

Soy and health: the latest evidence

LUIS VITETTA PhD, GradDipIntegrMed, GradDipNutrEnvironMed

AVNI SALI MB BS, PhD, FRACS, FACS, FACNEM

SAMANTHA COULSON BHSc, AdvDipNutr, AdvDipHerbalMed

The research evidence pertaining to the health effects of soybeans is subject to contentious interpretation. Nevertheless, clinical studies demonstrate that regular (daily) soybean consumption can be beneficial.

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Associate Professor Vitetta is Director of the Centre for Integrative Clinical and Molecular Medicine at the School of Medicine, The University of Queensland, Brisbane, Qld.

Professor Sali is Director of the National Institute of Integrative Medicine, Melbourne, and President of the Australasian Integrative Medicine Association, Melbourne, Vic.

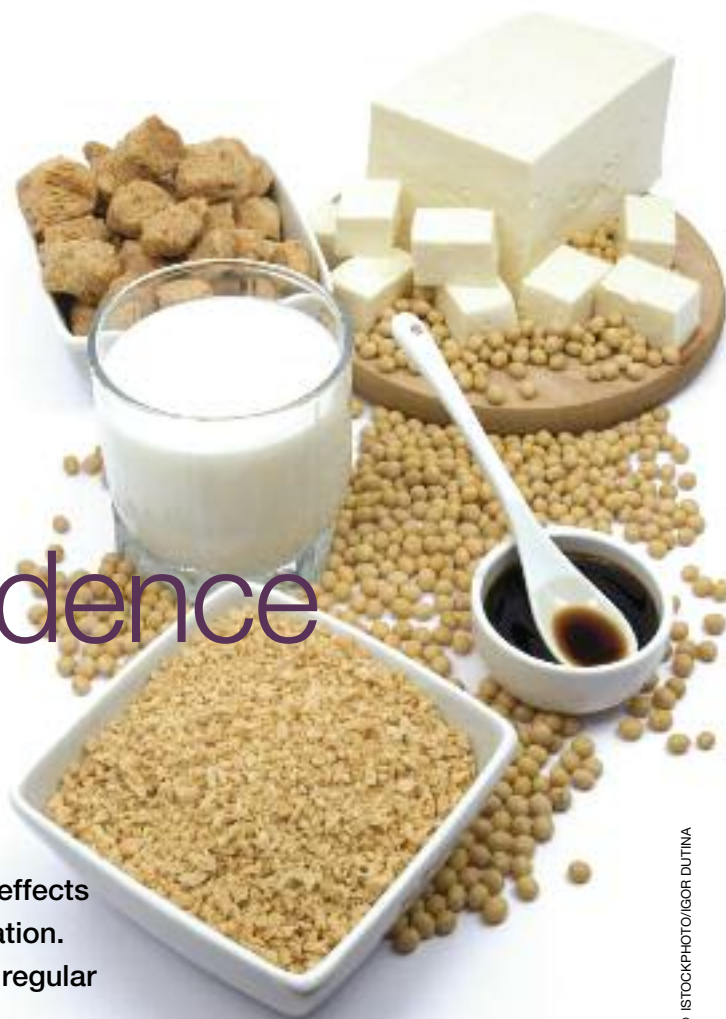
Ms Coulson is a PhD Scholar at the Centre for Integrative Clinical and Molecular Medicine at the School of Medicine, The University of Queensland, Brisbane, Qld.

The soybean (*Glycine max*) has a long history as a domesticated plant, with records of its use as far back as the eleventh century BC in China. Missionaries carried it into Korea and Japan in the third and fourth centuries AD.¹⁻⁴ The soybean is a member of the *Leguminosae* family of plants that form root nodules while harbouring nitrogen-fixing soil bacteria in a symbiotic association.

Soybeans are very rich in nutritive components. They have a high protein content and appreciable amounts of fibre, calcium, magnesium, phosphorus and potassium. They also contain isoflavones, compounds that have oestrogen-like structures (phytoestrogens).^{4,5} The dominant isoflavone in soy is genistein;

daidzein and glycitein are others that are present. Other bioactive components of soybeans include saponins, protease inhibitors and phytic acids. According to the US Department of Agriculture's National Nutrient Database for Standard Reference, soybean-based foods contain variable amounts of the nutritive components of the beans, including isoflavones.

