

EFFICACY OF PLANT STANOLS/STEROLS IN ENSURING HEART HEALTH

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Abstract: *In all civilized countries the first cause of mortality and morbidity is a cardiovascular disease. Cardiovascular diseases are a group of degenerative diseases of heart and blood circulatory system including heart disease, peripheral artery disease and stroke. To reduce LDL-cholesterol level two significant areas of functional foods development are based on the one hand on plant sterols and stanol esters use and respectively, on the other hand on soy proteins use. More recent studies have shown plant sterols' and stanols' (hydrogenated derivatives of sterols) capacity to reduce LDL-cholesterol under certain conditions. Recent technological advances have provided plant sterols and respectively stanols extractions and esterification opportunity and then their solubilization in matrix of fatty food has become possible so easily by their incorporation in food at effective levels. Dobrogea Group with Raisio Finland introduced on the Romanian market the first bread with added plant stanols esters showing that after 14 days only of regular consumption of this product the level of serum cholesterol decreased.*

Keywords: *functional food, plant sterols, health, heart, LDL-cholesterol, Benecol product*

Introduction

In all civilized countries the first cause of mortality and morbidity is a cardiovascular disease. In Romania, statistics shows a significant increase in the incidence of these diseases that are the main cause of death caused by cancerous disease. Most Romanians suffer from diseases with various forms of cardiovascular disorders. A Romanian of five has high blood pressure, while 17% have severe impairment of peripheral arteries caused by arteriosclerosis. Of these, more than half are obese [1]. Studies show that the diet of most people is based on carbohydrates and fat and contains an excess of salt. Besides food, other causes and more other characteristic factors of our times should be incriminated such as:

physical inactivity, stress, smoking, pollution, etc., heredity occupying the last position in the list [2].

PASSCLAIM and FUFOSE activities and revised some aspects of target functions available through diet could influence the health and welfare of the body. The concept was tested and evaluated to provide an initial characterization of the scientific basis to support innovation and development of functional foods and any claims related to.

Cardiovascular diseases are a group of degenerative heart diseases and blood circulatory system including coronary disease, peripheral artery disease and stroke.

Coronary disease is a serious problem in industrialized states and increasingly more acute problem in developing countries and

countries in transition. Predominant clinical manifestations are pectoris angina (chest pain), myocardial infarction (heart attack) and congestive heart failure.

Reduction and especially prevention of obesity and cardiovascular diseases is made by diet with a lower intake of carbohydrates, lipids and salt, respectively with a high level of fiber, specific attributes of hipocaloric diet food, gives positive results [1].

There is strong evidence that cardiovascular risk reduction is possible through the consumption of fruit and vegetables, fish and fish oils rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), linoleic acid and potassium rich foods, together with appropriate physical activity and moderate alcohol consumption. Docosahexaenoic acid (DHA) is a very important omega-3 fatty acid in brain development, in ensuring the maintenance of visual acuity and brain function for all age groups. Eicosapentaenoic acid (EPA) falls into the same class of omega-3 acids that are vital for cardiac function and general health maintaining [3]. Obesity and excessive alcohol consumption increase the risk of cardiovascular disease. A low risk is found in the consumption of products containing α -linolenic acid, oleic acid, fiber, plant sterols and stanols. A reduced risk was found for products rich in flavonoids [4].

Two significant areas of development of functional foods are based on the use of plant sterol and stanol esters, on the one hand and soy protein on the other hand respectively, to reduce LDL-cholesterol levels. Sterols are natural constituents of plants and common crops such as soybeans and maize, having a role similar to cholesterol in the body. For 50 years it has been acknowledged that sterols interact with cholesterol in the intestinal tract leading to reduced cholesterol absorption and significantly reduce blood cholesterol

levels respectively. More recent studies have shown that plant sterols and stanols (hydrogenated derivatives of sterols) reduce LDL-cholesterol under certain conditions. These substances are naturally found in the diet, but in much lower concentrations than those necessary to achieve an effect. However, recent technological advances have enabled the extraction and esterification of plant sterols and stanols respectively, and their solubilizing in the matrix of fatty foods makes it possible so easily to get them incorporated in foods at effective levels [5].

Materials and Methods

Demonstrating the effectiveness of bioactive compounds is critical in building a solid scientific basis to show the functional foods health claims.

In assessing the effectiveness of plants stanols and sterols on ensuring the heart health we applied the process developed by the US Institute of Food Technology to address critical issues in the design, development and marketing of functional foods (Fig. 1). Thus, after having identified the potential bioactive components, plants stanols and sterols respectively (Stage 1) some evaluation was made for efficacy and safety (Steps 2 and 3). When selecting food vector for these bioactive compounds (Stage 4), the characteristics of food, ingredients, nature and destination were taken into account. An independent assessment of compliance with regulatory aspects (Step 5) ensures the accuracy of health claim, which must be properly communicated to consumers (Step 6). Finally, by monitoring the product on market, there could be confirmed the findings from the market pre-evaluation (Step 7).

