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Review Article

ROLE OF DIETARY PROTEINS IN CARDIOVASCULAR DISEASES

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ABSTRACT

Observational studies indicated a negative association between the risk of vegetable protein and cardiovascular disease, but less robust intervention studies. Many interventional studies that measured soy protein's effects relative to animal protein have used casein. Relative to casein, soy protein tends to have a variable and less dramatic effect on lipids and lipoprotein than originally reported. Compared to animal proteins other than casein, relatively large soy protein intakes (almost 25 g/d) tend to have a consistent hypocholesterolemic effect, although small (almost 5%). No significant additional benefit of soy protein on other risk factors for cardiovascular disease has been identified when assessed; Lp(a), inflammatory markers, oxidative stress biomarkers, and endothelial function. The available data on the effect of dietary protein on plasma lipids, lipoprotein levels, and risk factors associated with cardiovascular disease is difficult to interpret and insufficient to account for the discrepancy between observational and interventional studies.

Keywords: Cardiovasular diseases, Proteins, Soya protein, Cholesterol

1. INTRODUCTION

Cardiovascular disease (CVD) is a type of heart or blood vessel disorders. CVD includes diseases of the coronary artery (CAD) such as angina and myocardial infarction (commonly known as heart attack). Other CVDs include stroke, heart failure, heart disease, rheumatic heart disease, heart disease, abnormal heart rhythms, congenital heart disease, heart disease, carditis, aortic aneurysm, peripheral artery disease, thromboembolic disease, and venous thrombosis [1].

Depending on the disease, the underlying mechanisms differ. Atherosclerosis is associated with coronary artery disease, stroke, and peripheral artery disease. This can be caused by high blood pressure, smoking, diabetes mellitus, lack of exercise, obesity, high blood cholesterol, poor diet and excessive alcohol consumption, among others. High blood pressure is estimated to account for about 13% of deaths from CVD, while tobacco accounts for 9%, diabetes 6%, lack of exercise 6% and obesity 5%. Untreated strep throat may be accompanied by rheumatic heart disease [2].

Cardiovascular diseases are the world's leading cause of death. Except for Africa, this is true in all parts of the world. In 2015, CVD combined resulted in 17.9 million deaths (32.1%), up from 12.3 million in 1990 (25.8%). Deaths from CVD are more common at a given age and have increased in many developing worlds, whereas rates have declined in most developed worlds since the 1970s [3]. Coronary artery disease and stroke account for 80% of male deaths from CVDs and 75% of female deaths from CVDs [4-6].

Dietary habits are a major factor of cardiovascular diseases like heart stroke, cardiac failure, coronary heart disease, Marfan syndrome, abnormal heart disease, aorta disease and type 2 diabetes mellitus. According to the survey poor diet donates to nearly half of all cardiovascular death. Expanding dietary protein may benefit cardiovascular wellbeing by supporting in weight reduction/maintenance, improving the lipid/lipoprotein profile and diminishing circulatory strain [7-11]. In any case, showing the medical advantages of dietary protein must be deciphered with alert in light of the fact that expanding the utilization of protein/protein-rich nourishments normally brings about different changes in the eating regimen (*i.e.*, vitality, supplements, and nourishments) since dietary protein Is gotten from various food sources. For instance, expanding protein/protein-rich nourishment filter modify the admissions of supplements (*e.g.*, soaked fat and refined starches) as well as nourishments (*e.g.* fruits, vegetables, and entire grains), depending on what protein nourishment sources are expanded and what they supplant [5]. In this way, the impacts of expanded protein utilization are affected by the particular protein

nourishment source and coming about macronutrient and micronutrient (and bio active) substitutions. Thusly, proof about absolute protein utilization must think about the wellspring of protein, which parts of the eating regimen it is superseding, and the supplements and bio actives that go with the protein in the nourishment grid [12].

