

The role of plant sterols/stanols in life-long management of blood cholesterol - from science to claims

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on behalf of the **International Plant Sterols and Stanols Association (IPSSA)**

Seminar Program – Functional Nutrition
“Cradle to Grave” - Hosted by Intertek

food matters live...

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International Plant Sterols and Stanols Association (IPSSA) - Introduction

- Established in **2015**; based in and operating from Brussels, Belgium
- Founding (and current) members are leading international companies in plant sterols and stanols
 - **Arboris, BASF, Cargill, Raisio, Unilever**
- IPSSA covers all aspects of the plant sterols and stanols sector
 - B2B (producers of plant sterols, plant stanols, and their esters)
 - B2C (producers of foods with added plant sterols and stanols)
- IPSSA has a global focus

IPSSA – Our mission

1. To educate the **media** and the **public** about the role of a healthy diet and lifestyle in reducing the risk of heart disease
2. To demonstrate in a clear and concise manner how plant sterols and stanols have been **scientifically proven to lower blood LDL-cholesterol**
3. To inform **policymakers** about the safety of plant sterols and stanols as well as their efficacy in lowering blood LDL-cholesterol and thus, their contribution to reducing the risk of heart disease



Cholesterol and Cardiovascular Disease (CVD)

- CVD is the leading cause of death in adults worldwide
- In Europe, CVD accounts for 45% of all deaths*
- Major burden on health care costs to EU economy with estimated costs of 210 billion Euro per year



- Elevated blood LDL-cholesterol is causal risk factor of atherosclerotic cardiovascular disease (ASCVD)**
- Lowering LDL-cholesterol \downarrow
The lower the better; the earlier the better!



- **Diet and lifestyle are the cornerstone in CVD prevention**
- With adequate changes, at least 80% of (premature) CVD mortality may be prevented**
- Introducing foods with added plant sterols and stanols as part of a healthy diet will contribute to blood cholesterol management of individuals



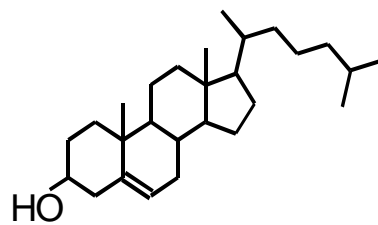
*European Cardiovascular Disease Statistics; 2017 Edition

**FERENCE et al, Eur Heart J 2017

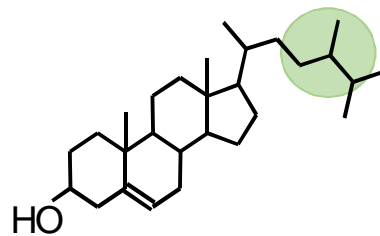
**Piepoli et al, European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2016

Plant sterols and stanols are natural compounds in the human diet

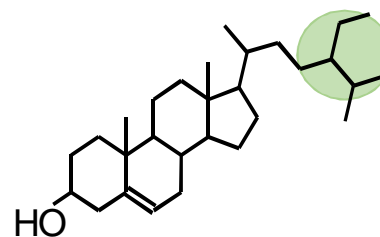
- Plant sterols and stanols are found in foods of plant origin, e.g. grains, seeds, vegetable oils, nuts, legumes, fruit and vegetables
- Average daily intake with habitual diets
 - 200 to 300 mg/day of naturally occurring plant sterols
 - ~50 mg/day of naturally occurring plant stanols
 - Up to 600 mg with vegetarian/vegan-type, plant-based diet
- Plant sterols and stanols are structurally similar to cholesterol with both different side chain configurations and lack of double bonds



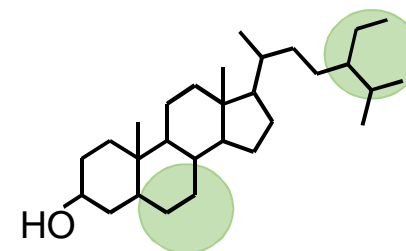
cholesterol



campesterol



sitosterol



sitostanol

Plant sterols/stanols - most thoroughly studied dietary ingredients for blood cholesterol-lowering

- Long history of knowing their cholesterol-lowering effect
- Since mid/late 1990s, foods with added plant stanols/sterols commercially available, with wide range of different food formats and food supplements
- Vast evidence for cholesterol-lowering effect
 - **>120 human studies** showing that plant sterols/stanols lower total and LDL-cholesterol without affecting HDL-cholesterol*
 - Plant sterols/stanols also modestly lower triglycerides (TG) esp. in individuals with high basal TG levels**



