LOWERING CHOLESTEROL WITH PLANT STANOL ESTER
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INTRODUCTION

Cardiovascular diseases (CVD) are still the most common cause of morbidity and mortality worldwide. The risk of developing CVD is strongly related to blood cholesterol levels, and numerous studies have established a direct relationship between cholesterol and the incidence of CVD. Recent studies indicate that elevated blood lipids are also associated with other diseases, such as dementia, which makes fighting elevated cholesterol levels even more important.

Meta-analyses suggest that for every 1% decrease in total cholesterol, there is a 2% decrease in CVD. These results have been demonstrated with medical treatments as well as with lifestyle changes. Lifestyle changes are always the cornerstone of the prevention and treatment of CVD, and they are recommended at any risk level.

A heart-healthy diet is low in saturated fat and cholesterol, and high in dietary fibre. Foods enriched with plant stanol ester are widely recommended as the second step if a conventional heart-healthy diet alone does not bring enough improvement. Plant stanol ester reduces serum total and LDL cholesterol by up to 10 to 15%. This effect is additive to those of other dietary changes and cholesterol medication.

Lack of motivation is a major barrier to successful long-term cholesterol reduction by dietary means. Importantly, consumption of plant stanol ester can motivate further dietary changes, because the effect of plant stanols is fast, significant and lasting.

This brochure provides basic information on plant stanol ester and Benecol® products for healthcare professionals. Benecol® products were the very first evidence-based, cholesterol-lowering functional foods introduced to the market in the 1990s. Today, Benecol® products are sold in almost 30 countries, and are backed by more than 50 clinical studies that have confirmed the efficacy and safety of plant stanol ester. The accumulating scientific data convincingly show that Benecol® products can be the basis of cholesterol management for all individuals at risk.
PLANT STANOLS AND PLANT STEROLS IN HUMAN NUTRITION

Plant stanols and sterols are cholesterol-like molecules with only minor differences in their molecular structure. The highest concentrations of plant stanols and sterols occur in vegetable oils and cereals. The daily intake of these substances in a typical Western diet varies between 30 to 50 mg/day and 150 to 450 mg/day, respectively, while cholesterol intake varies between 300 to 500 mg/day.

Plant stanols and plant sterols have been shown to reduce the absorption of cholesterol from the dietary tract. This reduction applies to both dietary and biliary cholesterol. However, the intake of plant stanols and plant sterols from an ordinary diet is not sufficient to effectively lower blood cholesterol levels. Therefore, plant stanols are added into foods as plant stanol ester, a soluble form of plant stanols, which has been shown to effectively reduce serum LDL levels by up to 15%.

The absorption of cholesterol in humans is effective - approximately 50% of it is absorbed. Plant sterols, and especially plant stanols, however, are much less readily absorbed from the diet. When foods with added plant sterols or plant stanols are consumed, approximately 0.5 to 2% of the plant sterols and only 0.04 to 0.2% of the plant stanols are absorbed. Furthermore, plant stanols are effectively eliminated from the body.

The efficacy of plant stanol ester in lowering cholesterol has been shown in more than 50 peer-reviewed clinical studies.

A daily intake of approximately 2 g of plant stanols reduces serum LDL cholesterol by up to 15%.

Such significant cholesterol-lowering effects have been shown in:

- normo- and hypercholesterolemic individuals;
- women and men, as well as in children;
- patients with coronary heart disease;
- patients with type 1 diabetes;
- patients with type 2 diabetes;
- in conjunction with typical Western diets;
- in conjunction with a strict lipid-lowering diet;
- in conjunction with cholesterol-lowering statin therapy.

In most studies, HDL cholesterol and triglyceride levels have remained unchanged. However, the most recent research indicates that plant stanol ester also reduces serum triglycerides in subjects with elevated triglyceride levels.
Most studies have assessed the effects of taking 2 grams of plant stanols in two or more portions per day. However, taking the daily dose of plant stanols in one dose with a main meal is just as effective in lowering serum LDL cholesterol concentrations as splitting the dose over three meals.

Consuming Benecol® products with daily meals is important for optimum efficacy. This is due to one phase of the mechanism of plant stanols, by which they replace cholesterol in mixed micelles formed in the digestive tract. Micelle formation requires sufficient amounts of fat and other macronutrients ingested in daily meals.

