Soyfoods, Soy Isoflavones & Health: Where Does the Science Stand?

Mark Messina, PhD, MS
Soy Nutrition Institute
Loma Linda University
Nutrition Matters, Inc.

April 10, 2017

- Perception of soyfoods
- Asian soy intake
- Macronutrient composition
- Health attributes of soy protein
- Isoflavones
- Breast cancer
- Hot flashes
- Bone health
- Concerns

Disconnect between Nutrition Professionals and the Public about the Healthfulness of Specific Foods

<table>
<thead>
<tr>
<th>Food</th>
<th>(% viewing as healthful)</th>
<th>Professionals</th>
<th>Public</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granola bars</td>
<td>28</td>
<td>↑3</td>
<td>71</td>
</tr>
<tr>
<td>Coconut oil</td>
<td>37</td>
<td>↑5</td>
<td>72</td>
</tr>
<tr>
<td>Frozen yogurt</td>
<td>32</td>
<td>↑4</td>
<td>66</td>
</tr>
<tr>
<td>Quinoa</td>
<td>89</td>
<td>↑21</td>
<td>58</td>
</tr>
<tr>
<td>Humus</td>
<td>90</td>
<td>↑24</td>
<td>66</td>
</tr>
<tr>
<td>Tofu</td>
<td>85</td>
<td>↑28</td>
<td>57</td>
</tr>
</tbody>
</table>

Poll conducted by Morning Consult for the NYT. July 2016. Nutritionists = ASN members

Why does 43% of the public think tofu isn’t healthful?

<table>
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<th>(% viewing as healthful)</th>
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Poll conducted by Morning Consult for the NYT. July 2016. Nutritionists = ASN members
Soy Misinformation

Estimated Asian Adult Soy Protein and Isoflavone Intakes
Mark Musha, Chikato Nagata, and Anne H. Wu

Abstract: There is substantial interest in the possible ameliorative effects of soy foods. Several studies have suggested that soy foods may be beneficial in the prevention and treatment of breast and prostate cancer. However, despite the relative simplicity of soy foods, the potential benefits of soy foods have been largely overlooked. The purpose of this study was to assess the potential benefits of soy foods in the prevention and treatment of breast and prostate cancer. The study was conducted in a randomized, double-blind, placebo-controlled trial. The results of the study suggest that soy foods may be beneficial in the prevention and treatment of breast and prostate cancer.

Asian Soyfood Consumption1

<table>
<thead>
<tr>
<th>Location</th>
<th>Serv./d2</th>
<th>Type of soyfood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shanghai</td>
<td>1 – 2</td>
<td>Unfermented</td>
</tr>
<tr>
<td>Singapore</td>
<td>½ – ¾</td>
<td>Unfermented</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>½</td>
<td>Unfermented</td>
</tr>
<tr>
<td>China</td>
<td>½</td>
<td>Unfermented</td>
</tr>
<tr>
<td>Japan</td>
<td>1 – 2</td>
<td>50% fermented</td>
</tr>
<tr>
<td>Korea</td>
<td>½ – 1</td>
<td>30% fermented</td>
</tr>
</tbody>
</table>

1Among older adults 2Servings: 240 ml milk, 85-100 g tofu
Soy protein products

Isolate: ~90% protein
Concentrate: ~70% protein
Flour: ~50% protein

• Routinely used in clinical studies
• Widely used by the food industry:  
  ▪ Functional purposes  
  ▪ Western (second generation) soyfoods

Macronutrient Composition

VS.
Macronutrient (% calories)
Composition of Soybeans in Comparison to Common Beans

<table>
<thead>
<tr>
<th>Macronutrient</th>
<th>Soybeans</th>
<th>Common beans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>27 *</td>
<td>70</td>
</tr>
<tr>
<td>Protein</td>
<td>33</td>
<td>27</td>
</tr>
<tr>
<td>Fat</td>
<td>40</td>
<td>3</td>
</tr>
</tbody>
</table>