Over the past three decades, scientific research has provided significant epidemiological and nutrition-based evidence for health benefits associated with soybean-based foods. Early epidemiological studies conducted in Asian populations that report a high intake of soybeans and soy products have demonstrated a lower incidence of



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NHMRC LEVELS OF EVIDENCE

Level I

Evidence from a systematic review of all relevant randomised controlled trials and meta-analyses.

Level II

Evidence from at least one properly designed randomised controlled clinical trial.

Level IIIa

Evidence from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

Level IIIb

Evidence from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies or interrupted time series with a parallel control group.

Level IIIc

Evidence from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.

Level IV

Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees.

Level V

Minimal evidence that represents testimonials.

TABLE 1. SOY AND BONE HEALTH: EVIDENCE FROM RECENT CLINICAL STUDIES¹¹⁻²³

Exposure	Clinical outcomes	NHMRC evidence level*
Soy isoflavones (aglycone form) ¹¹	Increase in lumbar spine BMD but no effects in femoral neck, hip total and trochanter BMD in menopausal women (Asian and Caucasian)	I
Soy isoflavones ¹²	Favourable effect on BMD unlikely at the lumbar spine and hip in postmenopausal women (Asian and Caucasian)	-I
Soy isoflavones ¹³	Attenuated bone loss of the spine in menopausal women (Asian and Caucasian)	I
Soy isoflavones ¹⁴	No BMD sparing effect for spine, femur, femoral neck or whole-body in non-osteoporotic postmenopausal women	-II
Soy isoflavones (aglycone form) ¹⁵	No effect in slowing bone loss at regional bone sites or in favourably altering biochemical markers of bone turnover in postmenopausal women	-II
Isoflavone-enriched foods ¹⁶	No prevention of postmenopausal bone loss and no effect on bone turnover in apparently healthy early postmenopausal Caucasian women	-II
Soy protein and isoflavones ¹⁷	No effect for soy protein and/or isoflavones (used alone or together) on BMD or markers of bone turnover in postmenopausal women	-II
Soy protein and isoflavones ¹⁸	No beneficial effect on BMD of the lumbar spine, femoral neck and total femur in postmenopausal women	-II
Soy isoflavones ¹⁹	Mild independent effect on the maintenance of hip bone mineral content in postmenopausal Asian women with low initial bone mass	II
Soy isoflavones ²⁰	Protective effect on BMD in postmenopausal Asian women	II
Natto (fermented soybeans) ²¹	Possible help in preventing postmenopausal bone loss through the effects of menaquinone 7 or bioavailable isoflavones, which are more abundant in natto than in other soybean products	IIIb
Soy protein ²²	Association (dose-response) with trochanteric, intertrochanteric and total hip BMD, as well as with total body bone mineral content in postmenopausal Asian women (>4 years after menopause)	IIIb
Soy isoflavones (dietary) ²³	Association between high intake and higher BMD values at both the spine and hip region in postmenopausal Asian women	IIIb

* In this article, a negative sign is used to indicate studies in which no association was found between exposure and outcome.

ABBREVIATION: BMD = bone mineral density.

cardiovascular disease, hormone-dependent cancers of the breast and prostate, colon cancer, menopausal symptoms and osteoporosis.⁶⁻¹⁰ These effects have been extensively appraised in subsequent reviews. However, some of the scientific evidence remains contentious.^{4,5}

It is beyond the scope of this review to assess the entire scientific literature pertaining to the effects of soybeans on health and chronic disease. We have endeavoured to assess the most recent clinical studies and score these according to NHMRC criteria (see the box on page 68). A MEDLINE search was performed to identify English language clinical studies on the association between soybean consumption (dietary or supplementary) and human health, published in the last decade. A total of

40 articles met the inclusion criteria. Relevant data are summarised in the Tables.

BONE HEALTH

A number of recent clinical studies have investigated the effect of soybean consumption on bone health (Table 1).¹¹⁻²³ The data remain largely contentious, which may be due to differences in the soy products under study, dosing and duration, and study population groups. However, the data appear robust enough to recommend that consumption of soybean or soybean-based foods containing at least 90 mg isoflavones per day can significantly increase bone mineral content and bone mineral density (BMD) of the lumbar spine, but not of other bone sites.

