



# Soy & Heart Health

## 2010 EDITION

In 2006, the most recent year for which data are available, an estimated 16.8 million Americans were affected by coronary heart disease (CHD), which includes myocardial infarction and angina pectoris. It is estimated that in 2009, nearly 800,000 Americans had a new coronary attack; 500,000 suffered a recurrent attack; and an additional 200,000 had a silent first heart attack.<sup>1</sup>

### FDA-Approved Health Claim for Soy:

*25 grams of soy protein per day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.*

The number of coronary deaths is split evenly between men and women, although the average age at which a first heart attack occurs is 64.5 for men and 70.3 for women. Approximately 424,892 Americans died of CHD in 2006, representing about 20 percent of all deaths in the United States and making CHD the number one killer of Americans.<sup>2</sup>

Despite these grim statistics, CHD death rates decreased by a remarkable 59 percent between 1950 and 1999, and by 33 percent between 1994 and 2004. While much of this decrease is due to improved medical treatment, improvements in lifestyle also greatly impact CHD morbidity and mortality. In most people, the etiology of CHD primarily involves risk factors that can easily be modified through lifestyle changes.

An analysis of three large prospective cohort studies that included approximately 400,000 participants found that about 90 percent of CHD patients have at least one of the following risk factors:<sup>3</sup>

- High total blood cholesterol levels ( $\geq 240$  mg/dl or 6.22 mmol/l) or current medication with cholesterol-lowering drugs
- Hypertension (systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg) or current medication with blood pressure-lowering drugs
- Current cigarette use
- Clinical report of diabetes

Dietary choices can significantly impact the risk of developing CHD. While markedly reducing CHD risk via dietary modification requires a comprehensive approach, there is no doubt that soyfoods can play an important role in heart-healthy diets.

### Effects of Soyfoods on Circulating Lipid Levels

Soyfoods have been recognized by nutritionists for decades as rich sources of high-quality protein. Over the past 15 years, the effect of this protein on blood cholesterol levels has attracted attention from the nutrition and medical communities. Research in this area was first conducted decades ago. The first rodent studies<sup>4,5</sup> showing that

soy protein lowered cholesterol levels were published more than 60 years ago, and the first clinical trial demonstrating this effect was published in 1967.<sup>6</sup> Throughout the 1970s and 1980s, Italian researchers were instrumental in showing that soy protein directly lowered blood cholesterol levels in very hypercholesterolemic patients.<sup>7-9</sup> Nevertheless, it was not until 1995 that the cholesterol-lowering effects of soy protein began to receive widespread recognition.

In that year, a meta-analysis of the clinical data, which included 38 different comparisons, found that soy protein reduced low-density-lipoprotein (LDL) cholesterol by approximately 13 percent.<sup>10</sup> This reduction was independent of the fatty acid content of soyfoods and was larger than that reported for any other single non-pharmacological treatment. Because statins were not yet widely used in clinical practice, the effect of soy protein was essentially equal to that of the available cholesterol-lowering medications.

The results of the 1995 meta-analysis prompted much investigation into the cholesterol-lowering effects of soy protein. Some of this research has been directed at identifying the specific soybean components and mechanisms responsible for cholesterol reduction, whereas other research explored the responses to soy protein by different subpopulations such as hypercholesterolemic subjects or premenopausal and postmenopausal women. In regard to mechanism, some data suggest that cholesterol reduction is a result of the upregulation of hepatic LDL receptors by the peptides formed upon digestion of soy protein.<sup>11,12</sup> Researchers also continue to explore whether isoflavones in soybeans impact the cholesterol-lowering effects of soy protein.<sup>13</sup>

In 1999, the U.S. Food and Drug Administration (FDA) approved a health claim for soy protein and CHD based on its cholesterol-lowering effects.<sup>14</sup> In total, more than 100 clinical trials investigating the hypocholesterolemic effects of soy protein have been published. However, despite the health claim, questions have



*Recent research indicates that soy protein lowers LDL cholesterol by 3 to 5 percent. On a population level, each 1 percent decrease in LDL reduces CHD risk and/or mortality by 2 to 5 percent. Therefore, even a 3 percent reduction in LDL could lower risk for heart disease by as much as 15 percent.*



recently been raised about the efficacy of soy protein.<sup>15</sup> There is no doubt that the current estimates of the degree to which soy protein reduces LDL are much lower than initially reported and that there is much variability among study results. Some variability is expected given the small sample size of many trials and the fact that such variability is also seen with all well-established cholesterol-lowering treatments, including low saturated fat diets<sup>16</sup> and phytosterol administration.<sup>17</sup>

