Symposium report

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Can food proteins affect the course and mortality caused by cardivascular diseases?

Report of the symposium of the Austrian Academic Institute of Nutritional Medicine, supported by the Alpro Foundation.

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Cardiovascular diseases cause more than 50% of all deaths in Europe. Elevated blood profiles, i.e. high LDL cholesterol levels, are considered as main cardiovascular risk factor (others include hypertension, overweight, diabetes and smoking). In the 1970s, the cholesterol-lowering effect of soy proteins was described for the first time [1]. Since then, a considerable amount of research has followed this line. Numerous researchers, such as the eminent expert C.R. Sirtori from Milano, have provided evidence for the cardioprotective properties of soy proteins in decreasing blood cholesterol levels.

On this highly topical issue, the Austrian Academic Institute of Nutritional Medicine and the Alpro Foundation organised an international symposium on April 15, 2004 in Vienna, Austria, which was held under the patronage of the Austrian Federal Ministry of Health and Women. At the symposium, renowned scientists and acknowledged nutritional experts reported on the state of knowledge on the impact of soy protein on cardiovascular diseases.

The following report summarises the main points of each presentation.

Professor K. Widhalm
Introduction: Current Research Report of the Department of Pediatrics/ University of Vienna – Devision of Nutrition and Metabolism

At the Department of Pediatrics/ Vienna University, soy protein has been used for more than 15 years to treat patients with the genetic form of hypercholesterolemia.

A current study investigated the acceptance of commercially available soy drinks, in particular the impact of the proteins contained on serum lipids and lipoproteins of children with familiar hypercholesterolemia. To this end, 21 children aged ten on average were put on a fat reduced and modified diet three months prior to the beginning of the study. The diet consisted of 20% proteins, 30% fat (rich on monounsaturated and restricted saturated fatty acids) and 50% carbohydrates. Over the following period 0,5 g of soy protein/ kg body weight has been administered to the children.

After six months, the use of soy proteins in powder form yielded usable data from 7 test people, who took their dose of soy protein reliably. Compared to their initial status, this group had 13% lower LDL cholesterol and a 9% lower level of triacylglycerol. The soy free and fat reduced nutritional intervention over three months had reduced LDL cholesterol by 6% and triacylglycerol by 4.4%. Despite the relatively small population (n=7), the study clearly shows the positive impact of soy protein as a substitute for animal proteins on the blood-fat profile of children with familiar hyper cholesterolemia.

Preliminary results from using novel products such as soy deserts, soy milk, etc., show a marked reduction of LDL-cholesterol and total cholesterol levels thanks to the fat reduced diet. Although data on the soy intervention is not complete yet, the fact that children accept soy products very well, is a very pleasant result.

Professor A. Rieder
Cardiovascular Diseases: Comparing Austria with other countries

In Austria, more than 40,000 people per year die from cardiovascular diseases. This corresponds to 52.5% of all fatalities, of which 67% are due to coronary heart diseases. Coronary Heart Disease (CHD) is the leading cause of death with women and men aged 65 and older. Within Austria, a regional disparity can be observed between the East and the West. Statistically, people living in Vienna face the highest risk of dying from cardiovascular diseases, followed by residents of the Burgenland and Lower Austria. In Vorarlberg and Tyrol mortality rates are 15% below the national average.

Statistical studies show a strong correlation between socio-economic indicators and illness and mortality rates. In other words, the greater the share of lower-income groups, the higher is the mortality rate from cardiovascular diseases.
Since the 1960s, mortalities due to cardiovascular diseases are declining in most industrialised countries. This trend is attributed to improved clinical prevention as well as primary and secondary preventive interventions. However, this trend is generally predicted to be reversed over the next couple of years and decades. This forecast is based on the rapidly increasing rates of obesity, the metabolic syndrome and type 2 diabetes as well as the massive increase in female smoking.

Looking at the European average, Eastern European countries record the highest and Mediterranean countries the lowest mortality rates due to cardiovascular diseases. Austria is positioned in the centre of this distribution, yet above the European average.

Conclusion: Preventive interventions represent feasible and very inexpensive ways to combat mortalities caused by cardiovascular diseases and should therefore receive top priority.

Professor G. Wolfram
Impact of life-style on cardiovascular risk

Nutrition, body weight, physical activity and smoking habits are major determinants of cardiovascular risk.

• **Nutrition:** excessive saturated fatty acids and the even more dangerous trans fatty acids, excessive energy and high levels of homocystein are deemed risk factors for cardiovascular diseases. In contrast, a high supply of n-3 fatty acids, monounsaturated fatty acids, fibres and antioxidants show a high cardioprotective potential [2,3]. The protective effect of n-3 fatty acids mainly owes to its demonstrated anti arrhythmic impact. Thanks to its ideal pattern of fatty acids, rapeseed oil is an exceptionally good non-animal source of n-3 fatty acids. Fibres (at least 30 grams) protect from myocardial infarction, as a diet rich on fibres automatically implies a nutrition with more vitamins and a more favourable pattern of fatty acids from vegetable sources.

