy isoflavones at 41 mg/day to the diet, 54.9% were equol producers. Chinese citizens consume on average less soy foods compared to Japanese citizens, so the pre-study result may have reflected pre-study diet. Epidemiological studies suggest that menopausal symptoms of equol producers are milder than those of non-producers, and that there may be other benefits. In the study conducted in China, the 320 equol producers had significantly lower serum cholesterol and uric acid compared to the 264 non-producers. In a study conducted in Japan, 145 peri- and post-menopausal women who were equol producers had significantly lower serum triglycerides and uric acid compared to 166 non-producers. In the latter study, neither total cholesterol nor LDL-cholesterol were different between groups. A published study of 127 Japanese pre-, peri- and post-menopausal women given either a placebo control or dietary supplements containing Natural S-equol at 10 or 30 mg/day showed that equol producers (34.3%) had significantly lower anxiety scores than non-producers (65.7%). After 12 weeks of supplementation with equol at 30 mg/day, the equol non-producers had improved menopause, anxiety, depression, and fatigue and vigor scores compared to the placebo group. However, women who were already equol producers did not benefit from supplemental equol. Taken all together, the population and intervention results suggest that the daidzein metabolite equol, either produced endogenously or provided exogenously, may have health benefits in areas of menopausal symptoms, blood lipids, and uric acid status.

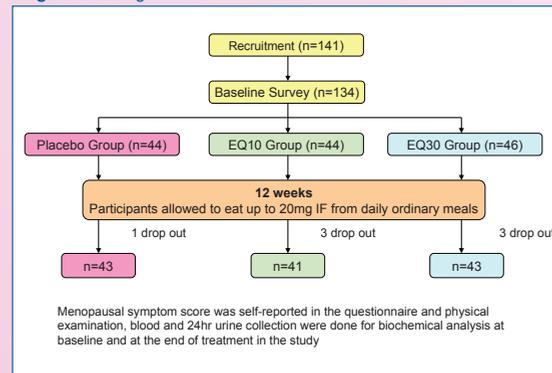
Ishiwata, et al, 2009 - Natural S-Equol Supplement for Relieving Menopausal Symptoms

- The objective of the study was to evaluate the effects of oral S-equol supplement on menopausal symptoms in a single-center, 12 week, double blind, randomized, placebo controlled trial in Japanese perimenopausal and post-menopausal women.

Methods and Materials

- Participants: 134 Japanese women (aged 40-59 yrs) randomly assigned to one of the two treatment or placebo groups
 - EQ 10 (n=44); 10 mg of S-equol per day
 - EQ 30 (n=46); 30 mg of S-equol per day
 - Placebo (n=44)

Figure 2. Design of Intervention Trial



Supplements

- Equol supplement (EQ) was made from soy germ by fermentation with *Lactococcus garviae*. The granulated supplement was packed in 10 mg EQ/stick. Placebo was similar in appearance size, color, taste and smell to EQ supplements.
- EQ10 group took one EQ stick each day before breakfast. The EQ30 group took three EQ sticks each day. One EQ stick was taken before the breakfast, lunch and dinner meal.

Measurements

- Physical examination: Ht, body wt, BMI, body fat, blood pressure, bone mineral density
- Hormones: LH, FSH, Estradiol (E₂), progesterone, prolactin, serum T₃ & T₄
- Serum Chemistries
- Urinary equol, daidzein, genistein, glycitein

Menopausal Symptom

- Participants were requested to access the severity of each of the 23 symptom questions on a 4 point score system. Twenty one symptoms were from the Menopausal Index for Japanese Women (Japanese Society of Obstetric and Gynecology) and two symptoms were added to assess sex and urogenital dysfunction. The Greene Climacteric Scale was used to calculate component symptoms for vasomotor, psychological, anxiety, depression, somatic and other symptom factors.

Profile of Mood States

- To evaluate effects of the equol supplement on mood, participants answered the validated Japanese version of the Profile of Mood States (POMS) at baseline and at the end of intervention. Included were 65 questions concerning weekly recall of six mood states: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor, Fatigue and Confusion.