The oxidative stress affects the children and adolescent people which lead to cardiovascular risk. Cardiovascular illnesses are significant reasons for mortality and dismalness both in industrialized and creating nations. Significance of CVD is given by a blend of elements that incorporate bulkiness, physical latency, reception of undesirable dietary partialities, and smoking [13-15]. Generally cardiovascular (CV) clinical signs are preventable or possibly can be deferred later in mature age lessening occasions, dullness, handicap, and clean expenses. Regardless, in spite of the fact that it is never past the point where it is possible to improve unfortunate way of life propensities, early commencement of aversion is bound to be powerful against beginning and advancement of ailment, postponing signs, and diminishing unfriendly occasions [16]. Table 1 summarizes the various proteins which are involved in cardiovascular diseases.

Table1: Various Dietary Proteins involved in Cardiovascular Disorders

Dietary Proteins Sources	Benefits	Risks Involved
Red Meat	Lean red meat is also a good source of protein, omega-3 fatty acids, vitamin B12, niacin, zinc and iron. It is consumed in a diet low in saturated fat does not increase cardiovascular risk factors.	Red meat has more saturated (bad) fat than chicken, fish and vegetable proteins such as beans. Saturated and trans fats can raise your blood cholesterol and make heart disease worse [17-19].
Egg	Eggs contain good quality protein and are a source of healthy fats including omega-3 fats.	Higher consumption of eggs or dietary cholesterol to a higher risk of cardiovascular disease and premature death. Diabetic patients, even moderate consumption of eggs and cholesterol was associated with significantly increased coronary heart disease risk [20].
Nuts	Lower levels of inflammation linked to heart disease. Risk of developing blood clots that can cause a fatal heart attack. Improve the health of the lining of your arteries.	Dyslipidaemia, Type2 diabetes and metabolic syndrome. Inversely associated with risk of myocardial infarction, heart failure, atrial fibrillation and abdominal aortic disorder [21].
Legumes	Reducing LDL cholesterol. Increasing HDL cholesterol. Lowering blood pressure. Helping maintain healthy blood glucose levels. Assisting with weight management.	Low consumption of legume leads to cardiovascular diseases and Type 2 diabetes [22].
K-Casein	Casein is a slow-digesting dairy protein that people often take as a supplement. It releases amino acids slowly, so people often take it before bed to help with recovery and reduce muscle breakdown while they sleep. Several studies have shown it helps boost muscle growth	A *casein* allergy occurs when your body mistakenly identifies *casein* as a threat to your body [23-25].
Calcium caseinate	Calcium caseinate is one of several milk proteins derived from casein in skim and 1% milk. It is primarily used in meal preparation and fat breakdown.	It may lead to cancer, digestive discomfort and gut inflammation [26].
Lactoferrin	Stimulates the immune system. Helping maintain healthy blood glucose levels. Assisting with weight management.	It may cause Diarrhoea. Inversely associated with risk of myocardial infarction, heart failure, atrial fibrillation and abdominal aortic disorder [27].
Bovine Serum Albumin	It is used in a variety of laboratory applications including its function as a protein concentration standard, its function as a cell nutrient and its ability to stabilize enzymes during restriction digest.	It can cause eye irritation and skin irritation [28].
Vegetable protein	They show lower risk towards stroke and heinous heart disorders.	The protein is inversely associated with Ischemic Heart Disease. It causes Drowsiness, Dizziness and Hypotension [29-30].

2. DIETARY PROTEIN AND CVD OUTCOMES

There are few studies on the relationship between the type of dietary protein and the incidence of CVD. A meta-analysis of five prospective studies comparing mortality between vegetarians and non-vegetarians adopting a similar lifestyle concluded after controlling potential confounding variables (i.e., age, sex, smoking status, alcohol use, exercise level, educational status and body mass index) that non-animal protein-consuming individual had a 24% lower ischemic mortality rate [31, 32].