Many studies, such as Vivekananthan et al. [4], show that if supplied as high-dose supplements, anti-oxidant vitamins, e.g. vitamin A, C and E, have no beneficial impact. However, even though appearing in much lower concentrations, they do have a beneficial impact if consumed via natural foods such as fruits or vegetables. This example demonstrates that nutrition is not just a sum of nutrients, but mainly the result of interactions and synergies between all components of a wholesome diet. Greater cardio-protection is also provide by **moderate alcohol consumption** (one to two drinks per day), whereas excessive consumption increases the risk of contracting cardiovascular diseases.

• **Physical activity:** physical activity has a beneficial impact on blood pressure, oxygen supply of the heart, the flow properties of blood, carbohydrate and protein metabolism and bone density. Also, it contributes significantly to an even energy balance. For these reasons, physical activity is generally regarded as an essential component of primary and secondary prevention against cardiovascular diseases. A study by Hambrecht et al. [5], published in the year 2000 in the New England Journal of Medicine reports a significant improvement in blood circulation of the heart muscle after only four weeks of physical activity. A study by Manson et al. [6] shows that physical activity can compensate the higher cardiovascular risk due to an elevated BMI but not due to smoking. Scientific evidence shows that regardless of age, it is always beneficial to start with moderate to intensive physical activity lasting at least 30 min for a few times per week.

• **Smoking:** smoking increases cardiovascular risk by lowering 'good' HDL cholesterol, increasing heart rate, blood pressure and oxygen consumption of the heart muscle, and decreasing coronary circulation. Moreover, smoking harms endothelial cells, which further amplifies the risk of coronary diseases. According to Rosenberg et al. [7], it takes three to five years after having quit smoking until the risk status returns to a level experienced by non-smokers.

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A meta-analysis by Stamler et al. (1991) covering 360,000 participants attests an increase in life expectancy of 6 to 9 years for men with a favourable risk profile and of 6 year for women.

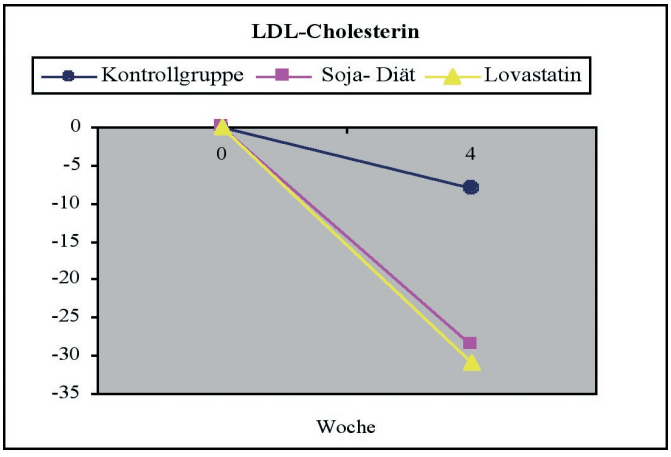
Professor Sirtori
The impact of soy proteins on lipides/lipoproteins and oxidation mechanisms

Prodded by the well-documented benefits of soy proteins on blood profile assembled over the past 25 years, the US FDA issued a recommendation in 1999 to use soy proteins for prevention of coronary diseases and approved respective 'health claims'. The frequently cited results from a meta-analysis by Anderson et al. [8] clearly shows that if compared to animal proteins, soy protein consumption induces a significant reduction of total cholesterol, LDL cholesterol and triacylglycerol levels in patients suffering from hypercholesterolemia. Because of its cholesterol reducing potential, the high consumption of soy products like tofu or miso is widely held as an important cause for the low cardiovascular mortality rates in Japan. Even a nutrition based on moderate soy uptake leads to a 20% reduction of coronary heart diseases.

A study by Widhalm et al. [9] published in the Journal of Pediatrics in 1993 shows for 23 children with elevated risks of familiar hypercholesterolemia shows a decline in LDL-cholesterol levels of 22-25% and a 16-18% reduction of triacylglycerols in the soy protein group. In comparison, the fat-reduced standard diet without any soy reduced LDL-cholesterol by only 7-13% and total cholesterol by 8-12%.

The significant discrepancy between the two nutritional diets suggests an early preventive nutritional intervention during child age for patients suffering from a familiar hypercholesterolemia, so as to avoid long-term drug treatment as far as possible and reduce the risk of cardiovascular diseases at an older age.

The cholesterol lowering mechanism appears to be linked to the raise of LDL receptors in the liver, which is typically depressed in hypercholesterolemic patients. To date, the hypothesis claiming an effect of soy-specific isoflavones from the group of phytoestrogenes lacks any scientific basis. Jenkins et al. [10] recently demonstrate a isoflavone-independent reduction of blood lipides, oxidised LDL, homocystein and blood pressure through substituting animal foodstuffs through soy products. A similar zero effect of isoflavones on blood cholesterol is described by Lichtenstein et al. [11]. They find a moderate benefit of isoflavone-free soy hydrolysates in cases of hypercholesterolemia.