*Mostly oligosaccharides (indigestible)
Capable of functioning as prebiotics

AJCN 70: 439S, 1999

<table>
<thead>
<tr>
<th>Protein Digestibility Corrected AA Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg white</td>
</tr>
<tr>
<td>Milk (casein)</td>
</tr>
<tr>
<td>Soy</td>
</tr>
<tr>
<td>Beef</td>
</tr>
<tr>
<td>Pea protein</td>
</tr>
<tr>
<td>Kidney beans</td>
</tr>
<tr>
<td>Pinto beans</td>
</tr>
<tr>
<td>Rolled oats</td>
</tr>
<tr>
<td>Rice</td>
</tr>
<tr>
<td>Peanut meal</td>
</tr>
<tr>
<td>Whole wheat</td>
</tr>
<tr>
<td>Wheat gluten</td>
</tr>
</tbody>
</table>

Highest score = 1.0 (truncated)


25 grams of soy protein per day ... may reduce risk of heart disease

Countries with approved health claims

- United States (1999)
- Indonesia
- Japan
- Korea
- Chile
- Turkey
- Malaysia
- Philippines
- Brazil
- Columbia
- South Africa
- Canada (2014)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
December 6, 2007

Reevaluating evidence in support of the health claim

AHA Science Advisory
Soy Protein, Isoflavones, and Cardiovascular Health
An American Heart Association Science Advisory for Professionals
From the Nutrition Committee
Frank M. Sacks, MD, Alice Lucia, TDS, Linda Van Horn, RD, William Harris, PhD, Penny Kris-Etherton, PhD, Sally Watson, PhD
for the American Heart Association Nutrition Committee

- Lowers LDL-C ~3% (22 studies)
- Doesn’t warrant health claim
- Didn’t conduct a meta-analysis

Key Words: AHA Scientific Advisory • cardiovascular disease • soy protein • isoﬂavones • cholesterol

Soy Protein Reduces Serum Cholesterol by Both Intrinsic and Food Displacement Mechanisms1–3

- Lowers LDL-C 4.3% (22 studies)
- Lowers LDL-C 5.2% (11 studies)
- Warrants health claim

1Vital Nutrition and Risk Factor Modification Group, Department of Medicine and Division of Endocrinology and Metabolism, McLean Hospital, Harvard Medical School, MA 02138. 2Department of Nutrition and Department of Biostatistics, Harvard School of Public Health, Boston, MA 02115. 3Department of Food Science and Nutrition, University of Minnesota, St. Paul, MN 55108.

2Soy protein intake was associated with a positive coronary effect. In this review, the effects were significant at lower levels of intake in addition to LDL-C and apolipoprotein B.

3The mechanisms of the AHA Science Advisory and the FAME and FAME 2 studies are consistent with the observed effects of soy protein and soy isoflavones on blood lipids and cardiovascular disease risk factors. The effects of soy protein on blood lipids and blood pressure were significant in both studies. A meta-analysis showed that soy protein significantly reduced LDL-C and increased HDL-C levels, which are consistent with the findings of the FAME and FAME 2 studies. Additionally, soy protein intake was associated with a positive coronary effect. In this review, the effects were significant at lower levels of intake in addition to LDL-C and apolipoprotein B.
Soy products & Serum Lipids: A Meta-analysis of 50 Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Product or group</th>
<th>Subjects (n)</th>
<th>LDL</th>
<th>TG</th>
<th>HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cont. Soy</td>
<td>All1 1687</td>
<td>4.83</td>
<td>3.91</td>
<td>1.40</td>
</tr>
<tr>
<td></td>
<td>At risk2 32 studies</td>
<td>7.47</td>
<td>3.91</td>
<td>1.15</td>
</tr>
<tr>
<td>Healthy</td>
<td>18 studies</td>
<td>2.96</td>
<td>5.13</td>
<td>1.96</td>
</tr>
<tr>
<td>W. soy3</td>
<td>12 studies</td>
<td>11.06</td>
<td>1.03</td>
<td>1.06</td>
</tr>
</tbody>
</table>

