SoyConnection

Health & Nutrition News About Soy

Brought to you by the United Soybean Board and the Soy Nutrition Institute

SUMMER 2017 | VOLUME 25, NUMBER 3

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The *Soy Connection,* funded by farmer checkoff dollars, is produced by the United Soybean Board and the Soy Nutrition Institute. An electronic version of this newsletter can be found at www.soyconnection.com/newsletters.

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FACTS VS. MYTHS—PART TWO

By Mark Messina, PhD, MS

Editor's Note:
This article is "Part Two" in The Soy Connection *newsletter series on the topic of soy "Facts vs. Myths." The series has been produced to help clear up confusion about the health attributes of soyfoods. The first installment of our series (Volume 25, No. 1) looked at fertility, breast cancer, and so-called "male feminization." The article in this issue reviews research on mineral status, development and cognitive function. In each case, for those who are busy, we first provide the overall conclusion, or "takeaway" message, followed by evidence underlying the concern, and then a summary of the evidence refuting the concern.*

Mineral Status

Takeaway

Despite being high phytate and oxalate, two compounds that inhibit mineral absorption—the absorption of calcium (and likely also iron) from soyfoods is only modestly inhibited as a result. Incorporating soyfoods into a healthy diet does not impair mineral status.

Evidence raising concern

The mineral status of those consuming plant-based diets can be compromised as a result of inadequate intake and/or reduced bioavailability.[1-3] Soybeans and soyfoods are high in compounds such as phytate[4] and oxalate[5] and possibly other components,[6] which can inhibit the absorption of divalent cations such as iron, zinc, and calcium. Vegetarians have lower iron stores because they consume high-phytate diets and do not consume heme iron.[1]

Evidence refuting concern

Soyfoods often replace animal foods in the diet so the primary concern with respect to mineral nutriture is their impact on calcium, zinc and iron status. Since relatively little meat is needed to satisfy iron and zinc requirements, the impact of soy is most relevant to vegetarians.[7] Vegan and mostly plant-based diets are typically a bit higher in iron, but a bit lower in zinc, and often much lower in calcium than typical Western diets.[8,9]

Soyfoods are high in phytate which inhibits mineral absorption to varying degrees. Heaney et al.[10] showed fractional calcium absorption from high-phytate soybeans was lower (0.310 vs 0.377) than from low-phytate soybeans, but was still remarkably good when compared with calcium absorption from cow's milk (0.414). More importantly, even though soybeans are also high in oxalate, a potent inhibitor of calcium absorption, calcium absorption from calcium-fortified soymilk[11] and calcium-set tofu[12] is similar to the absorption of calcium from cow's milk.

Acute studies show that both soy protein and phytate inhibit the absorption of iron from soy.[13] Polyphenols, which are found throughout the plant kingdom, may also have a similar effect.[6] However, methodological limitations may have underestimated the actual amount of iron absorbed from soy and possibly other plant foods because much of the iron in soy is in the form of ferritin.[18,19] Ferritin appears to be a form of iron insensitive to the effects of dietary compounds that inhibit non-heme iron absorption.

Furthermore, in contrast to prior understanding,[14] recent research shows that in response to the chronic consumption of a high-phytate diet, the effect of phytate on mineral absorption is greatly mitigated.[15] Therefore, acute studies almost certainly underestimate iron bioavailability from soy. Iron stores of vegetarians are lower than that of non-vegetarians (irrespective of their soy intake) but they are still within the normal range.[1]

Finally, soyfoods are not particularly good sources of zinc[16] and although estimates vary, zinc absorption from soyfoods is approximately 25% lower than from sources of animal protein.[17] Because it is difficult to assess zinc status,[18] it is often recommended that those consuming plant-based diets take a zinc supplement and/or incorporate zinc-fortified foods into their diet.

Development

Takeaway

Clinical research shows neither soyfood nor isoflavone exposure affect reproductive hormone levels in children, although the data are very limited. A cross-sectional study of U.S. girls shows high soyfood intake does not affect the onset of age of menarche. More research on the effect of soy on development is warranted.