A recent study by Jenkins et al. [12] provides a sensational result: it finds no significant difference for hyperlipidaemic patients in the effectiveness of a four week diet rich on soy proteins, fibres and vegetable sterol and the generally proven lipid-reducing drug Lovastin (28.6% vs. 30.9%) (see left diagramme).

According to the latest conclusions, the stimulation of LDL receptor expression in the liver, which is thought to stand behind the cholesterol-lowering mechanism, is to be attributed to soy-7s-globulin, in particular its most active Δ'- subfraction. A soon to be published study by Lovati et al. [12] will attempt to show that administering

isolated 7SΔ´- **globulin** to rats induces the impact of the hypocholesterolemic reference medication Lovastatin on total cholesterol and triacylglycerol levels by a factor of almost ten.

Moreover, soy proteins appear to have antioxidative potential, which has been confirmed recently in the animal model by Castiglioni et al. [13]. Not only did they find a marked reduction of plasmacholersterol and triacylglycerols in the soy protein group (16% of total protein intake), but also a highly significant decline in focal lesions in the aorta and of LDL-oxidability.

Professor M. Hamm
How can we implement a healthy nutrition based on vegetable proteins for the general population and risk groups?

From the perspective of nutritional medicine, a vegetable oriented food regimen oriented towards vegetables instead of animal (meat) products is a health improving measure. Among vegetable products, wholemeal cereals, nuts, oilseeds and pulses mainly serve to secure protein uptake. With a purely vegetarian or lacto-vegetarian nutrition, the following food combinations are suited to substitute amino acids and proteins from meat products: **cereals + milk; cereals + pulses; cereals + eggs; potatoes + eggs or pulses** (stew!).

Soy beans, which belong to the group of pulses, have a high share of proteins, which are of high biological quality. Applying the new method PDCAAS (Protein Digestibility-Corrected Amino Acid Score) to determine protein quality, soy proteins have the highest possible value of 1.0, which corresponds to the values of milk and egg protein. An increased inclusion of soy food or a partial substitution of animal foods assures a balanced ratio between vegetable and animal proteins. It has to be taken into account, however, that the milk typical nutrients calcium and vitamin B2 have to be consumed from alternative sources.

From a preventive perspective, the recommended daily uptake of 25g of soy protein is hardly compatible with western food culture. An example would be to consume 250 ml of soy milk (9g), 125 g of soy dessert (3.7g), 125 g of soy yofu (4.7g) and 100 g of tofu (7g) per day. The American soy expert Mark Messina therefore recommends a more realistic goal of 15g of daily soy uptake, which is likely to also have a positive effect on health.

Bsp. für Proteingehalt/ 100 g Sojaprodukte:

Sojabohnen	36 g	Sojasprossen	5,3 g
Sojamehl	37 g	Sojadrink	3,7 g
Tofu	8,3 g	Sojadessert	3,0 g

References

[1] Sirtori CR, Agradi E, Conti F. Soybean-Protein Diet in the Treatment of Type-II Hyperlipoproteinaemia. The Lancet 1977;5:275-77.

[2] DeLorgeril M, Renaud S, Mamelle N et al. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. The Lyon Diet Heart Study. Lancet 1994;343:1454-9.

[3] The GISSI-Prevenzione Investigators. Dietary supplemention with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 1999; 354: 447-55.

[4] Vivekananthan DP, Penn MS, Sapp SK et al. Use of antioxidant vitamins for the prevention of cardiovaskular disease: meta-analysis of randomised trials. Lancet 2003;361:2017-23.

[5] Hambrecht R, Wolf A, Gielen S et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. N Engl J Med 2000;342(7):454-60.

[6] Manson JE, Hu FB, Rich-Edwards JW et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in woman. N Engl J Med 1999;341(9):650-8.

[7] Rosenberg L, Palmer JR, Shapiro S. Decline in the risk of myocardial infarction amon woman who stop smoking. N Engl J Med 1990;322(4):213-7.

[8] Anderson JW, Johnstone BM, Cook-Newell ME. Meta-Analysis of the effects of soy protein intake on serum lipids. N Engl J Med 1995;332:276-82.

[9] Widhalm K, Brazda G, Schneider B. et al. Effect of soy Protein diet versus standard low fat, low cholestrol diet on lipid and lipoprotein levels in children with familial or polygenic hypercholesterolemia. J Pediat 1993;123:30-4.

[10] Jenkins DJ, Kendall CW, Jackson CC et al. Effects of high- and low-isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women. Am J Clin Nutr 2002;76:365-72.

[11] Lichtenstein AH, Jalbert SM, Adlercreutz H et al. Lipoprotein Response to Diets High in Soy or Animal Protein With and Without Isoflavones in Moderately Hypercholesterolemic Subjects. Arterioscler Throm Vasc Biol 2002;22:1852-58.

[12] Lovati et al. J Nutr 2004. Im Druck

[13] Castiglioni S, Manzoni C, D'Uva A. et al. Soy proteins reduce progression of al focal lesion and lipoprotein oxidiability in rabbits fed a cholesterol-rich diet. Atherosclerosis 2003;171(2);163-70.