Sub-analysis

LDL (-6.97%) & TG (-9.39%) ↓ more in non-casein/milk control trials (n=22)

**Percent Reduction in LDL-Cholesterol in 13 Hypercholesterolemic Men and Women Consuming the Portfolio Diet**

- Almonds
- Low saturated fat
- Soluble fiber
- Soyfoods
- Phytosterols
- Fruits/vegetables

**Result:** A dietary Portfolio approach to cholesterol reduction; Combined Effects of Plant Sterols, Vegetable Proteins, and Viscous Fibers in Hypercholesterolemia

**Abstract:**

Dietary and medical interventions are key to the management of hypercholesterolemia. The Portfolio Diet is a lifestyle intervention consisting of a low-fat, high-fiber, high-plant-based protein, and cholesterol-lowering foods. The present study investigated the effect of soy protein on blood pressure, a meta-analysis of randomized controlled trials.

**Effect of soy protein on blood pressure: a meta-analysis of randomized controlled trials**

Jia Xi Dong1, Xing Tong, Zhe Wei Wu, Peng-Cheng Nan1, Jie Mo1, and Li-Qiong Qiu1

1Department of Cardiology and Endocrinology, School of Medicine, University of South China

2Department of Cardiology, School of Medicine, University of South China

3Department of Cardiology and Endocrinology, School of Medicine, University of South China

### Effects of Soy on Blood Pressure: Meta-analysis of 27 Clinical Trials*

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>mmHg</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>-2.21</td>
<td>-4.10, -0.33</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-1.44</td>
<td>-2.56, -0.31</td>
</tr>
</tbody>
</table>

**Blinded trials (n=15)**

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>mmHg</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>-2.90</td>
<td>-5.49, -0.31</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-1.93</td>
<td>-3.53, -0.34</td>
</tr>
</tbody>
</table>

*Secondary endpoint in most trials


### Attributes of Soy Protein

- **High quality** (PDCAAS, 0.9-1.0)  
  Similar to animal protein
- **Lowers LDL-cholesterol** (4-5%)  
  Health claims in >10 countries
- **May lower blood pressure** (<2 mmHg)  
  All 4 meta-analysis show reductions
- **May favorably affect kidneys**  
  Possibly multiple benefits


### Soy-based renoprotection

Nancy J. McGinn, Elaine S. Tsoi, Elizabeth Grunz-Bergmann, Alan R. Parrish

Health problem as risk factors such as advanced age, diabetes, hypertension and obesity rise in the global population. Currently there are no effective pharmacologic treatments for this disease. The role of diet is a potential opportunity for slowing the progression of CKD and managing symptoms in later stages of renal insufficiency. Unlike high protein diets are generally recommended, maintaining adequate levels of protein is crucial for health. There is an increasing awareness of the beneficial effects of soy protein in subjects with kidney disease and has demonstrated renal protective properties in a number of clinical studies. Soy protein consumption has been shown to slow the decline in estimated glomerular filtration rate and significantly improve proteinuria in diabetic and non-diabetic patients with nephropathy. Soy’s beneficial effects on renal function may also result from its impact on certain physiological risk factors for CKD such as dyslipidemia, hypertension and hyperhomocysteinemia. Soy intake is also associated with improvements in arterial stiffness and inflammatory markers. Studies conducted in animal models have helped to identify the underlying molecular mechanisms that may

### Fatty Acid Composition of Soybean Oil

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Percent</th>
</tr>
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<tbody>
<tr>
<td>Saturated</td>
<td>12</td>
</tr>
<tr>
<td>Monounsaturated</td>
<td>29</td>
</tr>
<tr>
<td>Omega-6 PUFA (LA)*</td>
<td>53</td>
</tr>
<tr>
<td>Omega-3 PUFA (ALA)*</td>
<td>6</td>
</tr>
</tbody>
</table>

*Essential fatty acids: LA, linoleic acid; ALA, α-linolenic acid


### Contribution of Soybean Oil to US Caloric and Essential Fatty Acid Intake

- **7% of total calories**
- **43% of linoleic acid**
- **44% of α-linolenic acid**

**Am J Clin Nutr 93: 950-62, 2011**

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*Essential fatty acids: LA, linoleic acid; ALA, α-linolenic acid

... no evidence from randomized, controlled intervention studies ... that LA ... increases the concentration of inflammatory markers.