*Ras et al, Br J Nutr 2014

**Rideout et al, J AOAC International 2015

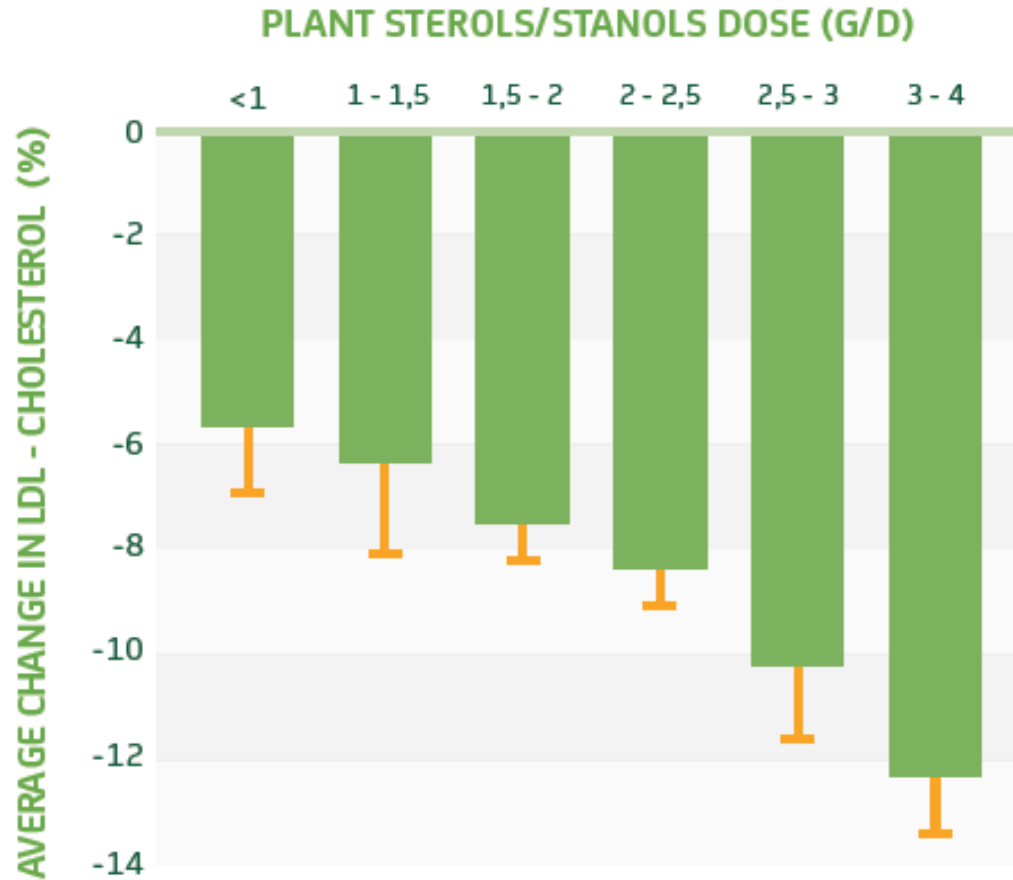
Building scientific evidence - basis for Health Claim authorisation

- Several **meta-analyses*** summarising evidence for the dose-dependent cholesterol-lowering effect of plant sterols and stanols
- Numerous humans studies addressing aspects, like
 - Efficacy of different food formats and food supplements
 - Efficacy in specific target groups
 - Factors that influence efficacy, e.g. intake occasion and frequency
 - Interaction with cholesterol-lowering drugs
 - Understanding of underlying mechanism of action

*Katan et al, Mayo Clinics Proceedings 2003; AbuMweis et al, Food Nutr Res 2008; Demonty et al, J Nutr 2009; Musa-Veloso et al, PLEFA 2011; Amir Shaghaghi et al. J Acad Nutr Diet 2013; Ras et al, Br J Nutr 2014



Cholesterol-lowering of plant sterols and stanol across different dose ranges



Meta-analysis based on 124 studies with 201 study arms;
9,692 study participants;
variety of food formats, e.g. margarine, milk, yoghurt,
food supplements

**Plant sterol/ stanol intakes of 1.5 - 3 g/day
dose-dependently reduce LDL-cholesterol by 7 - 12.5%**

LDL-cholesterol lowering of plant sterols and stanols demonstrated under various conditions

Cholesterol-lowering efficacy demonstrated in different populations

- Individuals with
 - Diabetes Mellitus
 - Familial hypercholesterolemia (FH)
 - Metabolic syndrome
- In combination with lipid-lowering drugs (statins, fibrates, ezetimibe)