Results

Table 1. Menopausal scores, POMS scores, and hormones at baseline and after 12 weeks of equol supplementation in perimenopausal / postmenopausal equol producers

	Placebo (n = 14)			EQ-1 (n = 10)			EQ-3 (n = 10)		
	Baseline	12 weeks	Significance	Baseline	12 weeks	Significance	Baseline	12 weeks	Significance
Menopausal Scores									
Psychological	5.3 (5.2)	3.4 (3.7)		2.4 (2.1)	1.9 (1.9)		5.6 (4.9)	4.4 (4.6)	
Anxiety	4.2 (4.2)	2.3 (2.8)	*	1.7 (1.6)	1.3 (1.5)		3.8 (4.3)	3.2 (3.8)	
Depression	1.1 (1.3)	1.1 (1.2)		0.7 (1.1)	0.6 (0.7)		1.8 (1.0)	1.2 (1.4)	
Somatic	7.0 (6.1)	5.8 (4.4)		6.1 (3.4)	5.8 (2.6)		6.6 (3.0)	5.7 (3.1)	
Vasomotor	3.3 (2.2)	1.8 (2.2)	*	1.2 (1.0)	1.1 (0.9)		2.1 (1.8)	1.6 (1.6)	
Total	20.8 (12.6)	14.6 (9.3)	*	13.7 (6.3)	11.7 (4.1)		20.4 (8.3)	15.9 (9.6)	
POMS									
Tension-Anxiety	45.6 (7.4)	45.0 (6.1)		45.9 (7.0)	44.7 (5.3)		48.6 (6.0)	47.9 (7.9)	
Depression-Dejection	48.0 (8.2)	48.1 (6.3)		46.2 (6.2)	44.5 (3.5)		48.3 (5.8)	50.1 (8.5)	
Anger-Hostility	46.8 (8.0)	47.1 (6.4)		47.7 (8.0)	45.8 (4.9)		52 (5.2)	50.6 (7.5)	
Vigor	47.4 (8.5)	42.5 (8.2)	*	49.5 (5.9)	46.4 (7.1)		46.6 (6.4)	49.8 (6.8)	
Fatigue	46.5 (8.6)	47.6 (10.6)		47.8 (9.9)	47.6 (8.5)		50.6 (6.1)	51.8 (8.1)	
Confusion	50.1 (9.3)	48.3 (9.2)		47.1 (8.0)	46.1 (2.2)		50.4 (9.4)	48.5 (7.4)	
Hormones									
LH, nmol/L	19.4 (8.0)	19.3 (11.9)		19.0 (16.2)	19.3 (14.3)		15.2 (9.2)	13.7 (8.8)	
FSH, U/L	54.7 (32.7)	55.0 (38.9)		37.1 (29.9)	40.1 (27.3)		43.8 (21.7)	48.2 (28.9)	
Estradiol, pg/mL	35.1 (26.4)	43.9 (32.8)		193.9 (97.9)	85.3 (65.6)		134.2 (109.3)	143.6 (109.5)	
Progesterone, ng/mL	0.27 (0.14)	0.26 (0.12)		1.17 (1.79)	1.72 (2.59)		0.53 (1.01)	0.26 (0.29)	

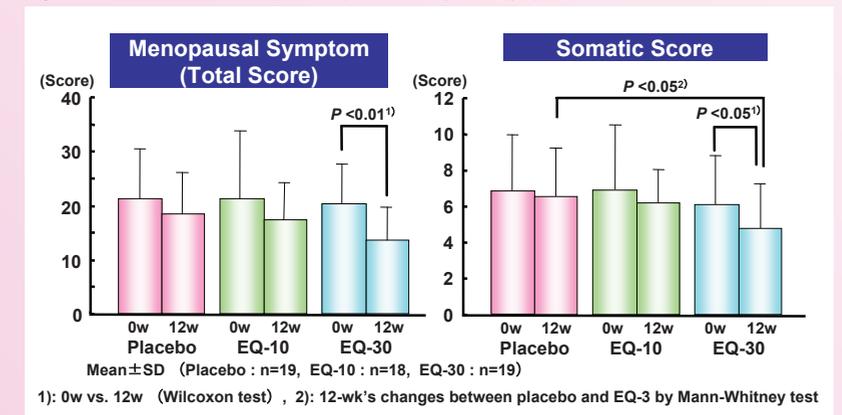
Values are presented as mean (SD). The EQ-1 group took 10 mg equal once a day, and the EQ-3 group took 10 mg equal three times a day. POMS, Profile of Mood States; LH, luteinizing hormone; FSH, follicle-stimulating hormone. *Significant differences between baseline and 12 wk in placebo group by Wilcoxon test. #Significant differences between baseline and 12 wk in EQ-3 by Wilcoxon test. *P < 0.05. #P < 0.01.