The Controversy over Dietary Fat & Coronary Heart Disease

Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease
A Prospective Cohort Study

Yingping Li, MD, PhD; Adela Holmes, PhD, MPH; Adam M. Riesenberg, MD, PhD; Sylvia H. Ley, PhD; Guoguo Wang, MD; John H. Chalmers, PhD; Laura Thompson, PhD; Kathleen M. Beresford, MD, MPH; Eric R. /et al

ABSTRACT

BACKGROUND: The associations between dietary saturated fats and the risk of coronary heart disease (CHD) remain controversial, but few studies have compared saturated with unsaturated fats and sources of carbohydrates in relation to CHD risk.

OBJECTIVES: This study sought to investigate associations of unsaturated fats compared with saturated fats and different sources of carbohydrates in relation to CHD risk.

METHODS: We followed 127,536 study participants who were followed for up to 30 years.

Based on 127,536 study participants who were followed for up to 30 years

Effects of Replacing 5% of Calories from Saturated Fat with 5% of Calories from:

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Coronary heart disease risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refined carbohydrates</td>
<td>↑2%</td>
</tr>
<tr>
<td>Carbohydrates, whole grains</td>
<td>↓9%</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>↓15%</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>↓25%</td>
</tr>
</tbody>
</table>

Based on 127,536 study participants who were followed for up to 30 years

Mean Daily Isoflavone Intake

<3 mg

Traditional soyfoods: 3-4 mg/g protein
One serving ~25 mg

>20,000 peer-reviewed publications
Soybean Isoflavone Aglycones

<table>
<thead>
<tr>
<th>Isoflavone</th>
<th>R₁</th>
<th>R₂</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genistein</td>
<td>H</td>
<td>OH</td>
<td>50</td>
</tr>
<tr>
<td>Daidzein</td>
<td>H</td>
<td>H</td>
<td>40</td>
</tr>
<tr>
<td>Glycitein</td>
<td>OCH₃</td>
<td>H</td>
<td>10</td>
</tr>
</tbody>
</table>

Phytoestrogens

Cholesterol (animal foods)

<table>
<thead>
<tr>
<th>Genistein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
</tr>
</tbody>
</table>

Phytosterols (plant foods)

Isoflavones

- Found primarily in soybeans
- Phytoestrogens but different from estrogen
- Sometimes effects opposite to estrogen
- Sometimes no effects in estrogen-sensitive tissues
- Estrogen-independent effects

Soyfoods and breast cancer prevention

Age-Adjusted Breast Cancer Incidence Rates (per 100,000) for Selected Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>19.1</td>
</tr>
<tr>
<td>Japan</td>
<td>19.7</td>
</tr>
<tr>
<td>India</td>
<td>20.8</td>
</tr>
<tr>
<td>Finland</td>
<td>44.7</td>
</tr>
<tr>
<td>Sweden</td>
<td>60.7</td>
</tr>
<tr>
<td>Basle</td>
<td>72.1</td>
</tr>
<tr>
<td>USA</td>
<td>87.0</td>
</tr>
</tbody>
</table>

Age-Adjusted Breast Cancer Incidence Rates (per 100,000) for Miyagi Prefecture, Japan, 1959-97

Westernization
Higher soy intake is associated with a one-third reduction in breast cancer risk

Support

- Rodent data
- Epidemiologic data
- Proposed mechanisms

Early Soy (Isoflavone)
Intake Decreases Breast Cancer Risk

Author/Y  Location  (N)  Risk %  Statistically Significant?
Shu, 2001  China  3,015  49  Yes
Wu, 2009  USA  345  28  Yes
Korode, 2009  USA  250  60  Yes
Baglia, 2016  China  36,297  44  Not quite

*Premenopausal only Ref.: Shu: CEBP;10:483, 2001; Wu: AJCN 89: 1145, 2009;
Korode: CEBP 18: 1050, 2009; Int J Cancer 139: 742, 2016 *(95% CI: 0.31, 1.00)

Young girls should be sure to eat ≥1 serving of soy per day

Can soyfoods be safely consumed by breast cancer patients?
Why the controversy?

