Editorial

Soy Intake and Metabolic Health: Beyond Isoflavones

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Cite the article as: Azadbakht L, Esmaillzadeh A. Soy Intake and Metabolic Health: Beyond Isoflavones. *Arch Iran Med.* 2012; 15(8): 460 – 461.

Metabolic syndrome is a combination of metabolic abnormalities that include abnormal glucose homeostasis, dyslipidemia, elevated blood pressure, and enlarged waist circumference.[1] Dietary intake has long been shown to play a key role both in the etiology and management of this syndrome.[2–5] Although several diets such as the Mediterranean[2] and DASH[3,4] might beneficially influence features of the syndrome, there is no consensus on the best dietary plan for these patients.[5] A recent study has recommended the use of a phytochemical-rich diet for improving features of the syndrome.[6] Diets that contain high levels of antioxidants and isoflavones have also been indicated as being potentially beneficial.[6] Soy products, which are a rich source of antioxidants and isoflavones, have recently attracted significant attention for their possible health benefits.[7] Experimental studies as well as randomized clinical trials have demonstrated a role for soy products in the management of the metabolic syndrome.[8–11]

In this issue of the *Archives of Iranian Medicine*, Bakhtiary et al.[12] have reported findings from a parallel-arm randomized clinical trial on the effects of either textured soy protein or soy nut consumption on cardio-metabolic risk factors among postmenopausal women with the metabolic syndrome. They found that both textured soy protein or soy nut consumption for 12 weeks resulted in reduced levels of serum total- and LDL-cholesterol, apolipoprotein B, and VLDL concentrations in addition to increased levels of serum apolipoprotein A1. However, the authors have failed to find significant effects of both products on serum hs-CRP, fibrinogen, triglyceride, and HDL levels as well as on blood pressure. Studying the effects of textured soy protein or soy nut on the metabolic syndrome is not novel. Earlier studies have shown the favorable effects of both soy products on this syndrome.[10,11] For instance, Azadbakht et al.[10] have conducted the same study in a three-arm crossover randomized clinical trial among postmenopausal women.[10] A comparison between the results of Azadbakht et al.[10] and those reported by Bakhtiary et al.[12] shows a similarity in the lipid profile results. However, Azadbakht et al.[13] have also observed beneficial effects of soy nut consumption on inflammatory biomarkers.

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Accepted for publication: 13 May 2012

Earlier studies have mostly attributed the health benefits of soy to its isoflavones. However, in addition to isoflavones, many other components of soy products, such as saponins, beta-conglycinin (7S globulin) protein fractions, dietary fiber, and unique unsaturated fats might be beneficial. Some *in vitro* studies have shown that soy contents of 7S globulin protein possibly up-regulate LDL receptors and thereby reduce serum LDL concentrations.[14] Although the findings on lipid profiles are conflicting, the combined results in a meta-analysis study have suggested significant reductions of 9% in serum concentrations of total cholesterol, 13% in LDL cholesterol, and 12% in triglycerides with an average consumption of 47 g/d of soy protein.[15]

Another meta-analysis has revealed that the isoflavone content of soy might be responsible for its lipid-lowering effects.[16] Major isoflavones of soy products include genistein, diadzein, and glycitin.[17] Data on the separate effects of these isoflavones on metabolic health is limited.[17] Some studies have indicated that genistein, as a main isoflavone in soy products, might affect cardiovascular health through its inhibitory effect on tyrosine kinase.[18] It has been hypothesized that the unique amino acid profile of soybean might play a role in the effects of soy.[19] Experimental data have shown the hypercholesterolemic effects of lysine and methionine as well as the hypocholesterolemic effects of arginine. Therefore, the higher arginine-to-lysine and methionine ratio in soy might explain, at least in part, its hypocholesterolemic effects.[19]

Findings on the effect of soy consumption on serum apolipoprotein levels in both normal and hyperlipidemic individuals are inconsistent.[20,21] Some investigators have not seen significant changes in circulating apolipoprotein B and apolipoprotein A1 levels following soy intake,[20] while others reported a significant decrease in serum apolipoprotein B levels in hyperlipidemic men.[18] As the effects of diets on cardio-metabolic health are mediated through inflammation, nutritionists have expressed interest in assessing the effects of soy on inflammation as well. Bakhtiary et al.[12] found no significant effects of soy intake on inflammation. Earlier studies on legumes, soy and inflammation have shown conflicting results.[13,22–24] It seems that the effects of soy consumption on inflammation are product-dependent. While the beneficial effects of soy nut and soy milk consumption on inflammation have been shown, textured soy protein or isoflavone supplements alone are reported to be neutral. Co-existence of unsaturated fats along with lecithin, isoflavones, essential fatty acids, phytoesterols, polyphenols, inositol, and dietary fiber as well as other bioactive compounds make soy nuts more effective food than other soy products in improving metabolic abnormalities[13,25] As concluded in a recent review,

whole-soy foods seem to be the best choice in influencing metabolic health.[25] Soy nut is a whole-soy product that contains all the beneficial ingredients of soy.[25] Various soy products are obtained through separate processing methods on soybeans. Due to processing-induced nutrient loss, each product has different levels of soybean ingredients. For instance, alcohol extraction and acid precipitation to produce soy protein results in isoflavone loss.[26] Other processing procedures can alter soybean fiber, fat, sugars, phytic acid, and saponin content.[26]

Although the study of Bakhtiary et al.[12] has several strengths including the comparison of two soy products, their findings should be interpreted cautiously. There are some limitations in the study that have not been acknowledged in the paper. The compliance to soy intake in RCTs is better assessed by measuring plasma phytoestrogen levels, or serum or urine isoflavone concentrations. Bakhtiary et al.[12] have used three day dietary records to assess compliance. This method of assessment cannot easily reflect the participants' soy intake throughout the study. Most studies on the effects of soy only administered soy products to participants and limited feeding trials are available in this regard. This would result in difficulties with the assessment of compliance to soy intake. Future studies are better designed as feeding trials. Bakhtiary et al.[12] have conducted a parallel-arm study; however, most soy trials have been designed as cross-over studies. The cross-over trials seem to be suitable for soy studies because the absorption of isoflavones varies substantially among individuals. Intestinal bacteria, genetic background and dietary habits might influence inter-individual variations in isoflavone absorption.[27]

In conclusion, it seems that consumption of soy products affects cardio-metabolic health to some extent. However, the effects from soy nut consumption might be superior to those of the soy protein. Further studies are required to determine the optimal amounts of soy nut and soy protein for inclusion in the diets of patients with metabolic syndrome. Well-designed feeding trials are also needed to arrive at a definite conclusion on the effects of soy on metabolic syndrome.

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