Table 2. Menopausal scores, POMS scores, and hormones at baseline and after 12 weeks of equol supplementation in perimenopausal / postmenopausal equol nonproducers

	Placebo (n = 19)			EQ-1 (n = 18)			EQ-3 (n = 19)		
	Baseline	12 weeks	Sig	Baseline	12 weeks	Sig	Baseline	12 weeks	Sig
Menopausal Scores									
Psychological	6.4 (3.7)	6.4 (4.0)		6.9 (5.4)	5.1 (3.4)		6.5 (4.0)	4.4 (3.1)	*
Anxiety	4.7 (2.8)	4.5 (3.2)		5.3 (4.0)	3.9 (2.7)		5.1 (2.7)	3.4 (2.3)	*
Depression	1.7 (1.5)	1.9 (1.1)		1.7 (1.7)	1.2 (1.0)		1.4 (1.1)	1.0 (1.2)	*
Somatic	6.8 (3.2)	6.3 (3.2)		6.7 (3.8)	6.1 (2.6)		6.1 (3.2)	4.7 (2.6)	*
Vasomotor	3.2 (1.9)	2.3 (1.5)	*	2.7 (1.8)	2.2 (1.7)		2.4 (1.9)	1.4 (1.9)	*
Total	21.4 (9.8)	18.4 (7.6)	*	21.3 (12.3)	17.3 (6.9)		20.2 (7.9)	13.6 (6.2)	*
POMS									
Tension-Anxiety	49.9 (6.4)	50.7 (9.1)		49.0 (8.8)	47.9 (7.5)		49.8 (9.2)	46.6 (4.6)	*
Depression-Dejection	51.3 (7.6)	53.3 (9.6)		49.4 (7.9)	45.6 (6.7)		48.5 (5.6)	45.4 (4.4)	*
Anger-Hostility	50.4 (8.4)	52.4 (7.1)		50.7 (10.1)	50.1 (7.7)		50.4 (7.7)	48.7 (4.7)	*
Vigor	44.8 (7.8)	42.6 (6.5)	*	44.2 (8.1)	45.2 (7.6)		43.4 (6.7)	45.6 (7.1)	*
Fatigue	50.3 (9.3)	54.3 (9.7)		49.8 (8.4)	49.7 (7.5)		49.2 (4.7)	46.5 (5.6)	*
Confusion	54.5 (8.2)	54.3 (8.8)		50.4 (10.1)	50.4 (7.8)		53.1 (10.2)	51.6 (6.8)	
Hormones									
LH, nmol/L	21.3 (9.2)	21.0 (9.1)		25.3 (13.3)	23.9 (12.2)		23.9 (10.0)	23.0 (14.3)	
FSH, U/L	50.8 (24.6)	54.6 (38.9)		63.9 (29.2)	65.4 (31.0)		56.5 (33.5)	59.6 (31.4)	
Estradiol, pg/mL	116.0 (154.6)	179.1 (127.8)		43.6 (56.0)	17.5 (7.9)		129.5 (162.9)	96.8 (166.3)	
Progesterone, ng/mL	0.76 (1.67)	1.38 (3.26)		0.28 (0.12)	0.25 (0.14)		0.55 (1.31)	0.46 (0.30)	

Values are presented as mean (SD). The EQ-1 group took 10 mg equal once a day, and the EQ-3 group took 10 mg equal three times a day. POMS, Profile of Mood States; LH, luteinizing hormone; FSH, follicle-stimulating hormone. *Significant differences between baseline and 12 wk in placebo group by Wilcoxon test. #Significant differences between baseline and 12 wk in EQ-3 by Wilcoxon test. *P < 0.05. #P < 0.01.

Figure 3. Effects of Natural S-Equol in Japanese Menopausal Symptom Score



Implications for Nurse Practitioners

- S-equol supplementation improved mood-related symptoms in both perimenopausal and postmenopausal Japanese equol and nonequol producers.
- Benefits included improvement in menopause, anxiety, depression, fatigue and vigor scores.
- The population and intervention results suggest that the daidzein metabolite equol may have health benefits for menopausal symptoms.
- Evaluation in the U.S. population is underway.

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