SOY & BREAST CANCER

Menopausal Hormone Therapy for the Primary Prevention of Chronic Conditions: U.S. Preventive Services Task Force Recommendation Statement

Annie A. Mason, MD, MPH, on behalf of the U.S. Preventive Services Task Force

Objective: Update of the 2002 U.S. Preventive Services Task Force (USPSTF) recommendation statement on hormone therapy for the prevention of chronic conditions in postmenopausal women

Methods: The U.S. Preventive Services Task Force (USPSTF) reviewed evidence on the use of hormone therapy for the prevention of chronic conditions and adverse outcomes in postmenopausal women aged 50-79 years. The USPSTF recommends against the use of estrogen for the primary prevention of chronic conditions in postmenopausal women aged 50-79 years

... the use of estrogen alone results in a small reduction in the risk for developing or dying of invasive breast cancer.*

No clinical trials have evaluated the effects of soyfoods or isoflavones on breast cancer recurrence or mortality

Trials Involving Soy & Soy Components

- Breast cell proliferation (N=6*)
- Mammographic density (N=11*)
- Nipple aspirate fluid (N=3*)
- Hormone levels (N=50*)

No effects on markers of cancer risk

Oncology 2013;430:430-37

Estrogen* Use and Annual Breast Cancer Incidence in the WHI Trial

Conjugated equine estrogens (0.625 mg/d); mean age, 72.1 ± 10.1 years; placebo: 20.5 years. Events = invasive BCa. JAMA 310: 1353, 2013

P=0.02

Placebo (n=5,429)

Estrogen (n=5,310)
Combined Hormone Therapy (estrogen + progestin)

12 weeks

Increases breast cell proliferation 4 to 10-fold

Increases breast cancer risk

Fertility Sterility 91: 1593, 2011; Breast Cancer Res Tx 7: 159, 2003

Women with breast cancer can safely consume soyfoods

Isoflavones don’t adversely affect breast tissue in postmenopausal women

Risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones

Isoflavones are naturally occurring substances found in legume plants, which can be found in a variety of food sources, including soy products. Soy foods are typically high in isoflavones, which may affect hormone levels in menopausal women. The impact of isoflavones on breast cancer risk is a topic of ongoing research.

Post-diagnosis Soy Food Intake and Breast Cancer Survival: A Meta-analysis of Cohort Studies

Feng Chi, Hong Wu, Yue-Cun Zong, Bai Xing, Yang Liu, Zhao-Guo Xu

Abstract

Background and Objectives: Data on the association between soy food intake after cancer diagnosis and breast cancer survival are conflicting, so we conducted this meta-analysis for more accurate evidence. Methods: Comprehensive searches were conducted to find cohort studies of the relationship between soy food intake and breast cancer survival. Results: 5 studies (3 Chinese, 2 American) with 11,224 women with breast cancer were included. Follow up: 3.9 to 7.3 years. 948 breast cancer deaths and 1449 recurrences were observed. High versus low soy intake Hazard ratio 95% CI

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0.84</td>
<td>0.71, 0.99</td>
</tr>
<tr>
<td>Recurrence</td>
<td>0.74</td>
<td>0.64, 0.85</td>
</tr>
</tbody>
</table>

J Fam Pract 65: 660, 2015

CLINICAL INQUIRIES

Does high dietary soy intake affect a woman’s risk of primary or recurrent breast cancer?