Meta-analyses and reviews published between 2004 and 2007, including those by the American Heart Association<sup>15</sup> and the federal Agency for Healthcare Research and Quality,<sup>18</sup> have concluded

*Substituting soyfoods for protein-rich foods higher in saturated fat may lead to a decrease in blood cholesterol.*

that soy protein lowers LDL by 3-5 percent,<sup>19</sup> which is similar to the effects of soluble fiber.<sup>20</sup> These estimates agree with a recently presented analysis that covered the relevant literature published since 1978 (see reference for a brief description of this research).<sup>21</sup> This analysis, which used the scientific guidelines recommended by the FDA for the evaluation of health claims to analyze the data, found the net reduction in LDL was approximately 7.1 mg/dl or about five percent.

The reasons for the lowered estimates are not entirely known, although compared to earlier studies, studies published after the 1995 meta-analysis involved subjects with lower baseline cholesterol levels and used somewhat lower amounts of soy protein. Also, many of the earliest studies that showed very large reductions in cholesterol reportedly used a soy protein processed differently than the products used in most other studies,<sup>22</sup> and these studies also involved very hypercholesterolemic individuals. In any event, the extent to which each of these factors influences the cholesterol-lowering effects of soy is unclear.

It is important to note that from a public health perspective, a 3-5 percent reduction in LDL is quite meaningful. Over time, each one percent decrease in LDL reduces CHD risk and/or mortality by as much as 2-5 percent.<sup>23,24</sup> Therefore, a three percent reduction in LDL levels could lower risk for heart disease by as much as 10 percent.

The amount of soy protein needed to lower cholesterol is uncertain. Twenty-five grams per day is generally considered to be the threshold intake required for cholesterol reduction and it is the amount set by the FDA. In large part, this figure has been adopted because few trials used less than 25 g, although there is evidence suggesting that lower amounts are also efficacious.<sup>25</sup>

The advantage of incorporating soyfoods into heart-healthy diets extends beyond the direct effect of soy protein on cholesterol levels. When soyfoods displace more traditional sources of protein in Western diets, overall saturated fat intake is reduced, polyunsaturated fat intake is increased and blood cholesterol levels will be lowered.<sup>26</sup> Approximately 84 percent of the lipids in soybeans are unsaturated.<sup>27</sup> Not surprisingly, comprehensive dietary approaches that have resulted in reductions in LDL ranging from 20-30 percent have relied heavily on soyfoods; the high-quality of soy protein and its hypocholesterolemic effects combined with the favorable fatty acid profile of soyfoods make these foods especially attractive in such diets.<sup>28</sup>

The predominant fatty acid in soybeans is the essential omega-6 fatty acid linoleic acid, which reduces blood cholesterol levels.<sup>27</sup> However, over the years, some concerns have arisen that too much of this fatty acid could increase CHD risk by increasing inflammation. Recently, the American Heart Association rejected concerns about the pro-inflammatory properties of omega-6 fats and concluded that that these fatty acids play a critically important role in heart-healthy diets.<sup>29</sup> In addition to providing omega-6 fats, soybeans provide alpha-linolenic acid (ALA), an essential omega-3 fatty acid.<sup>26</sup> Although ALA does not possess the same properties as the long-chain omega-3 fatty acids found in cold-water fish, evidence suggests that ALA has direct coronary benefits<sup>30,31</sup> although the degree is a matter of some debate.<sup>32</sup>

Finally, in response to the ingestion of soy protein, meta-analyses have found very modest increases (1-3 percent) in high-density-lipoprotein cholesterol (HDL) and modest decreases (5-10 percent) in triglyceride levels. Each one percent or one mg increase in HDL lowers CHD risk by 2-3 percent.<sup>33-35</sup> Although there is debate about whether an elevated triglyceride level is an independent predictor of CHD risk,<sup>36</sup> recent evidence suggests that the role of fasting triglyceride levels in the etiology of CHD has been underestimated.<sup>37,38</sup>