### EXAMPLES OF STUDIES WITH DIFFERENT PLANT-STANOL-ESTER-ENRICHED FOOD PRODUCTS

<table>
<thead>
<tr>
<th>Product</th>
<th>Plant stanols (g/day)</th>
<th>LDL reduction (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margarine</td>
<td>2</td>
<td>13</td>
<td>Hallikainen et al. 2000</td>
</tr>
<tr>
<td>Low-fat spread</td>
<td>2</td>
<td>15</td>
<td>Ketomäki et al. 2005</td>
</tr>
<tr>
<td>Yoghurt drink</td>
<td>2</td>
<td>13</td>
<td>Salo and Wester 2005</td>
</tr>
<tr>
<td>Yoghurt</td>
<td>3</td>
<td>14</td>
<td>Mensink et al. 2002</td>
</tr>
</tbody>
</table>

### ONCE-A-DAY WITH A MEAL IS ENOUGH

- **Control**
- **Once per day**
- **Three times per day**

Figure 2. The consumption of 2.5 g of plant stanols (as plant stanol ester) at lunch resulted in a similar LDL cholesterol lowering effect as the consumption of 2.5 g plant stanols divided over three meals ( Plat et al. 2000).
Plant stanols reduce the absorption of both dietary and biliary cholesterol from the digestive tract. Research shows that plant stanol ester is effective in all kinds of diets. It works in typical Western diets as well as in diets low in saturated fat and cholesterol. For people unwilling or unable to accomplish heart-healthy dietary changes, plant stanol ester can be the first significant dietary step in reducing serum cholesterol. For those who already follow a heart-healthy diet, plant stanol ester gives an additional cholesterol-lowering effect. Thus, modifying the diet to combine heart-healthy foods with Benecol® products may result in sufficient cholesterol reduction through diet alone.

According to international guidelines for the treatment of elevated serum cholesterol levels, the first step is to choose a diet low in saturated fat, trans fat and cholesterol, and rich in dietary fibre. These dietary choices are enhanced when plant stanol ester is added to the diet.

In specific cases, cholesterol medication may be needed. Statins are the most widely used cholesterol-lowering medications. They reduce serum cholesterol concentration by inhibiting the synthesis of cholesterol in the liver. The cholesterol-lowering effects of statins and plant stanols are additive because they have different mechanisms of action. Statins inhibit the production of cholesterol while plant stanols partly block the absorption of cholesterol from the digestive tract. Adding plant stanol ester to the diet of subjects already on statin medication further reduces serum LDL cholesterol by up to 10 to 15%.
PATIENTS WITH CVD

Measures taken to reduce the risk or prevent the recurrence of a cardiac event in individuals with an existing history of CVD are of utmost importance. Therefore, effective action must address the treatment of elevated cholesterol values. Research has shown that plant stanol ester is an effective means of lowering serum total and LDL cholesterol in individuals with existing cardiovascular disease.

DIABETICS

The prevalence of diabetes, especially type 2 diabetes, is increasing as populations age and unhealthy lifestyles are adopted. People with diabetes have a multiple risk of developing cardiovascular diseases compared with healthy individuals. This is why it is very important to treat diabetes’ risk factors as effectively as possible. Plant stanol ester has been shown to effectively reduce serum cholesterol values in type 1 and in type 2 diabetes.
PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA (FH)

The efficacy and safety of consuming products enriched with plant stanol ester has been shown in clinical studies with both adult and child subjects with FH. An early study concluded that a partial replacement of normal dietary fat by plant stanol ester margarine appeared to be an effective and safe hypocholesterolemic treatment in children with FH. A significant cholesterol-lowering effect was also seen in a recent study where FH children consumed yoghurt enriched with plant stanol ester. In a study with patients suffering from heterozygous familial hypercholesterolemia, spread containing plant stanol ester lowered serum cholesterol alone and in conjunction with statin medication by 11 to 20%. And a recent meta-analysis stated that plant stanols may offer an effective adjunct to the cholesterol-lowering treatment strategy of FH patients.

HEALTHY CHILDREN

Atherosclerosis may start to develop early in life. So it is important to follow a heart-healthy diet early in childhood. Research also shows that plant stanol ester is a safe and effective adjunct to a normal healthy diet in children. In these studies, children have easily adhered to a regular dietary regimen including products enriched with plant stanol ester. However, such products are not recommended for children younger than five years due to their special dietary needs.