Evidence raising concern

For the past four decades, the age at which puberty occurs among girls—manifested as breast development, appearance of pubic hair, and onset of menarche—has been commencing earlier.[19] Corresponding trends have also occurred in boys although probably to a lesser extent. There has also been a rise in the prevalence of precocious puberty (PP), which is defined as the development of pubertal changes, at an age younger than the accepted lower limits for age of onset of puberty, namely, before age 8 years in girls and 9 years in boys.[20] According to some experts, the advancement of development has resulted at least in part to exposure to hormonally active environmental agents including dietary constituents.[21] Two small Korean case-control studies found that urinary isoflavones in girls with precocious puberty were higher than in children serving as controls.[22,23]

Evidence refuting concern

Concerns about the impact of soy on development are focused on the potential hormonal effects of isoflavones.[24] The impact of soy infant formula (SIF) has received most attention in this regard.[25-27] SIF is not discussed here so the reader is referred to the references,[28-32] although it is important to point out that after an extensive review, the U.S. National Toxicology Program concluded there was minimal concern about the adverse developmental effects of SIF, although they also acknowledged the need for more research.[28]

In adults, isoflavone intake even when greatly exceeding typical Japanese intake, does not affect testosterone levels in men,[33] or estrogen levels in men[34] or women.[35] Limited clinical research has been conducted in children, but two very small studies found neither soyfood intake nor isoflavone exposure affected reproductive hormone levels in boys or girls.[36,37] Indirectly, intriguing research indicating that soy consumption during adolescence reduces later risk of developing breast cancer argues against soy causing puberty to occur earlier in life because early puberty is associated with an increased risk of this disease.[38,39]

In contrast to the two aforementioned Korean studies,[22,23] a prospective study involving 1,239 U.S. girls aged 6–8 who were followed for seven years, found no relationship between pubertal development and urinary isoflavone excretion.[40] Another U.S. study found isoflavone exposure was associated with delayed breast development, although this cross-sectional study was quite small in size.[41] Nevertheless, this finding agrees with the results of a German longitudinal

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study.[42] Finally, in a British study, gestational urinary levels of genistein and daidzein, two main isoflavones in soybeans, were unrelated to menarche age in the offspring.[43] However, these U.S. and European studies are of very questionable value for understanding the health effects of soy because soy intake among the participants is so low.[44]

An exception to this generalization is a U.S. cross-sectional study involving 327 Seventh-day Adventist (SDA) girls aged 12 to 18.[45] SDAs are a high-soy-consuming population. To this point, the mean number of servings of soyfoods among the adolescent girls was 12.9 per week and 21.1% of the girls consumed soyfoods ≥4x/day. The mean age of menarche among the girls was 12.5 years. The intake of total soyfoods and three specific soyfoods was unrelated to age of menarche.[45]

Cognitive Function

Takeaway

Clinical evidence suggests that in postmenopausal women, isoflavone exposure may improve some aspects of cognitive function, such as memory. In contrast, epidemiologic research evaluating the relationship between soy intake and cognitive function has produced mixed and conflicting results. Decisions about incorporating soy into the diet should not be based on its possible effects on cognition.

Evidence raising concern

Isoflavones have the potential to affect cognition via their interaction with estrogen receptors.[46] A Hawaiian prospective study found that mid-life tofu intake was associated with poor cognitive test performance and low brain weight.[47] Likewise, among elderly Indonesians, intake of tofu (but not tempeh) was associated with worse memory among elderly Indonesians.[48] In Shanghai, tofu intake was associated with worse cognitive performance.[49]

Evidence refuting concern

The aforementioned Hawaiian study, initiated in 1965, was not designed to evaluate cognitive function, but rather coronary heart disease.[47] The dietary questionnaire included only 26 questions, which pales in comparison to questionnaires commonly used today that include >100 questions. The questionnaire was designed primarily to differentiate between Western and Japanese dietary patterns, not so much to gather information about specific foods. Furthermore, the questions used to evaluate tofu intake changed throughout the course of the follow up period so an arbitrary classification had to be created to evaluate the relationship between tofu and cognition.

