

# The SOY Connection

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## UPDATE AND PERSPECTIVE ON SOYBEAN ISOFLAVONES AND THE ALLEVIATION OF HOT FLASHES

By Mark Messina, Ph.D.

### Introduction

Much of the recent nutritional interest in soyfoods can be attributed to these foods being a unique, rich dietary source of isoflavones. The estrogen-like effects of isoflavones have led some to suggest soybean constituents might serve as alternatives to conventional menopausal hormone therapy. Not unexpectedly, therefore, there has been considerable investigation into the ability of isoflavones and isoflavone-rich soyfoods to alleviate menopause-related hot flashes. A hot flash produces a sudden sensation of warmth or even intense heat that spreads over various parts of the body, especially the chest, face, and head.

Estrogen use is known to effectively alleviate flashes,<sup>1,2</sup> however, the search for alternatives to estrogen has intensified following the results of the Women's Health Initiative (WHI), which showed the overall harmful effects of estrogen plus progestin outweighed the potential benefits.<sup>3,4</sup> In 1992, Adlercreutz et al.<sup>5</sup> were the first to suggest that the estrogen-like properties of isoflavones might account for the low incidence of hot flashes experienced by women in Japan. According to surveys conducted by Lock et al.<sup>6,7</sup> during the early 1990s, the percentage of women reporting hot flashes in Japan was only about one-third that of North American women. However, these kinds of comparisons between East and West don't provide insight into whether soyfood intake per se is a factor in this difference.

More meaningful data come from epidemiologic studies showing that among women in Japan, those who consume more soyfoods are less likely to report having hot flashes.<sup>8,9</sup> On the other hand, not all studies show this to be the case. The incidence of hot flashes is lower in Asian countries where soyfoods are consumed to a much more limited extent than in Japan.<sup>10,11</sup> Further, although the Study of Women's Health across the nation found the incidence of hot flashes was lower among Asian-American women (in comparison to white American women),<sup>12</sup> a recent study found that soy intake was not a factor in the lower incidence of hot

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## RESEARCH UPDATES

By Mark Messina, Ph.D.

### Soy Intake Early in Life

Not surprisingly, most clinical research involving soyfoods or soybean constituents such as isoflavones has been conducted on adults, and in particular, postmenopausal women. However, there is a need to understand the impact of soyfood/ isoflavone intake on the nutritional and

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## FOCUS ON // HOT FLASHES

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# RESEARCH UPDATES

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health status of children and to understand the role of traditional soyfoods in the diets of young Asians. Two recent studies provide some insight in this regard. One provides a very detailed look at the soy/isoflavone intake of young children in Korea. Many studies are available on the isoflavone intake of adult Asians, but few are available on the isoflavone intake of children. The other study, which has thus far only been presented, examines the relationship between soy intake during childhood and adolescence, and adult breast cancer risk among U.S. Asians.

## Korean Isoflavone Intake

Isoflavone intake results were derived from the daily food intake collected by the 1998 National Nutrition Survey. Intake was expressed on an absolute basis and per kilogram (kg) body-weight (bw) for different age groups, using the average weight for each group according to previously published data. As Figure 1 on page 5 shows, on a body-weight basis, soy (as assessed by isoflavone exposure) intake plays as big a role among children ages 1-12, as it does for adults. Peak soy intake occurred during the 30-49 year period, but on a body-weight basis that was only slightly higher than age 3-6 years. For comparison purposes, the maximal intake of 33.6 mg isoflavones is the amount found in about 1½ servings of traditional soyfoods. Note, there is a wide range of intake among any given age group and the mean intake is not necessarily ideal.

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# SOY AND HOT FLASHES

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flashes among American women of Japanese descent in comparison to European descent, living in Hawaii.<sup>13</sup> In any event, definitive conclusions about the ability of isoflavones to alleviate hot flashes can only be made on the basis of results from intervention trials.

## Clinical Trials

Since the first clinical trial was published in 1995, more than 40 others have examined the impact of soyfoods or isoflavone supplements derived from soybeans and red clover on hot flash frequency and/or severity. It is beyond the scope of this article to review the results of these trials in detail but it is quite clear from the many published reviews of the literature, and even a superficial examination of the relevant studies, that the data are quite mixed and inconsistent.<sup>2, 14-19</sup> This having been said, the data appear sufficiently suggestive to recommend that women at least try isoflavone supplements or soyfoods for relief. This sentiment is especially warranted since soyfood intake does not appear to be associated with any adverse health effects in generally healthy women, the efficacy can be personally determined, and any benefits should be apparent within 4 weeks. Women in the clinical trials have been generally exposed to between 50 and 100 mg isoflavones per day.