Plant sterols/stanols are effective with different background diets

- As part of a typical (habitual) diet
- Additive to cholesterol lowering effect of a low-fat diet
- As part of a whole diet (dietary pattern)



Positive EFSA opinion for plant sterols and stanols in 2008 forms basis of authorised health claim

Plant Sterols and Blood Cholesterol

Scientific substantiation of a health claim related to plant sterols and lower/reduced blood cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006¹

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2008-085)

Adopted on 11 July 2008

A clinically significant LDL-cholesterol lowering effect of about 9% can be achieved by a daily intake of 2 - 2.4 g of phytosterols in an appropriate food (e.g. plant sterols added to fat-based foods and low-fat foods such as milk and yoghurt). The size of the cholesterol lowering effect may differ in other food matrices.

A cause-effect relationship has been established between the consumption of plant sterols and lowering of LDL cholesterol, in a dose-dependent manner.

SCIENTIFIC OPINION

Plant stanol esters and blood cholesterol

Scientific substantiation of a health claim related to plant stanol esters and lower/reduced blood cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006¹

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2008-118)

Adopted on 02 October 2008

A clinically significant LDL-cholesterol lowering effect of about 10% can be achieved by a daily intake of plant stanol esters equivalent to 2 g of plant stanols in an appropriate food (e.g. fat-based foods and low-fat foods such as yoghurt), preferably with a meals. The size of the cholesterol lowering effect may differ in other food matrices. **A cause-effect relationship** has been established between the intake of plant stanol esters and lowering of LDL cholesterol, in a dose-dependent manner.

Authorised disease risk reduction claim for plant sterols and stanols and conditions of use in EU

‘Plant sterols and plant stanol esters have been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease.’

Conditions of use

- Information to consumer that beneficial effect is obtained with a **daily intake of 1.5 - 3 g plant sterols/stanols**
- Reference to magnitude of effect may only be made for foods within the following categories: **yellow fat spreads, dairy products, mayonnaise and salad dressings.**
- When referring to magnitude of effect, the range **“7 to 10 %”** for foods that provide a daily intake of **1.5-2.4 g plant sterols/stanols** or the range **“10 to 12.5%”** for foods that provide a daily intake of **2.5- 3 g plant sterols/stanols** and duration to obtain the effect **“in 2 to 3 weeks”** must be communicated to the consumer.

EFSA opinion from 2012 forms basis for increasing the cholesterol-lowering efficacy from 10 to 12.5%

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to 3 g/day plant sterols/stanols and lowering blood LDL-cholesterol and reduced risk of (coronary) heart disease pursuant to Article 19 of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from Unilever PLC and Unilever NV, submitted pursuant to Article 19 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of an application to modify the conditions of use of an authorised Article 14 claim related to 1.5 - 3.0 g plant sterols/stanols per day and lowering blood LDL-cholesterol by 7 - 12 % and reduced risk of (coronary) heart disease. The applicant has further requested that the minimum

On the basis of the data presented, the Panel concludes that ... **plant sterols and stanol esters at a daily intake of 3 g (range 2.6 g to 3.4 g) plant sterols/stanols in matrices approved by Regulation (EC) No 376/2010 lower LDL-cholesterol by 11.3 % (95 % CI: 10.0 - 12.5) and that the minimum duration required to achieve the maximum effect of plant sterols and stanols on LDL-cholesterol lowering is two to three weeks.**

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to 3 g/day plant stanols as plant stanol esters and lowering blood LDL-cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from Raisio Nutrition Ltd, submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Finland, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to 3 g/day plant stanols as plant stanol esters per day and lowering blood LDL-cholesterol by 12 % and reduced risk of (coronary) heart disease. The applicant has further requested that the minimum

On the basis of the data presented, the Panel concludes that **plant stanol esters at a daily intake of 3 g plant stanols (range 2.7 g to 3.3 g) in matrices approved by Regulation (EC) No 376/2010 lowers LDL-cholesterol by 11.4 % (95% CI: 9.8 – 13.0) that the minimum duration required to achieve the maximum effect of plant stanol esters on LDL-cholesterol lowering is two to three weeks.**

Examples of approved health claims for plant sterols/stanols across the globe



USA

- Foods containing at least 0.5 g per serving of phytosterols [plant sterols, plant stanols, or plant sterols and stanols] eaten with meals or snacks for a daily total intake of 2 g as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.