Demonstrating the effectiveness of bioactive compounds is essential in building a solid scientific basis necessary

to render evident the contribution of functional foods.

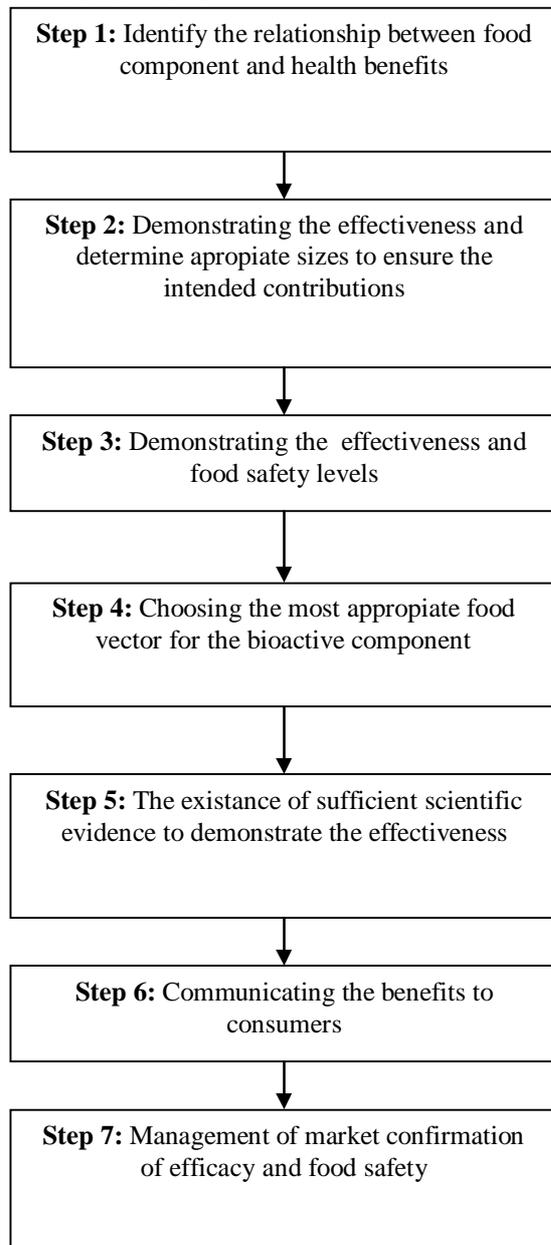


Figure 1. Process of design, development and marketing of functional foods. Source: IFT, 2005

The ability of identifying and quantifying key components of functional foods is an important first step in determining their effectiveness. Nutrients and bioactive substances must be stable in set in food to become functional at the time of consumption. Tests of long-term stability assessment are used to assess the efficacy of bioactive compounds in commercial

products. Bioavailability of bioactive compounds, essential to the pursuit of their functional effects is influenced by physical and chemical form, the overall effect of diet, effect of food processing technology and environment factors [6].

To ensure the health benefit, bioactive substance must be consumed in adequate amounts. The increase or decrease of bioactive components consumption has an effect on efficacy and safety of food. The impact assessment on safety and effectiveness requires quantitative knowledge on the consumption of target population, potential increased consumptions, population segments that present special risks or benefits.

The food vector selection depends on their acceptability, stability and bioavailability of bioactive compounds in food, consumption and lifestyle practices.

Once the health claim is scientifically validated, this information must be communicated to consumers. If they are not informed about the possible beneficial effects induced by food, few of them will know the benefits of these products, and manufacturers will be less motivated to develop other functional foods. This communication must submit significant links between the attributes of functional food and the consequence of their consumption on health care needs. Specific regulations should allow manufacturers to characterize accurately the health benefits of functional foods and scientific support of these claims. All parties involved must ensure that the message is correct and easily understood by consumers. The results obtained in the first five stages form the basis of messages to consumers, to convey the benefits of functional foods consumption.

Supervision of the functional food on market refers to the process of obtaining information on functional ingredients effects induced after having released the product on the market. This information

was obtained by monitoring the consumption patterns and the consumer's impact can complement the results obtained during market pre-evaluation, such as food safety and effectiveness of bioactive compounds, and any adverse effects (complaints) were not been identified in market pre-testing.

Results and Discussion

Phytosterols, widely distributed in the vegetal area, significantly reduce blood LDL-cholesterol and therefore, the risk of cardiovascular disease.