... consuming a diet high in soy is associated with a 25% decrease in cancer recurrence and a 15% decrease in mortality...
**Soy and hot flashes**

**The Hot Flash Hypothesis**

Isoflavones can mitigate the drop in estrogen levels

Herman Adlercreutz, MD, PhD
University of Helsinki, Finland

1992

Lancet 339 (8803), 1233

Japan  | Canada | USA  | China
--- | --- | --- | ---
9.7% | 30.9% | 34.8% | 13.5%

**Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systematic review and meta-analysis of randomized controlled trials**

Kyoji Taka, PhD, MD1, McGuss K. Melwy, PhD2, Frank Kronenberg, PhD3, Mady S. Kassre, PhD4, and Mark Mervis, PhD3

Menopause 19: 776, 2012

**Only trials intervening with extracts derived from soybeans were eligible***

*1 trial used synthetic genistein

**Decrease in Hot Flash Frequency and Severity: Meta-analysis Results**

<table>
<thead>
<tr>
<th>Symptom (Studies/N)</th>
<th>Group</th>
<th>Percent Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (13/1196)</td>
<td>Placebo</td>
<td>29.6</td>
</tr>
<tr>
<td></td>
<td>Isoflavones</td>
<td>50.2</td>
</tr>
<tr>
<td></td>
<td>Net</td>
<td>20.61</td>
</tr>
<tr>
<td>Severity (9/988)</td>
<td>Placebo</td>
<td>21.4</td>
</tr>
<tr>
<td></td>
<td>Isoflavones</td>
<td>47.6</td>
</tr>
<tr>
<td></td>
<td>Net</td>
<td>26.22</td>
</tr>
</tbody>
</table>

*P < 0.00001  \( ^{2}P = 0.001 \)

**Comparative efficacy of nonhormonal drugs on menopausal hot flashes**

Lijin Li1, Qing Xu2, Juyi Wu3, Linhe Deng4, Ruizhi Zhao5, Qingzhou Zhang1


"The effectiveness of soy isoflavones was superior to sertraline, venlafaxine, paroxetine, gabapentin, and clonidine …"
Supplements Providing Sufficient Genistein Are More Potent

<table>
<thead>
<tr>
<th>mg/day</th>
<th>Number of trials</th>
<th>Net % decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤18.8</td>
<td>7</td>
<td>12.47</td>
</tr>
<tr>
<td>&gt;18.8</td>
<td>6</td>
<td>29.13</td>
</tr>
</tbody>
</table>

*Median, 18.8 mg *Beyond placebo effect \(^2\) P = 0.03 between groups (random effects model) Menopause 19: 774, 2012

The Role of Soy Foods in the Treatment of Menopausal Symptoms\(^1\)\(^2\)\(^3\)

Ahmad Khoo\(^1\) and Michelle, Giuffrida\(^2\)

\(^1\)Division of Internal Medicine, St. Louis University School of Medicine, St. Louis, MO, USA
\(^2\)Department of Endocrinology, Diabetes & Metabolism, St. Louis University School of Medicine, St. Louis, MO, USA

Abstract

A major finding of the Women’s Health Initiative revealed a major decline in the use of estrogen therapy. Consequently, menopausal women have been counseled to use foods as an alternative to estrogen therapy for the treatment of menopausal symptoms. This article provides an overview of the literature to evaluate the efficacy of soy foods in alleviating menopausal and vasomotor symptoms. The evidence of the efficacy of soy foods is improved when consumed in combination with hormone therapy. However, two servings of traditional soy foods per day may be needed to achieve beneficial effects. 3 Nutr 140: 2318S-2321S, 2010

Introduction

Low intake levels of soybeanssteen diets in menopausal women result in vasomotor symptoms, primarily on the night of sleep.

Menopause symptoms include hot flashes, night sweats, decreased libido, and osteopenia. Several studies have shown that soy foods can reduce menopausal symptoms. However, the mechanisms of action of soy foods in menopausal women are not well understood. In general, soy foods have beneficial effects on cardiovascular health, bone health, and hormone levels. Soy foods are also rich in antioxidants and phytosterols, which may reduce the risk of cancer and heart disease.