In the case of the Indonesia study,[48] follow up research by the authors failed to confirm the tofu finding; in fact, among those individuals with an average age of 67, results showed significantly positive associations between weekly tofu and tempeh consumption and better immediate recall.[50] Also, in the initial study, tempeh intake was associated with better memory. The authors speculated that the opposing findings between tofu and tempeh were because the latter contains higher levels of folate. However, not only is the relationship between folate and cognition unclear,[51] but the possible slightly higher folate content of tempeh in comparison to tofu almost certainly is not sufficient to affect cognition.[52] Thus, the results of this study are internally inconsistent. Overall, epidemiologic research that has evaluated the impact of soy intake on cognition has produced very mixed findings.[49,53-55]

Furthermore, the clinical data suggest that isoflavone exposure may improve cognition.[56] More specifically, a meta-analysis of 10 placebo-controlled randomized clinical trials involving 1,024 postmenopausal women found that soy isoflavones favorably affected summary cognitive function and visual memory in postmenopausal women.[56] A second meta-analysis also found isoflavones improved memory (episodic) and possibly also global cognition.[57] However, the data are inconsistent. Notable in this regard is a 3-year trial involving over 300 postmenopausal women which failed to show that isoflavone-rich soy protein affected global cognition.[58] More recently, a six-month study found that 100 mg/d isoflavones did not improve cognition in older men and women with Alzheimer's disease.[59]

Overall, given the inconsistency of the data, it is not surprising that the authors of a recently published comprehensive review concluded that ". . . the evidence to date is not sufficient to make any recommendations about the association between dietary intake of soy isoflavones and cognition in older adults."

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CHILDREN'S NUTRITION CENTER FOCUSED ON SOY FORMULA

By Aline Andres, PhD

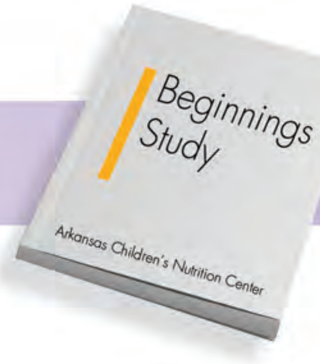
Soy formula has been in use since the 1960s and estimates are that 20 million Americans consumed this food at some point in their development. Currently, approximately 13% of formula-fed infants use soy formula.[1] After an extensive review in 2008, the American Academy of Pediatrics concluded that soy formula produces normal growth and development.[2] Similarly, in 2010, the U.S. National Toxicology Program (USNTP) concluded that there is minimal concern about the safety of soy formula.[3] Nevertheless, soy formula has become controversial because infants are exposed to high levels of isoflavones. To help address this controversy and to answer a call by the USNTP for more data, investigators at the Arkansas Children's Nutrition Center (ACNC) undertook the "Beginnings Study" in 2002.

Soy formula became controversial when some scientists revisited results of studies from the 1940s in sheep that ate clover which indicated that some chemical components similar to those in soy protein, known as isoflavones, impaired reproduction. Since then reports from several animal studies indicated that purified isoflavones produced adverse effects, including changes in sexual development with estrogen-like effects. It should be noted, however, that results of animal studies at the ACNC using the same soy protein used in soy formula, rather than purified isoflavones used in previous reports, showed no adverse effects. In fact, these results showed potential health benefits and no estrogen-like effects.[4-6] These discrepant results sparked the ACNC to initiate the Beginnings Study in children, as well as more mechanistic studies in animals, to compare the side by side growth and development of children fed breast milk, milk formula or soy formula.

In the Beginnings Study, children are followed from the first weeks of life through puberty: 388 children were fed breast milk (BM, n = 138), milk formula (MF, n = 130), or soy formula (SF, n = 120). Developmental landmarks are carefully studied at ages 3, 6, and 9 months and at 1, 2, 3, 4, 5, 6, and 14 years using state of the art methodology. Growth/development, body composition (relative amounts of muscle, fat, and bone), organ development (physical/functional exams, ultrasonography), metabolism (fluid markers, metabolomics), brain development (standardized behavioral testing, EEG, MRI), and bone development/integrity (fluid markers, pQCT) are assessed. To date, data from 376 children have been processed through age 5 years.

This study found growth and development of children in all three groups to be within the reported national and international norms. These data include: growth curves,[7] organ development[8,9] and performance on mental, psychomotor, language,[10] and brain development.[11-13]

While birth weights and body composition do not differ at birth, body composition profiles differed significantly between diet groups



over the first year of life. BM-fed infants accrue fat at greater rates than formula-fed infants and SF-fed infants have less fat and more lean body mass than BM-fed infants at 3–6 months. By age 1 year, body composition does not differ between groups.[7] Ultrasonography showed the size, shape and structural integrity of primary sex organs (ovary, testes), as well as secondary sex organs (uterus, breast, prostate) were within the normal range at age 4 months (when maximal formula intake/weight occurs) and at age 5 years.[8,9] MF-fed infants had significantly larger ovaries compared to BF- or SF-fed children at age 4 months. No other differences were noted at 4 months or 5 years.