MENOPAUSAL SYMPTOMS

Descriptive epidemiological studies have reported that the incidence of hot flushes is far lower for menopausal women in Asian countries than for those in Western countries. Early studies have reported the prevalence of hot flushes to be between 70 and 80% for women in the USA and Europe, compared with only 10 to 20% for women in Japan, Singapore and China.²⁴

Various preparations of phytoestrogens are marketed as effective in the treatment of menopausal symptoms, and these have become popular alternatives to conventional oestrogen products. A number of efficacy-related clinical studies and meta-analyses have been conducted (Table 2).²⁵⁻³³ Several of these studies have provided moderate evidence that

TABLE 2. SOY AND MENOPAUSAL SYMPTOMS: EVIDENCE FROM RECENT CLINICAL STUDIES²⁵⁻³³

Exposure	Clinical outcomes	NHMRC evidence level*
Isoflavones (from soy and red clover) ²⁵	Inconclusive: some indication of a benefit of soy isoflavones on hot flush frequency or severity	I
Soy isoflavones ²⁶	Benefit on menopausal symptoms for overall combined results and subgroup results, but definitive conclusions contentious given the high heterogeneity of the studies	I
Isoflavones (from soy and red clover) ²⁷	No reduction in frequency of hot flushes for red clover isoflavone extracts Mixed results for soy isoflavone extracts	-I
Phytoestrogens (from soy and red clover) ²⁸	No improvement in hot flushes or other menopausal symptoms	-I
Genistein (a soy isoflavone) ²⁹	Effective management for hot flushes in postmenopausal women not treated with HT	II
Genistein (a soy isoflavone, aglycone form) ³⁰	Effective management for vasomotor symptoms – reduced number and severity of hot flushes and night sweats in postmenopausal Caucasian women	II
Soy isoflavone (supplement) ³¹	Alleviation of vasomotor symptoms, such as hot flushes, without increase in endometrial thickness in postmenopausal South American women Decrease in LDL-cholesterol levels	II
Daidzein-rich isoflavone supplement (aglycone form) ³²	Improvement in hot flushes composite score of 54% in postmenopausal women	IIIb
Soy and isoflavones (dietary) ³³	Protective effect against hot flushes	IIIc

* In this article, a negative sign is used to indicate studies in which no association was found between exposure and outcome.

ABBREVIATION: HT = hormonal therapy.

isoflavone supplementation is effective in alleviating vasomotor symptoms such as hot flushes, and the authors of one study concluded that a daidzein-rich isoflavone supplement may be an effective and acceptable alternative to hormonal therapy.³²

However, the current overall evidence remains very much contentious. The consumption of soybeans may materialise as a secondary benefit that is due to lifestyle modifications. Lifestyle changes have been associated with modifications

in dietary patterns associated with lifestyle and dietary changes, such as decreased consumption of hydrogenated trans fats and saturated fats together with a concomitant increase in phytoestrogen-rich plant foods.³⁴