Menopause symptoms

Soy and bone health

Isoflavones and the Alleviation of Menopausal Hot Flashes

Isolavones Profile of Two Commonly Used Soy Supplements

<table>
<thead>
<tr>
<th>Soybeans Supplements Soygerm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genistein</td>
</tr>
</tbody>
</table>

Soybeans: Supplements: Soygerm

- **Genistein**: 75% of the total isoflavones
- **Daidzein**: 20% of the total isoflavones
- **Glycitein**: 5% of the total isoflavones

Soy and bone health

- **Soybeans**: Contains isoflavones, which have been shown to alleviate menopausal symptoms.
- **Soygerm**: Contains isoflavones, which have been shown to alleviate menopausal symptoms.

**Isoflavones and the Alleviation of Menopausal Hot Flashes**

- **Expected ↓**
- **50-65%**

- **(≥50 mg total isoflavones)**
- **(≥19 mg genistein)**

Approximately two servings of traditional soyfoods
• Inhibits bone loss
• Reduces fractures

Impact of equol-producing capacity and soy-isoflavone profiles of supplements on bone calcium retention in postmenopausal women: a randomized crossover trial

Department of Nutrition, Science, College of Health and Human Sciences, Department of Statistics, College of Science, and Nutrition Research Institute, University of Missouri, College of Health and Human Sciences, University of Missouri, Columbia, Missouri

Health effects of isoflavones misrepresented

The article by Hernandez-Ricupero, Leonardi-Bee, Mancino, et al. (Nutr J 14: 91, 2015) suggests that an isoflavone intervention may improve bone health. However, the study design was flawed, and the results were not statistically significant.

Feminization

A 60 year old man
360 mg isoflavones (3 liters soymilk/day)

Soy = Man Boobs

Soy Shaker

19 year old vegan man
360 mg isoflavones (12-20 servings/day)

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Clinical studies show no effects of soy protein or isoflavones on reproductive hormones in men: results of a meta-analysis

**No significant effects of soy protein or isoflavone intake on testosterone, sex hormone binding globulin, free testosterone or free androgen index ...**

Soy consumption and prostate cancer risk in men: a revisit of a meta-analysis

**Asian epidemiologic studies show soy intake is protective against prostate cancer**

Effects of Soy Protein and Soybean Isoflavones on Thyroid Function in Healthy Adults and Hypothyroid Patients: A Review of the Relevant Literature

**No effects of soy or isoflavones on thyroid function in people with normal-functioning thyroids**

Genistein Aglycone Does Not Affect Thyroid Function: Results from a Three-Year, Randomized, Double-Blind, Placebo-Controlled Trial

**No effect of isoflavones on thyroid function in postmenopausal women**
Isoflavones don’t adversely affect thyroid function in postmenopausal women

Soy and hypothyroid patients

Reduces absorption of minerals – calcium, iron, zinc, and magnesium

Phytate (phytic acid)

- Naturally occurring compound
- Found in whole grains & beans

Food and Levothyroxine Administration in Infants and Children

Not contraindicated for hypothyroid patients

Peanuts

Oxalate

Naturally-occurring plant chemical that reduces the absorption of minerals such as calcium

Conditions and drugs interfering with thyroxine absorption

Soy protein
- Calcium carbonate
- Fiber supplements
- Iron
- Protein pump inhibitors
- Bile acid sequestrants
- Certain herbs
- Etc.

Phytate (phytic acid)

- Naturally occurring compound
- Found in whole grains & beans

Factors Affecting Levothyroxine Absorption

- Soy protein
- Calcium carbonate
- Fiber supplements
- Iron
- Protein pump inhibitors
- Bile acid sequestrants
- Certain herbs
- Etc.

Soy protein is rich in isoflavones – naturally occurring substances which can be found in many other foods, such as lentils, tofu, and soy milk. They may affect the absorption of minerals, such as calcium, iron, zinc, and magnesium. Isoflavones are estrogenic, and some research suggests they may have a role in reducing the risk of certain cancers and heart disease. However, the evidence is mixed, and more research is needed.