Oxford Vegetarian Study results show that after age change, there is a direct relationship between meat and cheese intake and total concentrations of cholesterol in both men and women. In a prospective study comparing Seventh-Day Adventists with non-vegetarians, following age change, smoking, exercise, body mass index, obesity, and bread intakes, nuts, fish, cheese, coffee, legumes, and fruit intakes; beef consumption was associated with an increased risk of ischemic heart disease in men, but not in women [33-34].

Results from a cross-sectional study in Japanese men and women suggested a negative association between self-reported soy intake and total concentrations of cholesterol after age adjustment, smoking status and dietary energy, fat and protein in men and adjustment for menopausal status, age, body mass index, coffee consumption, total intake of energy and vitamin C in women. Nagata et al. recently reported a modest but significant inverse correlation between soy protein intake and isoflavone intake and serum homocysteine concentrations in a cohort of Japanese premenopausal women, focusing on a risk factor for CVD other than plasma lipid levels [35]. This finding is likely to be confirmed further.

3. PROTEINS TYPE AND CVD

Jacques et al. reported that the exchange of lean white fish for other animal protein sources resulted in higher concentrations of total cholesterol, high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL)-apo B in postmenopausal women, regardless of the dietary fatty acid profile. Gascon et al. examined the effects of replacing lean white fish in premenopausal women with a combination of meat (beef, pork, and veal), eggs, and milk after adjusting the diets to have comparable fatty acid profiles [21]. The fish protein diet resulted in lower concentration of very low density lipoprotein triglycerides (TG) relative to the meat, eggs, and milk diet [36].

In contrast with a mixture of beef, pork, veal, eggs, milk, and milk protein in normalmolipidemic male subjects, Lacaille et al. tested the effects of diets rich in lean fish protein. Although the polyunsaturated: monounsatu - rated: saturated fatty acid ratios have been modified to be identical, the lean fish protein diet has more docosahexaenoic acid and eicosapentaenoic acid (docosahexaenoic acid + eicosapentaenoic acid= 1 g) than the dietary nonfish protein [37]. The diet of fish protein led to higher levels of HDL2-cholesterol, total apo B and LDL-apo B, and lower levels of TG: apo B and cholesterol: apo B. The behaviors of lipoprotein lipase and hepatic lipase did not differ substantially between the two diet phases at the end of the feeding periods. The findings of these studies comparing the impact of fish protein to other animal protein sources suggest that changes in plasma lipid levels were not consistent when detected and, in some cases, were not beneficial with regard to risk factors for CVD.

4. SOYA PROTEIN AS A RISK FACTOR FOR CVD

In a 1995 published meta-analysis of the effects of soy protein on serum lipid concentrations, *Anderson et al.* concluded that dietary soy protein significantly decreased total cholesterol, LDL cholesterol, and TG concentrations compared to animal protein, primarily casein [38]. They also found that the percentage of reducing LDL cholesterol was higher with increased initial concentrations of LDL cholesterol. The presence or absence of bioactive compounds retained in soybean after processing was potentially confusing in these observations.

Naturally, soybeans contain a group of compounds called isoflavones collectively. Genistein, daidzein, and glycitein are the major ones present. We have a low production of estrogen. The method of processing performed by the soybeans determines the absolute quantity of isoflavones in soy protein products. Most studies evaluating the effect of soy protein on casein or other animal proteins have variable isoflavone quantities. For this reason, these studies using soy protein with indigenous isoflavones are considered separately in this review, as part of the study design, from those in which the level of isoflavones relative to soy protein was varied [39].

5. SOYA PROTEIN WITH INDIGENOUS ISOFLAVONES RELATIVE TO CASEIN

Many research based on lipids and lipoprotein concentrations compared soy protein preparations

containing isoflavones to casein. Research that used a parallel study design and then research that used a hybrid design were first addressed. *Gooderham et al.* reported no significant difference in total cholesterol concentrations in normocholesterolemic men compared to 60 g SPI containing 131 mg isoflavones to 60 g casein [40-42]. There have been no reports of the effects on LDL cholesterol. In mildly hypercholesterolemic postmeno - pausal women, Vigna et al. compared 60 g of "Supro" SPI with 76 mg isoflavones to 60 g of casein.