Given the number of trials already conducted, it is unlikely that further research of a general nature will allow a definitive conclusion about the efficacy of isoflavones for alleviating hot flashes to be reached. However, as discussed below, at least three explanations have been proposed for the inconsistent clinical data. These hypotheses warrant testing and provide a further basis for suggesting that at least some "soy" products in at least some women will result in a reduction of hot flash frequency and/or severity.

## Proposed Explanations for the Inconsistent Clinical Trial Results

In 2003, on the basis of a regression analysis that included 13 trials, Messina and Hughes<sup>16</sup> concluded that isoflavones are efficacious but only among women with very frequent (more than four or five per day) hot flashes. A recent meta-analysis by Howes *et al.*<sup>15</sup> also found efficacy to be related to initial hot flash frequency. Thus, at least some evidence suggests that women who experience very frequent hot flashes are more likely to benefit from isoflavones than those whose symptoms are more mild.

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Efficacy may also be determined by the specific manner in which isoflavones are metabolized, which varies greatly among individuals.<sup>20</sup> There is at least a theoretical basis for speculating that women with high serum isoflavone levels, in response to supplements or soyfoods, may be more likely to experience a reduction in hot flashes than those with lower serum levels. In addition, Setchell *et al.*<sup>21</sup> have argued that producers of equol, a large intestine bacterial-derived metabolite of the soybean isoflavone daidzein, are more likely to experience benefits from isoflavone and soyfood intake. Limited direct research indicating equol-producers are more likely to experience reductions in hot flashes is available at this time.<sup>22, 23</sup> Note that only approximately 30% of individuals make equol.<sup>21</sup> Although, evidence suggests this figure varies among populations and the percentage of equol-producers is higher among Japanese<sup>24-26</sup> and vegetarians.<sup>27</sup> Parenthetically, there is also anecdotal and very speculative evidence suggesting the percentage of equol producers in the United States is decreasing.

Finally, a new analysis of 11 trials involving isoflavone supplements has concluded that efficacy is dependent upon the genistein (primary isoflavone in soybeans) content of the supplement.<sup>28</sup> There are two common methods for producing isoflavone supplements; one leads to a product that contains an isoflavone profile (relative content: genistein>daidzein>>>glycitein) similar to that found in the soybean whereas the other produces a supplement that is high in daidzein and glycitein but very low in genistein. Williamson-Hughes *et al.*<sup>28</sup> found that of the six trials involving low-genistein supplements only one was efficacious whereas in all five trials involving the high-genistein supplements isoflavones were efficacious. Thus, supplements that list genistein as the first isoflavone may be more effective than those that are high in glycitein and low in genistein.

## SUMMARY AND CONCLUSIONS

The estrogen-like effects of isoflavones in combination with the low incidence of hot flashes among Japanese women prompted speculation that soyfoods may alleviate hot flashes. However, results from the more than 40 clinical trials involving isoflavones or soyfoods have produced inconsistent results. Nevertheless, the findings are sufficiently encouraging for health professionals to recommend that women at least try soy or isoflavone supplements for relief. Clinical trials have used between 50 and 100 mg isoflavones daily. One serving of a traditional soyfood provides approximately 25 mg isoflavones. Several explanations for the inconsistent clinical trial results have been proposed. Research aimed at determining the veracity of these explanations is warranted.

## ABOUT THE AUTHOR

Mark Messina, Ph.D. is the co-owner of Nutrition Matters, Inc., a nutrition consulting company, and is an adjunct associate professor at Loma Linda University. His research is primarily on the health benefits of soyfoods.