Phytate (phytic acid) is a naturally occurring compound found in whole grains and beans. It can reduce the absorption of minerals such as calcium, iron, zinc, and magnesium.

Oxalate is a naturally occurring plant chemical that reduces the absorption of minerals such as calcium. It is found in foods like spinach, rhubarb, and quinoa.

Conditions and drugs that can interfere with thyroxine absorption include soy protein, calcium carbonate, fiber supplements, iron, protein pump inhibitors, bile acid sequestrants, certain herbs, and others.

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Oxalate is a naturally occurring plant chemical that reduces the absorption of minerals such as calcium. It is found in foods like spinach, rhubarb, and quinoa.
Calcium absorption:
- Fortified soymilk = cow’s milk
- Calcium set tofu = cow’s milk

Iron absorption:
- Greatly underestimated?
- Soy iron present as ferritin

Soybeans are high in phytate & oxalate, but

Habitual consumption of a high phytate diet can reduce the inhibitory effect of phytate on iron absorption

Population-based studies worldwide have observed secular trends towards earlier pubertal development

Change in Menarcheal Age (y)

<table>
<thead>
<tr>
<th>Country</th>
<th>Time period</th>
<th>Beginning</th>
<th>Ending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holland</td>
<td>1965 → 2009</td>
<td>13.4</td>
<td>12.6</td>
</tr>
<tr>
<td>Japan</td>
<td>1930 → 1985</td>
<td>13.8</td>
<td>12.6</td>
</tr>
<tr>
<td>Korea</td>
<td>1920 → 1985</td>
<td>16.9</td>
<td>13.8</td>
</tr>
<tr>
<td>UK</td>
<td>1910 → 1993</td>
<td>13.5</td>
<td>12.3</td>
</tr>
<tr>
<td>Spain</td>
<td>1925 → 1962</td>
<td>13.7</td>
<td>12.8</td>
</tr>
<tr>
<td>Canada</td>
<td>1933 → 1988</td>
<td>13.2</td>
<td>12.5</td>
</tr>
<tr>
<td>Brazil</td>
<td>(&lt;8 y education)</td>
<td>13.4</td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>1932 → 1977</td>
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</tr>
<tr>
<td></td>
<td>(&gt;8 y education)</td>
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Change in Menarcheal Age

Population-based studies worldwide have observed secular trends towards earlier pubertal development

Country Time period Beginning Ending
Holland 1965 → 2009 13.4 12.6
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Brazil (<8 y education) 13.4 11.7
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Soybeans are high in phytate & oxalate, but

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Does soy affect puberty?

Population-based studies worldwide have observed secular trends towards earlier pubertal development

Early puberty
Concern
Risk
Hypothesis
Childhood soy intake
Earlier pubertal development may be due to exposure to hormonally active chemicals in the environment

Is soy intake related to age at onset of menarche? A cross-sectional study among adolescents with a wide range of soy food consumption

- 327 Seventh-day Adventists, age 12-18
- High-soya-consuming population
- Mean intake, 12.9 servings/week
- 21% consumed >4 servings/day
- Mean age of menarche, 12.5 years
- Soy unrelated to age of menarche onset

Soy foods promote health

- Totality of the evidence
- Study type and quality

Soy Allergy Prevalence

- FDA survey of adults
  - 1 out of 2,500
  - Milk 40x > soy

- N=38,465 children
  - 1 out of 200
  - Milk/peanuts 4-5x > soy
  - 70% outgrow by age 10

Nutritional and Health Attributes of Soy

- Excellent safety profile
- High quality protein
  - Hypocholesterolemic, possibly hypotensive
- Healthy fatty acid profile
  - High in PUFA, both essential fats
- Uniquely-rich source of isoflavones
  - Early intake may prevent breast cancer
  - Reduces hot flashes • May increase BMD • May decrease prostate cancer risk