Soy and Thyroid: Vindication for Soy

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Over the past 30 years, soyfoods have been plagued by several controversies. The soy and breast cancer relationship has unquestionably been the most contentious one. A close second may be the relationship between soy and thyroid function. As discussed in detail below, the reasons why this relationship has played such a prominent role in shaping the image of soy are easy to identify.

However, within just the past few years, the conclusions of scientific bodies that soy does not adversely affect thyroid function have helped allay concerns about the anti-thyroid effects of soy. These bodies include the European Food Safety Authority,[1] The Permanent Senate Commission on Food Safety of the German Research Foundation[2] and the US Food and Drug Administration (FDA).[3] The results of a recently published meta-analysis of clinical studies to examine the effect of soy on thyroid hormones – the first of its kind – may help to further reduce concerns about the impact of soy on thyroid function.[4]

Concerns that soy may impair thyroid function have garnered considerable public and media attention considering the numbers of people with thyroid disorders. According to data from the National Health and Examination Survey (1999-2002), nearly 4% of adult Americans are hypothyroid; the rate is approximately 5 times higher among those at least 80 years of age.[5] In addition, as much as 17% of the population have subclinical hypothyroidism.[6] Subclinical hypothyroidism is characterized by elevated serum levels of thyroid-stimulating hormone (TSH) in the presence of normal serum levels of free thyroxine (fT4).

Two other observations about the prevalence of thyroid disorders warrant

mention. One is that there are anecdotal data indicating that more people think they have a “sluggish” thyroid than do. The other is that thyroid disorders are more common in women than men.[5] This latter observation is pertinent because women are more likely to be consumers of soy than men.

The impact of soy on thyroid function has been investigated for more than 80 years as the first animal study examining this relationship was published in 1933.[7] Studies published around 1960 included case-reports of infants developing hypothyroidism in response to the consumption of soy infant formula, a problem that ended soon thereafter when the formula began to be fortified with iodine.[8,9] Nearly four decades later, the soy and thyroid relationship received renewed attention as a result of comments made in 1999 by researchers affiliated with the U.S. Food and Drug Administration (FDA).

These comments, which raised concern about the possible goitrogenic effects of soybean isoflavones, were submitted during the public comment period associated with the eventual approval of a health claim for soyfoods and coronary heart disease.[10] Although the concerns were based primarily on in vitro data,[11,12] because they were submitted by researchers affiliated with the same institution granting the health claim, and despite the fact the FDA rejected these concerns, they likely received more attention, especially from social media, than they might have otherwise.

In contrast to these comments raising concern, in 2006 a narrative review that evaluated 14 clinical trials concluded neither soy nor isoflavones affect thyroid function in euthyroid individuals.[13] However, this review acknowledged that research determining the effect of soy on patients with a compromised thyroid function and in those whose iodine intake was marginal (because of the possibility of isoflavones being iodinated in vivo instead of tyrosine, thereby inhibiting thyroid hormone synthesis[14]) needed to be conducted. The latter issue was addressed in 2012; researchers found that the iodination

of isoflavones was negligible and clinically irrelevant.[15] Thus, concerns about soy adversely affecting thyroid function in individuals with marginal iodine intake were not supported. Of course, everyone, regardless of their soy intake, should be sure to consume adequate iodine.

The other issue – the effect of soy on those with a compromised thyroid function – was addressed in 2011[16] and 2018.[17] In 2011, a small British study conducted by Sathyapalan et al.,[16] found that modest isoflavone exposure (16 mg/day) increased the likelihood of progressing from subclinical to overt hypothyroidism. However, there are at least three reasons to be skeptical of this finding.

The first reason is that the study found that in all participants, regardless of whether they progress to over hypothyroidism, isoflavone exposure caused marked and statistically significant reductions in systolic and diastolic blood pressure, insulin resistance and inflammation (as assessed by C-reactive protein).[16] The magnitude of these effects was much greater than had been observed in other studies and were truly remarkable considering the low dose of isoflavones used in this study.

The second reason is that in 2018 follow up research by this same research group failed to find an effect of isoflavones on the progression of subclinical hypothyroidism even though a much larger dose (66 mg/day) was used.[17]

The third reason is that the comparison in both studies was between an isoflavone-rich isolated soy protein and an isolated soy protein devoid of isoflavones. Chemically removing isoflavones from soy protein, as was done in these two studies, can alter the tertiary structure of the protein, thereby raising questions about the appropriateness of isoflavone-poor soy protein serving as the control protein.

Finally, there is the recently published meta-analysis referred to at the onset, which included 18 trials.[4] The studies intervened primarily with soy protein or isoflavone supplements; isoflavone doses ranged from 40 to 200 mg/d. The low end of this range represents the average intake of native Japanese.[18] The analysis found

no effects of the intervention on fT4 or free triiodothyronine, the two primarily thyroid hormones.

However, there was a very modest increase in thyroid stimulating hormone levels, a finding that was barely statistically significant (p=0.049). The authors noted that the clinical significance of this finding, if any, is unclear. Furthermore, a look at the forest plot from this paper shows very clearly, that the findings from four studies by one research group, the group who studied subclinical hypothyroid patients, were responsible for the increase in TSH.[16,19-21]

Also noteworthy is the 2018 study that found soy did not affect the progression of subclinical hypothyroidism, did not find an effect on TSH, but it was published too late to be included in the meta-analysis.[17] If it had been, the finding from the meta-analysis that TSH was increased might no longer have been statistically significant. So, there is reason to question even the modest increase in TSH reported in the meta-analysis. All in all, the evidence is very reassuring about the lack of effect of soy on thyroid function.

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