Structurally, phytosterols are close to cholesterol. Scientific plausibility of phytosterols' benefits is well understood. Phytosterols compete with cholesterol for incorporation sterol into micelles of intestinal lumen, interfering with both intestinal absorption of cholesterol ingested and the endogenous, secreted in the intestinal lumen [7]. Scientific evidence indicates that phytosterols affect proteins that form the membrane structure [8]. Action mechanisms of plant sterols and stanols are not fully clarified. However, two separate and sequential mechanisms seem to inhibit the cholesterol absorption with plant stanol. The first mechanism occurs in the intestinal lumen, while stanols replaced cholesterol from mixed micelles. The second mechanism occurs in the epithelial cells of the intestinal wall. The stanols plant that captures these cells activates specific protein carriers, which pump a part of cholesterol from the epithelial cells in the intestinal lumen [9]. This reduction in cholesterol influx reduces cholesterol availability for incorporation into LDL particles [10]. Interference of cholesterol intestinal absorption has been demonstrated in both animal studies and in humans [11, 12].

Clinical trials using double-isotope method showed that the intake of plant stanols reduces cholesterol absorption by 50% to 80%. Decreased cholesterol absorption occurs in both exogenous and endogenous cholesterol. This explains the effectiveness of cholesterol reduction by plant stanols even when consumed in a low cholesterol diet.

Vanstone et alia (2002) have established the parity of the two families of compounds (stanols and sterols) in lowering LDL-cholesterol and free non-esterified stanols and sterols equivalence in reducing cholesterol. It is shown that free and esterified sterols and stanols act similarly in lowering serum cholesterol levels and interfering with intestinal absorption of cholesterol [13]. Table 1 presents the FDA and EFSA conclusions regarding data supporting the stanols/sterols esters health claim and coronary diseases. In October 2000 FDA approved a health claim for certain foods and dietary supplements containing stanols or sterols esters, and later on, has expanded the health claim for additional food and other free forms and mixtures of stanols and sterols. In May 2010, some results of evaluation of the applications submitted and data presented by the European Food Safety Authority stated that a causal relationship between the consumption of foods containing plant sterols and plant stanols esters and lower cholesterol level has been established, and the European Commission by the CE Regulation no. 384/2010 has approved the health claim that *"it was found that plant stanols esters reduce blood cholesterol; high cholesterol is a risk factor for coronary heart disease"*[14,15, 16].

Table 1.
Plant sterols and stanols esters and coronary heart diseases

Hill Criteria	Scientific evidence
1. <i>How strong the association is:</i> strong	In the most intervention studies conducted on subjects who had moderate to high cholesterol levels (total cholesterol <300 mg/dl, plant sterols esters have significantly reduced the serum total cholesterol and LDL-cholesterol.
2. <i>Consistency of association observed:</i> association was observed by various people, places, times and different circumstances	Four studies indicated a close correlation between the consumption of plant sterols and reduced serum cholesterol levels in hypercholesterolemia subjects. The results of three studies support the effect of plant sterols to reduce cholesterol levels among subjects who had normal cholesterol levels. Two studies have shown a relationship between the consumption of plant stanols esters and reduced serum cholesterol levels in hypercholesterolemia subjects who consumed stanols esters as part of a low cholesterol and saturated fat diet. Eight studies have shown a relationship between the consumption of plant stanols and reduced levels of total cholesterol or LDL – cholesterol in hypercholesterolemia subjects' case.
3. <i>Association specificity:</i> an association is obvious for specific causality.	Given the variation both in content and foods containing plant sterols and sterols esters, which have been the subject of these studies, the response of serum cholesterol levels appear to be consistent and substantial. Given the variability in content and sterols food transporters used in these studies, cholesterol levels, the answer seems coherent and substantial.
4. <i>Biological gradient:</i> evidence of dose response variations.	Plant sterols may be more effective than previously thought, used in small doses. Researchers have found that reducing serum cholesterol

	level is even greater as the daily intake of plant stanols esters is higher. A minimum consumption of 0.8 g/day free plant sterols esters showed a substantial reduction of serum total cholesterol and LDL-cholesterol levels.
5. <i>Plausibility:</i> the association is biologically plausible	Long ago it was shown that plant sterols (β -sitosterols and its compounds) prevent the cholesterol absorption by blocking cholesterol absorption in the intestine.
6. <i>Consistency reasons:</i> the association is consistent with current knowledge on the disease / biomarkers known to be associated with	FDA and EFSA concluded that it is generally accepted that serum total and LDL - cholesterol are major risk factors of cardiovascular disease and dietary factors that influence serum cholesterol levels affect the risk of developing cardiovascular disease.