The mental development index (MDI) was slightly better in BF compared to formula-fed infants, with no difference between MF and SF infants even after controlling for mother's IQ, gestational length, education, total income and age, at ages 6 and 12 months. The psychomotor development index was also higher for BF infants compared to SF infants at age 6 months after controlling for socio-economic status, maternal age, maternal IQ, gestational age, child's race, gender, birth weight, weight, head circumference and diet history. The Preschool Language Scale-3 (which evaluated the expressive communication and auditory comprehension) was lower in MF compared to BF and SF infants at age 3 and 6 months.[10]

In other studies of infant pigs fed BM, MF or SF, we have replicated many clinical results and showed that the three diet groups have organ specific gene expression profiles; meaning that each diet results in a different and specific pattern in which genes are turned on or off. These studies also showed that SF does not activate the estrogen receptor or display estrogenic properties or gene expression/metabolic profiles, which suggests that SF does not act as an estrogen.[14-16]

When considered together, these data demonstrate that: 1) early exposure to diet factors can influence the course of normal development; 2) SF-fed children perform as well as MF children, and 3) no evidence was found thus far to support concerns about adverse effects of SF feeding.

The Beginnings Study participants are now being recalled at age 14 years to assess growth, development, bone health, brain function and pubertal onset. Results will inform the long term effect of early infant feeding on overall health.

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Highly Refined Soybean Oil Not Allergenic

By Mark Messina, PhD, MS

The U.S. Food Allergen Labeling & Consumer Protection Act (FALCPA) mandates labeling of all ingredients derived from commonly allergenic foods. In the United States, eight foods have been identified as the most frequent human food allergens, accounting for 90 percent of food allergies. These foods are milk, eggs, fish, crustacea, wheat, peanuts, tree nuts and soy.[1,2] However, these foods are not equally allergenic—in fact, soy protein allergies are relatively uncommon.[3] Being allergic to soy protein is much less common than being allergic to milk or peanuts.[4,5]

Importantly, the FALCPA exempts highly refined oils from these labeling provisions because highly refined soybean, peanut and sunflower seed oils have been clinically documented to be safe for consumption by individuals allergic to the source food.[6-9] Soy is viewed similarly in Europe, where soy protein is classified as one of the 14 most common foods that induce allergic reactions, yet fully refined soybean oil is exempt from labeling.[10]

The process of commercially refining soybean oil involves extraction with hot solvents, bleaching and deodorization, which serve to eliminate almost all soy protein (and thus allergens) from the oil.[11] However, it is extremely difficult to quantify the protein content of oil. Attempts to do so indicate that crude oils contain about 100–300 mg/kg, whereas fully refined oils contain at least 100 times less.[11] This difference explains the lack of reaction observed in response to ingesting highly refined oils, unlike ingesting unrefined or partially refined culinary oils, which have been found to elicit allergic reactions in sensitized individuals.[12] While highly refined soybean oil does contain residual soy protein, the residue levels are extremely low—too low to elicit an allergic response in nearly all cases.[11,13-15] Analytical data from Rigby et al.[16] on cumulative threshold doses for soy protein suggest that even the most sensitive individuals would need to consume at least 50g of highly refined oil to experience subjective symptoms.[16]

There have been a few cases where soybean oil elicited an allergic response, but these instances followed intravenous infusion of an emulsion containing soybean oil, which seems far removed from typical consumption.[14,17,18] There is also one unusual case of a possible soy oil-induced allergy after an infant was fed exclusively on an amino acid-based formula containing a soybean oil-based component.[19] The circumstances of exposure in this exceptional case are unusual and the association with the soybean oil component of the formula was somewhat speculative.

In addition to the clinical studies cited here showing that highly refined soybean does not elicit an allergic response, circumstantial evidence supporting the clinical results comes from the work of the Swedish National Food Administration. Since 1994, this group has been recording and investigating all cases of fatal and severe reactions to foods.[20,21] While soy protein featured in about 25 percent of the reported cases (compared to ~33 percent for peanuts), none implicated soybean oil, or a product containing soybean oil as the only source of soy.

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