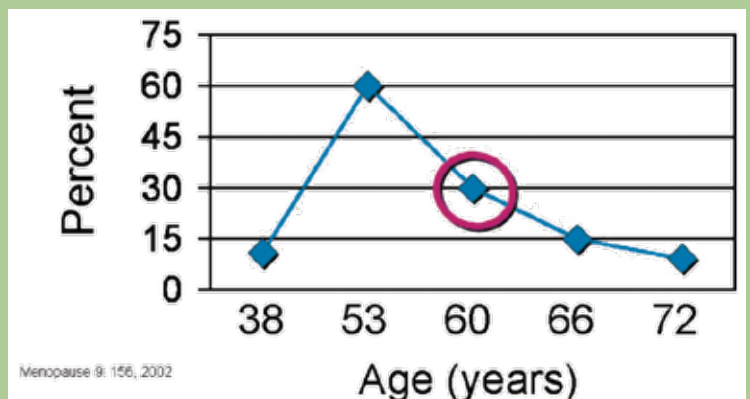
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Figure 2

## PREVALENCE OF HOT FLASHES AMONG SWEDISH WOMEN ACCORDING TO AGE





**F.Y.D.**  
From Your Dietitian

# MENOPAUSE, HOT FLASH TREATMENT OPTIONS

By Elisabeth Trimarchi, R.D. & Patricia Samour, R.D.

“Is it hot in here or is it me?” If you or someone you know is going through menopause, this question may be all too familiar. While menopause itself is a naturally occurring experience, many women choose alternatives to reduce potential symptoms such as hot flashes and night sweats.

Menopause is a period of physical change that most women go through between our 40s to late 50s. During this time, our body makes less estrogen and progesterone; ovulation, menstruation, and fertility gradually end. With these hormonal changes, a number of symptoms can occur such as hot flashes, night sweats, vaginal dryness and mood swings. A hot flash, or flush, is a feeling of warmth that spreads over the body and is often associated with perspiration.

Hot flashes are reported to be less common among Chinese women (10-25%) than western women (58-93%). Figure 2 on page 3 displays the prevalence of hot flashes in Swedish women between 38 to 72 years of age. Note that the incidence of hot flashes peaks at 60% of women at age 53, and reduces to 30% by age 60 but is still almost 15% by age 72 years. Hot flashes can occur once a month or as often as every 10 minutes. The magnitude, duration, and intensity of hot flashes vary considerably among women and severe hot flashes can significantly affect one's overall quality of life.

Estrogen has been used as a hormone replacement for over 60 years to treat menopausal symptoms and is still the most effective modality over all other non-hormone treatment options in reducing hot flashes. Results of the 2002 Women's Health Initiative study, revealed considerable side effects associated with the use of combined hormone therapy (0.625 mg conjugated estrogen and 2.5 mg medroxyprogesterone acetate) including an increased risk in breast cancer, stroke, and thromboembolism. Since then, the use of the lowest effective dose of steroids in Hormone Replacement Therapy (HRT) is recommended and many of these low dose preparations are available in oral, transdermal or percutaneous forms.<sup>3</sup> To find out which option is best suited to you, check with your physician.

Due to concerns of estrogen and its side effects, there is much interest in women seeking out alternative therapies. Women with breast cancer who cannot take estrogen are also seeking alternatives.<sup>1</sup> A summary of these alternative findings is listed below.

- Antidepressant medications including selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs) --paroxetine, venlafaxine, fluoxetine, citalopram-- veralipride, and moclobemide have been shown in clinical trials to reduce the number and severity of hot flashes. Additionally, studies using antihypertensive medications including clonidine and gabapentin have similar results.<sup>1</sup> Although these medications are less effective than estrogen in reducing hot flashes, they may be worth considering as a treatment option. Unfortunately, adverse side effects and cost may prohibit use by some women.
- Clinical trials using soy and isoflavones have shown mixed results in reducing hot flashes. However, the data are certainly sufficiently suggestive to justify women trying soyfoods and isoflavone supplements for relief. These products may be especially beneficial in women who experience very frequent hot flashes. Efficacy may also be determined by isoflavone metabolism which varies markedly among individuals. Also, products that are especially high in genistein, a type of isoflavone, may be most effective.
- Recent studies on oral supplements containing trifolium pretense (red clover) isoflavones, may offer another alternative for treating hot flashes. Although the evidence is marginally significant, the long term effects are unknown.<sup>4</sup>
- Other alternative products that have not been shown to reduce hot flashes in clinical studies include

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By Elizabeth Trimarchi, R.D.

A healthy, portable snack that includes soy protein, fiber and is rich in antioxidants.