TABLE 3. SOY AND CANCER PREVENTION AND MANAGEMENT: EVIDENCE FROM RECENT CLINICAL STUDIES³⁵⁻⁴⁴

Exposure	Clinical outcomes	NHMRC evidence level
Soy foods ³⁵	Dose-dependent association between soy food intake and reduced breast cancer risk (approximately 16% risk reduction per 10 mg of isoflavones intake/day) in Asian populations (relatively high levels of consumption) No relation between soy intake and breast cancer risk in studies conducted in Western populations (relatively low levels of consumption)	I
Soy foods ³⁶	In overall analysis, no association with colorectal cancer risk Reduced risk of colorectal cancer for women but not men (Asian and Caucasian) Reduced risk of colorectal cancer for soy foods/products and miso consumption but not for tofu	I
Soy foods ³⁷	Decreased risk of prostate cancer associated with high consumption of nonfermented soy foods (benefit attributed to tofu) but not with fermented soy foods	I
Soy foods ³⁸	Protective effects against risk for endocrine-related gynaecological cancers (endometrial and ovarian)	I
Soy protein and isoflavones (dietary) ³⁹	Small reduction in breast cancer risk; inverse association between soy exposure and breast cancer risk stronger in premenopausal women than in postmenopausal women (Asian and Caucasian)	I
Soy foods ⁴⁰	Inverse dose-response relation between intake and risk of endometrial cancer in Asian women	IIIb
Isoflavones ⁴¹	Association between increased intake and decreased risk of lung cancer in Asian men and women who have never smoked	IIIb
Soy protein and isoflavones (dietary) ⁴²	Inverse association between intake of soy products/isoflavones and breast cancer risk in Asian women, most evident among premenopausal women and women with BMI ≤ 25 kg/m ²	IIIb
Miso soup and soy isoflavones ⁴³	Consumption of miso soup and isoflavones, but not any soy foods, associated with a reduced risk of breast cancer in premenopausal and postmenopausal Japanese women Women with highest isoflavone intake (as genistein 25.3 mg/day) or highest consumption of miso soup (≥ 3 bowls/day) had approximately 50% reduced risk of breast cancer compared with women with the lowest isoflavone intake (as genistein 6.9 mg/day) or those with the lowest consumption of miso soup (< 1 bowl/day)	IIIc
Soy foods ⁴⁴	In premenopausal and postmenopausal Asian women with breast cancer, reduced risk of death and cancer recurrence	IIIc

ABBREVIATION: BMI = body mass index.

CANCER PREVENTION AND MANAGEMENT

A number of studies with moderate or high levels of evidence from Asian locations have reported on the beneficial effects of soybean consumption in the prevention of cancers from various sites; these are described in Table 3.³⁵⁻⁴⁴ These include cancers of the breast, prostate, large bowel, lung, endometrium and ovaries.

CARDIOVASCULAR HEALTH

As shown in Table 4, findings from recent studies suggest that consumption of soybeans can significantly improve cardiovascular health.⁴⁵⁻⁵² Specifically, it has been reported that soy protein can be used to replace foods high in saturated fats and trans fats. A meta-analysis of 41 randomised controlled trials (RCTs) concluded that soy protein supplementation leads

to small reductions in total cholesterol and LDL-cholesterol levels of approximately 0.13 mmol/L and 0.10 mmol/L, respectively; further, small increases in HDL-cholesterol levels (0.02 mmol/L) were also achieved.⁴⁶ The amounts of soy protein investigated in the studies covered in the meta-analysis ranged from 28 to 42 g/day, and the reviewers recommended an intake of 22.5 g soy protein (e.g. soy milk, soy meat analogues) per 1000 kcal consumed.⁴⁶

DISCUSSION

Intake of specific phytochemicals or their precursors does not necessarily equate with their exposure at the tissue level. Phytochemical pharmacodynamics, like that of pharmaceutical drugs and other xenobiotics, involves absorption, metabolism, distribution, and excretion, and each of these processes may contribute to

overall exposure and the effects displayed.⁵³

It is interesting to note that native Asian women and men have the lowest rates of breast cancer⁵⁴ and prostate cancer,⁵⁵ respectively. Migration to Western countries and adoption of a Western diet increase the incidences of these cancers among migrant Asians to levels similar to those seen in Western populations.⁵⁶ Similarly, a cross-sectional study in Japan has demonstrated an inverse association between soybean consumption and serum total cholesterol concentration,⁵⁷ but an increase in the incidence of cardiovascular disease is reported for migrant Japanese.⁵⁸ For these reasons, dietary factors – and particularly the consumption of soybeans and its constituent isoflavones – have been implicated as affording some protection against these hormone dependent cancers and cardiovascular disease.