CANADA



- Serving size of product provides x% of the daily amount* of plant sterols shown to help reduce/lower cholesterol in adults.
- "Plant sterols help reduce (or help lower) cholesterol. High cholesterol is a risk factor for heart disease."

AUSTRALIA/NEW ZEALAND

- Food products authorized for enrichment with plant sterols, stanols, and their esters are
- eligible for *high level health claim***, "reduces blood cholesterol".
- Foods must contain at least 0.8 g of plant sterols/stanols for a daily intake of 2 g.

*The "daily amount" referred is 2 g. This amount is based on the evidence available concerning the amount of plant sterols shown to help reduce cholesterol in adults.

***High level health claim* means a health claim that refers to a serious disease or a biomarker of a serious disease

Target population for foods with added plant sterols and stanols*

- Individuals with **elevated serum cholesterol**, but **intermediate or low global CVD risk**, who therefore do not (yet) qualify for drug treatment
- **As an adjunct to drug (statin) therapy** in individuals, who fail to achieve LDL-cholesterol targets, or are statin-intolerant in conjunction with other lifestyle interventions
- In adults and children (>6 yrs.) with familial hypercholesterolemia



Medical and scientific associations recognise foods with added plant sterols and stanols

Recognition of efficacy and safety of plant sterols/stanols as a dietary option for lowering LDL-cholesterol, a risk factors of CHD



Plant sterols and stanols in comparison to other diet and lifestyle approaches

Dietary Component	Dose or change in intake/ habit	Approximate LDL-cholesterol reduction	Strenghts of evidence
Reduce and replace SAFA with unsaturated fats , (PUFA and MUFA)	Exchange 5% energy of SFA with PUFA Exchange 5% energy of SFA with MUFA	7% ^a 6% ^a	★ ★ ★
Reduce dietary cholesterol	<300 mg/day	3% ^b	★ ★
Other LDL-lowering options			
Increase dietary fibre intake from foods rich in soluble fibre	≥3 g/day β-glucan	5-6% ^{c,d}	★ ★ ★
Consider plants sterols/stanols	1.5-3 g/day	7-12.5%	★ ★ ★
Consider soy protein	≥25 g/day	3-4% ^f	★ ★
Lifestyle			
Body weight	-10 kg	5% ^h	★ ★
Physical activity	3-4 sessions/week	2-4% ⁱ	★ ★

★★★ Level of Evidence A= Data derived from multiple randomized clinical trials or meta-analysis

★★ Level of Evidence B = Data derived from a single randomized clinical trial or large non-randomized studies

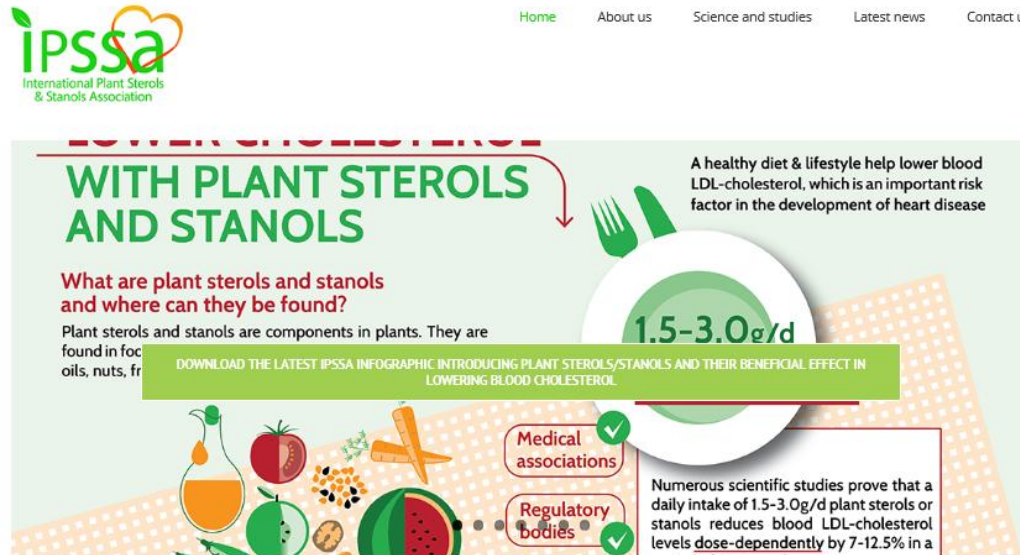
- Vast number of human intervention studies shows LDL-cholesterol lowering benefit of foods with added plant sterols and stanols
- **Intake of 1.5-3 g/day** lowers LDL-cholesterol dose-dependently by **7-12.5%**
- Plant sterols/stanols **are effective in all food formats and in food supplements**
- **Additive effect** to a heart healthy diet and to lipid-lowering medication
- **Authorized health claims** by e.g. EU Commission, *FDA* (US), Health Canada
- Included in **recommendations** for diet and lifestyle approaches for management of dyslipidaemia as an additional adjunct to a healthy diet
e.g. 2016 EAS/ESC guidelines on the management of dyslipidaemias



Thank you!