**Yield:** 4 servings of about ¼ cup each

**Ingredients:**

- ¼ cup Roasted soynuts
- ¼ cup Dry roasted almonds
- ¼ cup Dried cranberries
- ¼ cup Dried blueberries
- 2 Tbsp. Dark chocolate chips

**Preparation:** Mix all ingredients together and separate into 4 servings.

**Nutritional Analysis:**

¼ cup serving Calories 190; Total Fat 7.5 g; Saturated Fat 1.5 g; Carbohydrates 24 g; Dietary Fiber 3 g; Sodium 13 mg; Total Protein 4 g; Soy Protein 2 g. 🍌

# MENOPAUSE, HOT FLASH OPTIONS

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vitamin E, dong quai, ginseng root, evening primrose oil, and wild yam. Black cohosh may be effective but it has some mild adverse effects and has not been studied more than 6 months duration.<sup>2</sup>

In treating your hot flashes, discuss your treatment options, their side effects and your overall health status with your physician.

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## Breast Cancer

The possibility that early soy intake reduces breast cancer incidence later in life is arguably one of the most exciting hypotheses in the entire diet-cancer field. The first animal study in support of this hypothesis was published in 1995 and the first epidemiologic study in 2001. A recent epidemiologic study presented at the American Association for Cancer Research meeting in Washington, DC, late last year provides additional support as well as new insight into the critical period of exposure to soy for protection against breast cancer to occur. This study involved 99 cases and 156 controls. The women were interviewed about their soy intake during childhood (5 – 11 years of age) and adolescence (12 – 19 years of age). Women who were in the third tertile for soy intake during these two periods of life were 58% and 23%, respectively, less likely to have developed breast cancer during adulthood as were women in the first intake tertile. One proposed mechanism for the observed protection against breast cancer is that the isoflavones in soy stimulate differentiation of breast cells making them permanently more resistant to becoming cancer cells.

Am Assoc Cancer Res Annual Meeting (abstract - 06-AB-667-AACRCPR) 2006. 🍌

Age (years)	Intake (mg)	Intake(mg)/kg bw
1-2	14.5	1.0
3-6	8.9	0.5
7-12	12.4	0.4
13-19	10.1	0.2
20-29	21.0	0.4
30-49	33.6	0.6
50-64	26.4	0.4
≥65	18.8	0.3

Figure 1

Int J Food Sci Nutr 2006;57(5):325-44.

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## STEARIC ACID: DOES IT RAISE BLOOD CHOLESTEROL LIKE A SATURATED FAT?

By Brent Flickinger, Ph.D.

Partially hydrogenated vegetable oils, the primary source of trans fatty acids, provide a stable medium for frying applications and a solid, functional fat for spread and baking applications. The reformulation of food products to remove trans fatty acids is a major issue facing food and restaurant industries. Reformulation of spread and baking applications has been more challenging due to the need for specific physical/functional properties in a fat which is imparted by saturated and/or trans fatty acids. As a result, interest has been refocused on saturated fatty acids.

Saturated fat in the U.S. food supply is primarily composed of three saturated fatty acids: myristic, palmitic and stearic acids. From a structural standpoint, these fatty acids differ only in their size (a.k.a. fatty acid chain length). This structural difference can play a role in the functionality of a solid fat. Major sources of these fatty acids are animal fats, tropical fats/oils and fully hydrogenated vegetable oils. Animal fats predominantly contain palmitic and stearic acids; tropical fats/oils predominantly contain

palmitic, myristic, lauric or stearic acids (depending on the plant source); and fully hydrogenated vegetable oils contain predominantly stearic and palmitic acids.

Governmental agencies and non-governmental organizations have evaluated data on the serum cholesterol effects of these fatty acids. Consistently, myristic and palmitic are viewed to raise serum cholesterol levels while stearic is viewed as being neutral on serum cholesterol levels.<sup>1,3</sup> Stearic acid has been observed in some, but not all studies, to increase a specific factor related to blood clotting at intake levels very much greater than its level in the typical U.S. diet.<sup>4,9</sup> In the current context of replacing trans fatty acids, stearic acid has received attention both for its impact on serum cholesterol neutrality and blood clotting. The blood clotting issue has been commented upon by the 2005 U.S. Dietary Guidelines Advisory Committee. Based on their review of the scientific data, their report states "Thus, at intakes of stearic acid that are equal to or slightly higher than amounts consumed in the United States, no adverse effects on fibrinogen levels would be expected."<sup>10</sup>

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