Wang et al. assessed the effect of soybean protein's high molecular-weight fraction (HMFSP), produced after digestion of intact soy protein with microbial proteases, compared to an equivalent amount of SPI or casein (8% of energy) in mildly hypercholesterolemic women. HMFSP resulted in a decrease of 20 percent in LDL cholesterol, while SPI and casein both resulted in an Increase of 4 percent. When half the amount of HMFSP or casein was given in a high cholesterol diet (500 mg/d), HMFSP decreased the concentration of LDL cholesterol by 18%, significantly higher than casein, which increased LDL cholesterol by 5%.

5.1. *HDL Cholesterol and TG*

Focusing on the response of HDL cholesterol to soy protein with isoflavones relative to casein, there was no significant effect in most studies. All of them used SPI with isoflavones as the source of protein in the studies that reported a significant effect [43-44]. Baum et al. reported an increase of 3% and 6% in HDL cholesterol concentrations with SPI (56 mg / d and 90 mg / d, respectively) Nilausen et al., and an increase of 11%; and Kurowska et al. and an increase of 9% compared to milk. Wang et al. recorded a 13% decrease in HDL cholesterol compared to casein and a 7% increase compared to HMFSP.

5.2. *Lipoprotein (a)*

Two groups reported that consumption of diets containing soy / isoflavones results in higher concentrations of lipoprotein (a) [Lp(a)] than diets based on casein. In three other tests, however, soy protein was not reported to have a significant impact on concentrations of Lp(a).

5.3. Other CVD risk factors

5.3.1. Inflammatory Markers

Just one study examined the effects on inflammatory biomarkers of soy protein. In a crossover study, Blum et al. reported no significant effect of soy protein on the soluble interleukin-2 receptor (sIL-2R), E-selectin, P-selectin, molecule-1 (ICAM-1) intercellular adhesion and molecule-1 (VCAM-1) vascular cell adhesion after 6 weeks of supplementation compared to milk protein [45].

5.3.2. Blood Pressure and Endothelial Function

There are insufficient and inconclusive data on the impact of soy protein on blood pressure or vascular function. In contrast with casein, Teede et al. reported a hypotensive effect of soy protein. *Kurowska et al.,* on the other hand, found that soy protein resulted in increased blood pressure, both systolic and diastolic, relative to milk [46]. A caseinate compared to a soy protein supplement (40 g protein and 80 mg isoflavones) was reported in hypercholesterolemic postmenopausal women to significantly improve endothelial function as measured by flow-mediated dilatation, despite the lack of effect on plasma lipids. *Teede et al.* reported 40 g of soy protein in males, but not females, containing 118 mg isoflavones. The findings of more recent studies examining the impact of soy protein on the levels of plasma lipid and lipoprotein were variable and less drastic than originally reported [47].

Crossover studies have not recorded a major protein type effect for the most part. Parallel design experiments, although with highly variable outcomes, were more likely to find an effect of soy protein. There was no evidence in the studies examined in this section that the isoflavone soybean portion may explain the differences between the data observed to date. Such results are identical to those published for isolated isoflavone supplementation alone. Based on reported observations on Lp(a), inflammatory markers, and endothelial function, no consistent additional effects on CVD risk factors can be attributed to soy protein at this time.

6. SOY PROTEIN-ENRICHED AND DEPLETED IN ISOFLAVONES RELATIVE TO CASEIN; STUDIES ASSESSING THE INDEPENDENT EFFECT OF ISOFLAVONES

Studies also compared the effects on lipid concentrations and other risk factors for CVDs of soy-enriched and depleted isoflavones relative to casein.

6.1. Total and LDL Cholesterol

Crouse et al. compared 25 g / d of casein to 25 g / d of SPI containing increasing amounts of isoflavones (3, 27, 37, or 62 mg / d) in a parallel study of moderately hypercholesterolemic men and pre-and postmenopausal

women. In total (6 percent) and LDL cholesterol (4 percent) concentrations relative to the casein group, only the soy group with the highest isoflavone content experienced significant reductions [48].