For more information on plant sterols and stanols visit
<http://www.ipssa-association.com> and follow us on Twitter @IPSSAglobal

Downloadable
Infographic



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WITH PLANT STEROLS AND STANOLS

A healthy diet & lifestyle help lower blood LDL-cholesterol, which is an important risk factor in the development of heart disease

1.5-3.0g/d

What are plant sterols and stanols and where can they be found?
 Plant sterols and stanols are components in plants. They are found in foods such as vegetable oils, nuts, fruits and vegetables.

DOWNLOAD THE LATEST IPSSA INFOGRAPHIC INTRODUCING PLANT STEROLS/STANOLS AND THEIR BENEFICIAL EFFECT IN LOWERING BLOOD CHOLESTEROL

Medical associations
Regulatory bodies

Numerous scientific studies prove that a daily intake of 1.5-3.0g/d plant sterols or stanols reduces blood LDL-cholesterol levels dose-dependently by 7-12.5% in a

Link to Voices of Lowering cholesterol campaign

6
07, 2017

Publication by Frost & Sullivan commissioned by FSE on Healthcare Cost Savings of Phytosterol Food Supplements in the European Union
 In order to understand better the potential value of supplementation to society, Food Supplements Europe (FSE) has commissioned economic consultants of Frost & Sullivan to evaluate the potential healthcare cost savings that could be derived [...]

7
06, 2017

Plant stanol and sterol containing foods further lower blood cholesterol in patients treated with statin medication
 Plant stanols/sterols work in a different way to statins and can help people who take statin medication achieve further cholesterol reduction
 Current expert advice supports a lower the better strategy for blood cholesterol
 Healthy diet is an [...]

7
06, 2017

Study shows the cholesterol-lowering efficacy of plant stanols in a new type of food supplement
 A new study shows that a chewable food supplement with added plant stanol esters can be used to help reduce elevated blood cholesterol levels
 Plant stanols work by reducing the absorption of cholesterol from the gut [...]



Back up

Mandatory labelling requirements for foods with added plant sterols/stanols

1. 'with added plant sterols' or 'with added plant stanols' in the same field of vision as the name of the food
2. the amount of added phytosterols, phytosterol esters, phytostanols or phytostanol esters content (expressed in % or as g of free plant sterols/plant stanols per 100 g or 100 ml of the food) shall be stated in the list of ingredients
3. **a statement that the food is not intended for people who do not need to control their blood cholesterol level**
4. **a statement that patients on cholesterol lowering medication should only consume the product under medical supervision**
5. **an easily visible statement that the product may not be nutritionally appropriate for pregnant and breastfeeding women and children under the age of five years**
6. **advice that the food is to be used as part of a balanced and varied diet, including regular consumption of fruit and vegetables to help maintain carotenoid levels**
7. in the same field of vision as the statement required under point 3 above, a statement that the **consumption of more than 3 g/day of added plant sterols/plant stanols should be avoided**
8. **a definition of a portion of the food or food ingredient concerned (preferably in g or ml) with the amount of the plant sterol/plant stanol that each portion contains**

Novel Foods (NF) authorisation of plant sterols

Plant stanols were already on the market prior to May 1997, hence implemented Novel Foods Regulation was not applicable

- Plant sterols are authorized under EU NF Regulation
- Extensive pre-market safety program basis for authorisation
- **Post-launch monitoring** as requirement of NF authorisation shows no over-consumption in target consumers and no unwanted consumption in un-target groups (e.g. children)

COMMISSION DECISION
of 24 July 2000
on authorising the placing on the market of 'yellow' fat spreads with added phyosterol esters' as a novel food or novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council
(notified under document number C(2000) 2121)
(Only the English text is authentic)
(2000/500/EC)

COMMISSION DECISION
of 31 March 2004
authorising the placing on the market of milk type products and yoghurt type products with added phyosterol esters as novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council
(notified under document number C(2004) 1245)
(Only the English text is authentic)
(2004/335/EC)