### Beyond Effects on Lipid Levels

There is epidemiologic evidence that soyfoods exert coronary benefits independent of their effect on blood cholesterol levels. For example, after controlling for a wide variety of CHD risk factors, a prospective study involving nearly 65,000 postmenopausal women from Shanghai found that soy protein intake was associated with an 86 percent reduction in the risk of non-fatal myocardial infarction.<sup>39</sup> In agreement, a cross-sectional study involving 406 Chinese adults ages 40-65 years (134 males, 272 females) without confirmed relevant diseases found that soyfood intake was inversely related to bifurcation intima-media thickness, although the association was more apparent in men than women.<sup>40</sup> Also, a prospective study involving 40,462 Japanese participants (40-59 years old, without cardiovascular disease or cancer at baseline) found that when comparing women with frequent ( $\geq 5x/week$ ) versus infrequent ( $\leq 2x/week$ ) soy consumption, the multivariable hazard ratios were 0.64, 0.55 and 0.31 for risk of the incidence of cerebral infarction, myocardial infarction and CHD mortality, respectively.<sup>41</sup>

For two reasons, it is highly unlikely that the cholesterol-lowering effects of soyfoods were primarily responsible for the effects observed in these three epidemiologic studies. First, soy protein consumption in the upper intake categories was between 8 and 16 g/day, which, based on the results from the clinical studies, is likely too little to lower cholesterol. Second, the protective effects were far greater than could be expected from the cholesterol reduction typically associated with soy protein. Perhaps it is possible the observed protection could simply be the result of soyfood intake

being associated with a healthier overall lifestyle (i.e., healthy user effect). This explanation is also unlikely because most of the studies controlled for a wide range of potentially confounding variables, and in Asia soy consumption is much less reflective of an overall lifestyle than it is in countries where soyfoods have not been part of the traditional diet.

*Heart disease is the leading cause of death for both men and women in the United States.*

In support of the epidemiologic studies are various clinical studies that show soyfoods, soy protein or soybean isoflavones favorably affect a number of biological measures that impact heart disease risk. The proposed hypotensive effects of soyfoods are particularly intriguing. A recent meta-analysis found that soyfoods reduced systolic and diastolic blood pressure by about 6 and 4 mm Hg, respectively, although these data were based on only five studies.<sup>42</sup>

Despite the intriguing results from some clinical studies, the very inconsistent findings overall prevent firm conclusions about the effects of soy on these lipid-independent risk from being made. Recent studies do provide possible explanations for some of the inconsistency. For example, endothelial function, which is regarded as an independent CHD risk factor, was found to be improved by isoflavones primarily only among subjects whose endothelial function was impaired at baseline.<sup>45</sup> In fact, a recent meta-analysis confirmed this finding.<sup>46</sup>

Similarly, the anti-inflammatory effects of isoflavones may be observed only in subjects at risk of CHD who have elevated levels of inflammatory markers.<sup>47</sup> The clinical studies in which effects of different soy products on biological measures of CHD risk were examined involved subjects at both normal and elevated risk. Thus, the differences in baseline subject characteristics may account for some of the overall inconsistent clinical results.

### Summary and Conclusions

*In summary, soyfoods may make important contributions to heart healthy diets by:*

- *Providing high-quality protein but minimal amounts of saturated fat*
- *Directly lowering blood cholesterol levels*
- *Modestly elevating HDL and decreasing triglyceride levels*
- *Providing omega-6 and omega-3 essential fatty acids*
- *Favorably affecting CHD risk factors independent of lipid levels such as endothelial function, systemic arterial compliance, LDL oxidation, LDL particle size and blood pressure*

### Heart Healthy Sources of Soy Protein

Soyfood	Serving size	Grams of soy protein
Fortified soymilk	1 cup	6-7
Soy cereal	1 ¼ cup	7
Soy yogurt, vanilla	1 cup	6
Soy breakfast patty	2 patties	11
Soy bar	1 bar	14
Soy chips	1 bag	7
Soy nut butter	2 Tbsp	7
Soy nuts, roasted, unsalted	¼ cup	11
Tofu	½ cup	10
Edamame	½ cup	11
Soy burger	1 patty	13-14
Soy pasta	½ cup (cooked)	13
Soy pudding	½ cup	6

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The United Soybean Board (USB) is a farmer-led organization comprised of 68 farmer-directors. Working with independent academic researchers affiliated with the National Institutes of Health (NIH) and academic institutions, USB has invested millions of dollars into health and nutrition research related to soy. Soybean farmers take pride in producing one of the healthiest food crops in the world. To access healthy soy recipes and more nutrition information, please visit [SoyConnection.com](http://SoyConnection.com).