FAST EFFECT AND LASTING CHOLESTEROL REDUCTION

The full cholesterol-lowering effect of plant stanol ester can occur in as little as one to two weeks. From a treatment point of view, it is more important that this effect be sustained. The lasting cholesterol-lowering effect of plant stanol ester has been shown in two controlled, double-blind studies. One was a 12-month study with mildly hypercholesterolemic subjects. A second was a recent 18-month study with subjects on statin treatment. The lasting effect was also demonstrated in a 5-year study in a free-living population.

THE CHOLESTEROL-LOWERING EFFECT OF PLANT STANOL ESTER IS SUSTAINED

![Graph showing the cholesterol-lowering effect of plant stanol ester over time.](image-url)
PLANT STANOL ESTER – MECHANISM OF ACTION

Plant stanol ester partially blocks cholesterol absorption from the gut but the exact mechanism of action is not fully understood.

In the digestive tract, plant stanol ester is first hydrolysed into plant stanols and fatty acids. Because of the structural similarity of plant stanols and cholesterol (see page 4), plant stanols can partially replace cholesterol in so called mixed micelles, which are needed for cholesterol absorption. Thus, cholesterol absorption is significantly reduced. Furthermore, plant stanols may activate still unknown transport proteins in intestinal enterocytes. These transport proteins most likely excrete cholesterol into the gut lumen and, accordingly, out of the body.

SAFETY

More than 50 published clinical studies, extensive safety evaluation studies and the long experience of Benecol® products on the market have shown that plant stanol ester is safe to use, well-tolerated and without adverse effects.

Plant stanol ester has obtained Generally Recognised As Safe status (GRAS) in the USA. It has also been evaluated by food authorities in several EU countries prior to introduction in these countries. Food authorities in Europe have evaluated the use of plant stanols in foods and their recommendation is that the daily intake should range from 1 to 3 grams.

Plant stanols are virtually unabsorbable, and are effectively eliminated from the body. Levels of plant stanol in blood remain very low even after continuous long-term use of Benecol® products.

Data from clinical studies show that the lipid-standardized blood concentration of β-carotene may be reduced in connection with plant stanol ester consumption. However, adherence to dietary recommendations including a daily consumption of vegetables and fruit prevents this decrease in carotenoids.
recommended by international expert bodies

According to all international and national guidelines and recommendations, dietary intervention is always the cornerstone of therapy for dyslipidemia. This is the case even when cholesterol-lowering drug therapies have been initiated because diet may have other beneficial cardiovascular effects beyond its effects on lipid concentrations, such as antithrombotic effects and improved endothelial function. Several international bodies have included the use of foods with added plant stanol esters in their recommendations for cholesterol-lowering dietary therapies. Examples of these are:

- US National Cholesterol Education Program NCEP (2001)
- International Lipid Information Bureau (2003)
- American Diabetes Association & American College of Cardiology Foundation (2008)


Benecol® products are recommended as part of a diet low in saturated fat and cholesterol and rich in dietary fibre.

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BENECOL® PRODUCTS – A TASTY AND CONVENIENT WAY OF REDUCING CHOLESTEROL

Plant stanol ester is available for consumers as Benecol® products in many countries worldwide. These products have been formulated to fit local cultures, eating habits and attitudes, but the important common feature that links them all is that they contain enough plant stanol ester to significantly reduce cholesterol. The overall nutritional profile of all Benecol® products also fits into current dietary guidelines and recommendations.

Examples of Benecol® products:
• Benecol® margarines and spreads
• Benecol® milk and soy-based yoghurts
• Benecol® milk and soy-based yoghurt mini drinks
• Benecol® cream cheese style spreads
• Benecol® oatmeal porridge
• Benecol® bread

Please visit www.benecol.net to find out which Benecol® products are available in your country

SUMMARY

• Plant stanol ester, the cholesterol-lowering ingredient in Benecol® products, reduces serum total cholesterol by up to 10% and LDL cholesterol by up to 15%.
• Such clinically relevant results are gained from a daily dose of approximately 2 grams of plant stanols in conjunction with meals.
• The cholesterol-lowering effect is lasting when Benecol® products are consumed on a daily basis.
• Plant stanol ester is recommended by numerous national and international expert bodies and it is considered as efficient and safe.
• Benecol® foods are tasty, and they fit well into a recommended heart-healthy diet.