Among participants with LDL cholesterol above the median (164 mg / dL; 9% and 10% respectively), the decline among total and LDL cholesterol was largest and only significant in groups consuming the two highest levels of isoflavones. Gardner et al. fed 42 g of SPI supplements enriched or depleted from isoflavones (80 mg or 0 mg) or casein to moderate postmenopausal hypercholesterolemic women following a similar study design. The final concentrations of total cholesterol among the three groups were not significantly different [49].

6.2. HDL Cholesterol and TG

Four of the studies compared the effects of depleted or enriched soy protein in isoflavones with casein and concluded that there were no significant effects of soy protein on concentrations of HDL cholesterol or TG. In one case, Meinertz et al. reported that concentrations of HDL cholesterol were 10 percent higher and, paradoxically, after the high-isoflavone SPI phase, concentrations of TG were 25 percent higher than casein.

6.3. Lipoprotein (a)

Of the three studies recording concentrations of Lp(a), two recorded no significant effect, while one reported that soy consumption resulted in>2-fold higher concentrations of Lp(a) compared to casein or soy protein extracted when the isoflavone fraction was present.

6.4. Other CVD Risk Factors

6.4.1. Oxidative Stress

Two groups assessed LDL's oxidation susceptibility. None of the diet's protein or isoflavone content affected LDL oxidation, measured as the formation of conjugated diene.

6.4.2. Homocysteine

Jenkins et al. identified no significant differences between diets containing soy (high or low in isoflavones) or dairy products in plasma homocysteine concentrations. However, when the results of the two soy phases were combined, homocysteine concentrations were significantly lower (7%) than after the dairy products phase had been fed to the subjects [50].

6.4.3. Markers of inflammation

No major effect of soy protein or soy-derived isoflavones has been reported on the acute-phase proteins C-reactive protein and serum amyloid-A (SAA) of the various inflammation biomarkers tested. In hyperlipidemic men and postmenopausal women, no major effect was found in the pro-inflammatory cytokines interleukin (IL)-6 and tumor necrosis factor (TNF)-α, with the exception ofIL-6, which was significantly higher in women after high-isoflavone soy diet [51].

6.4.4. Endothelial function

Steinberg et al. identified no significant differences in nitric oxide metabolites, endothelin-1 or flow-mediated dilatation assessed as markers of endothelial function, with and without soy, or milk protein in normocholesterolemic men and women. Nonetheless, following treatment with soy protein with isoflavones, the peak flow rate after occlusion was significantly lower compared to milk protein.

7. CONCLUSION

The data available from studies that focus on the effects of dietary protein form on the levels of plasma lipids and lipoproteins and CVD risk factors are difficult to interpret and do not clarify the protective role of vegetable proteins initially reported from observational studies. Most of the intervention researches are centered on investigating soy protein and soy-derived isoflavones' lipid-lowering ability. Although earlier work indicated a possible beneficial effect of soy protein on plasma lipids and lipoproteins, less promising results have been given by more recent studies. The soy protein's cholesterol-lowering effects were more robust, albeit limited, when compared to animal protein sources other than casein. In most studies, confusion attributable to small decreases in the consumption of saturated fatty acids when animal protein was replaced by soy protein cannot be absolutely removed. Soy protein effects on other risk factors for CVD are low if recorded. In addition, the effects of non-casin animal protein sources have not been studied extensively. A comprehensive dietary assessment is needed to assess the impact of specific nutrients on older people's physical performance. In order to establish the optimal blend of protein sources to support physical performance in old age, future interventional studies are needed. While the usual displacement of animal protein with vegetable protein may have a beneficial effect on risk factors for CVD, most of the benefit is likely due to a

shift in the diet's fatty acid profile favoring unsaturated fatty acids.

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