Source: ISLI, 2002

Rye bread Benecol Dobrogea is the only product in Romania with the optimal dose of plant stanols esters, supported ingredients in Europe for over 50 clinical studies. This product is the best choice for reducing cholesterol with a healthy diet. Benecol is the name of food ingredient with plant stanols, which lower cholesterol and is now found on the market in Romania.

Clinical studies show that daily consumption of Benecol products for two consecutive weeks reduced total cholesterol by 10% and LDL-cholesterol by 15% and these values remain low for a period of 12 months if products containing plant stanols esters are daily consumed [17].

Plant stanols esters of Benecol product reduce total cholesterol by 10% and the combined effect of nutritional recommended fatty acids and plant stanols esters of Benecol reduced cholesterol level by 15%.

Blood cholesterol concentration is the sum

of their synthesis, absorption and excretion. Decrease intestinal absorption of cholesterol by 50-80% is possible when the plant stanols are included in food. In response, the liver increases the cholesterol synthesis from its precursors. Despite the increased level of cholesterol synthesis, the final result is a decrease of plasma LDL - cholesterol. HDL - cholesterol concentrations remain unchanged.

Plant stanols esters' efficacy in reducing blood cholesterol has been confirmed by double-blind, randomized and placebo controlled clinical studies. The effect of cholesterol reduction was seen at subjects with high and normal cholesterol levels, patients with cardiovascular disease, patients with I or II degree of diabetes, subjects in Europe, North America, Australia and Asia, in case of combination with typical western diet, with a low-fat diet or a vegetarian diet [17].

The lasting effect of cholesterol-lowering with plant stanols esters was demonstrated by two double-blind controlled clinical studies. One study lasted 12 months and was conducted on subjects with mild hypercholesterolemia. This study involved 153 subjects with moderate hypercholesterolemia who changed margarine typically consumed for rapeseed oil margarine with or without the addition of 24 g / day plant stanols esters.

The intervention began with a dose of 2.6 g of sitostanol per day and continued for six months. After six months the amount of sitostanol ingested was reduced for half of the subjects at 1.8 g while the other half continued with 2.6g. In the first subgroup LDL-cholesterol was reduced by 15.2%, respectively 14% compared with that receiving placebo margarine. Statistically there were no significant differences between the two doses studied [17].

Similar results were obtained, for example, in a study on diabetic patients: dressing for salads with plant sterols esters added reduced cholesterol in the first weeks of

consumption, an effect that was attenuated during eight weeks. Furthermore, in another study lasting 52 weeks made on margarine added by sterol esters there was a reduction of only 4-6% of total cholesterol and LDL-cholesterol, for a daily dose of 1.6g of sterols. Clearly, more studies are needed to assess long-term efficacy of sterols.

Studies were made using stanols esters both for men's and women's diet and the effects were similar in both cases. In contrast, the effectiveness of cholesterol reduction when using sterol esters was not as consistent as in the case when studying plant stanol esters.

The efficacy and safety of consuming products enriched with plant stanol esters has been shown in clinical trials made both on adult subjects and children with familial hypercholesterolemia (FH). An initial study concluded that a partial replacement of usual dietary fats by margarine enriched with plant stanols esters is a treatment of hypercholesterolemia, safe and effective in children with FH.

A significant cholesterol lowering effect was demonstrated recently in a study where children with FH consumed yoghurt enriched with plant stanols esters. In a study made on patients suffering from heterozygous familial hypercholesterolemia, a serum cholesterol decrease by 11-20%, after a consumption of spreads containing plant stanols esters alone or in conjunction with statin-based medication has been observed.

The study was performed on 11 patients suffering from hypercholesterolemia, non-insulin dependents and mellitus diabetes studying cholesterol absorption and metabolism such as kinetic LDL-cholesterol and HDL-cholesterol in a plant stanols esters (3 g/day) treatment [17].

Total cholesterol and LDL-cholesterol decreased significantly between 6 and 9%, in that order. VLDL serum cholesterol values and lipoprotein B decreased

significantly between 6 and 12%, while HDL-cholesterol increased by 11% for consumption of plant stanols esters.

Conclusion

One risk factor in developing coronary heart disease is high cholesterol level.

Stanols increase cholesterol-lowering effect, with recommended changes in diet. Several clinical studies have shown that Benecol effectively reduces total cholesterol level by 10% and respectively LDL-cholesterol level by 15% when products are consumed as part of a recommended diet, at least for 14 days.

Dobrogea Benecol bread consumption is recommended to any age group or different present or future pathologies that the patient may be faced with as a prevention or curative way, being fully supported by the Romanian medical community.

All these analyses suggest that for every 1% decrease in total cholesterol, there is a 2% decrease in the incidence of cardiovascular disease. These results can be obtained firstly by a change of lifestyle, and secondly by drug therapy.

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