TABLE 4. SOY AND CARDIOVASCULAR HEALTH: EVIDENCE FROM RECENT CLINICAL STUDIES⁴⁶⁻⁵²		
Exposure	Clinical outcomes	NHMRC evidence level
Soy protein ⁴⁵	Decrease in total cholesterol, LDL-cholesterol and triglycerides associated with consumption of soy protein rather than animal protein (men and women)	I
Soy protein (supplement) ⁴⁶	Reduced total cholesterol and LDL-cholesterol and increased HDL-cholesterol	I
Soy protein ⁴⁷	Soy protein (containing isoflavones) associated with decreased total cholesterol, LDL-cholesterol and triglycerides, and increased HDL-cholesterol Changes related to level and duration of intake, gender and initial serum lipids Effects more pronounced in men than in women; in subjects with hypercholesterolaemia than in those with normal cholesterol levels; in pre- and perimenopausal women than in postmenopausal women; with low-fat and low-cholesterol diets; and with a daily consumption of ≥80 mg isoflavones (contained in soy protein)	I
Soy protein isolate ⁴⁸	Modulation of serum lipid ratios in a direction beneficial for cardiovascular disease risk in healthy young men Lower total HDL-cholesterol, ratio of LDL-cholesterol to HDL-cholesterol and ratio of apoB to apoA-I with consumption of soy protein isolate, irrespective of isoflavone content, than with milk protein isolate	II
Soy isoflavones ⁴⁹	Improvement in lipid profile across the menstrual cycle in normocholesterolaemic premenopausal women Changes in total cholesterol, HDL-cholesterol and LDL-cholesterol across menstrual cycle phases During specific phases of the cycle, the high-isoflavone diet lowered LDL-cholesterol by 7.6 to 10.0%, the ratio of total cholesterol to HDL-cholesterol by 10.2%, and the ratio of LDL-cholesterol to HDL-cholesterol by 13.8%	II
Isoflavones (as constituent of isolated soy protein) ⁵⁰	Improvement in the lipid profile of normocholesterolaemic and mildly hypercholesterolaemic postmenopausal women, with reduction in LDL-cholesterol and the LDL-cholesterol to HDL-cholesterol ratio No effect on total cholesterol, HDL-cholesterol, triglycerides, apo A-I, apoB, lipoprotein(a) or LDL peak particle diameter	II
Soy protein isolate ⁵¹	Decrease in LDL-cholesterol and ratios of LDL-cholesterol to HDL-cholesterol and ratio of apoB to apoA-I compared with milk protein isolate in patients with type 2 diabetes	IIIa
Soy protein ⁵²	Beneficial effects for fasting plasma glucose, total cholesterol, LDL-cholesterol, triglycerides, CRP and kidney-related indexes (proteinuria and urinary creatinine) in patients with type 2 diabetes with nephropathy	IIIa
ABBREVIATIONS: Apo = apolipoprotein, HDL = high-density lipoprotein, LDL = low-density lipoprotein.		

Interindividual differences in phytochemical metabolic activity in the gut may be influenced by many factors. These include:

- the microbial environment
- genetic determinants of biotransformation enzyme expressions, stability and activity
- environmental exposures that influence gut micro-organisms and biotransformation enzymes
- variation in concentrations of endogenous compounds that modulate biotransformation pathways.⁵⁹

It is possible that soybean efficacy in the prevention of diseases such as breast and prostate cancers and the decreased risk for cardiovascular disease may be highly dependent on a symbiotic relationship with the gut microflora. Bacteria and fungi play a significant role in the fermentation of soybean products. The traditional fermentation products (which are also known as functional foods) consumed by the Japanese include black rice vinegar, soy sauce (shoyu), miso, natto and tempeh. South-east Asian populations consume an average of 20 to 80 g of traditional soy foods daily, the most common of which are tofu, miso and tempeh. In comparison, Westerners consume much less soy, only about 1 to 3 g daily, and this is predominantly in the form of processed soy drinks, breakfast cereals, energy bars and soy burgers.⁶⁰ Fermented soybeans that can be chemically modified further by the gut flora may provide a significant health advantage in the form of soybean secondary and/or tertiary metabolites that are beneficial to human health.

SUMMARY

- The research evidence pertaining to the health effects of soybeans is subject to contentious interpretation, given the heterogeneity of clinical studies. Nevertheless, clinical studies demonstrate that regular (daily) soybean consumption can be beneficial to health.
- Health improvements as a result of soybean consumption have been documented for BMD of the lumbar spine, menopausal symptoms, blood lipids and blood pressure. Soybean consumption also has been shown to prevent some cancers (gynaecological, breast, prostate, large bowel and lung).
- If a healthy gut flora is established then the regular consumption of fermented soybeans can have beneficial effects.

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A list of references is available on request to the editorial office.

COMPETING INTERESTS: None.

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LUIS VITETTA PhD, GradDipIntegrMed, GradDipNutrEnvironMed **AVNI SALI** MB BS, PhD, FRACS, FACS, FACNEM
SAMANTHA COULSON BHSc, AdvDipNutr, AdvDipHerbalMed

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