

DANACOL REDUCES CHOLESTEROL: TRUE OR FALSE?

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1. Abstract:

Atherosclerosis and its main clinical complication, ischemic heart disease, are the leading cause of mortality in the western world. In their aetiology many **risk factors** are involved, among which **hypercholesterolemia**. As a result, many therapies have been proposed to reduce cholesterol levels and some products with this feature have flooded the market.

Danacol is a dairy fermented product enriched with **plant sterols**, present in the Spanish market since 2004. Active ingredients are plant sterols from vegetable oils. To achieve a significant biological effect in lowering LDL cholesterol a daily intake of **1.6g/day of active compounds** is required. The goal of the study is to make a review of Danacol and its active compounds in order to analyse the functional property of the product.

2. Cholesterol:

Cholesterol was discovered in 1770 by Pulletiere La Salle, who was able to isolate it from the liquid bile. Since 1843, atherosclerosis and its heart complications have been related to the abnormal metabolism of the lipids, connecting **cholesterol** with **heart diseases**.

However, it cannot be ignored that cholesterol is essential for most cells in the body, being of vital importance to the structure and function of the cell membrane, among other functions.

Cholesterol in mammals can be obtained through the diet (**exogenous pathway**) or by the novo synthesis in the cells of the body (**endogenous pathway**). Cholesterol can be stored in the cell in the form of an ester or as part of cell membranes as free cholesterol. Due to its insolubility in water, in order to be transported by biological fluids, cholesterol binds with phospholipids and proteins to form **lipoproteins**. In humans, LDL (low density lipoproteins) are responsible for transporting most of the cholesterol through blood plasma. Free cholesterol is found mainly on the surface of the lipoprotein along with phospholipids and proteins, while esterified cholesterol and triglycerides are part of the hydrophobic matrix. It is considered that a subject suffers **hypercholesterolemia** when they present values of total cholesterol ≥ 200 mg / dl and LDL-C values ≥ 130 mg / dl.

3. Danacol:

Danacol is a fermented low fat dairy product **enriched with phytosterols** (sterols / stanols), which aims to lower blood levels of LDL cholesterol and total cholesterol.

The active ingredients of the product, phytosterol esters, are from vegetable oils and are a mixture of β -sitosterol $\leq 80\% \leq 40\%$ campesterol, stigmasterol $\leq 30\% \leq 15\%$ β -sitostanol, campestanol $\leq 5\%$ brasicasterol $\leq 3\%$ and $\leq 3\%$ other phytosterols.

Danacol is aimed at a segment of population with concentrations of total cholesterol and LDL-C on blood considered **risky**.

Danone says that daily consumption of Danacol, along with a healthy lifestyle, is an easy and powerful way to **reduce cholesterol levels** with visible results after three weeks.

Use specifications proposed by Danone:

Consumers should take 1.6 g per day of the active component. The content of phytosterols in Danacol is 1.6 g in the drinking product and 0.8 g in the gel product (only sold in France). So the recommendation described by Danone is 1 serving of liquid product and 2 portions of gel product.

To achieve the reduction of blood cholesterol described, the consumer must **take** the product **daily**.

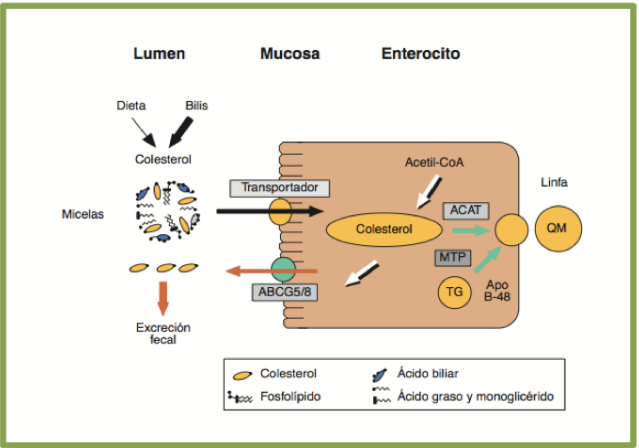
4. Plant sterols and stanols:

Phytosterols and phytostanols (saturated forms of phytosterols that have no double bond present in their molecule) come from **plant sterols**, which are found in fruits, seeds and leaves of almost all known plants. This means that we found them as part of the **human diet**. However, unlike cholesterol, these sterols are not synthesized by the body and are poorly absorbed by the intestine.

Phytosterols chemically identified add to more than **25 different structures**. However, those who are in greater proportion are **α -sitosterol (C29), campesterol (C28) and stigmasterol (C29)**.

It is estimated that the daily intake of phytosterols, which obviously is very variable because it depends on the eating habits of the population, is between 160 mg/day and 500 mg/day, with a higher proportion in vegetarian diets.

2. Intestinal absorption of cholesterol:



5. Mechanism of action of phytosterols and phytostanols:

The mechanism of action by which phytosterols and phytosterol make their hypocholesterolemic effect can be placed in **three different levels**.

1. Plant sterols inhibit cholesterol absorption in the intestine **moving it from mixed micelles**. Because plant sterols are more hydrophobic than cholesterol (greater length and complexity of the side chain) they have more affinity to join micelles than cholesterol.

2. Plant sterols **inhibit ACAT-2** preventing the re-esterification of cholesterol and its incorporation into chylomicrons, stimulating this way the flow towards the intestinal lumen.

3. Plant sterols increase the activity and **expression of ABC type transporters**, accelerating the flow of cholesterol from the enterocyte into the intestinal lumen.

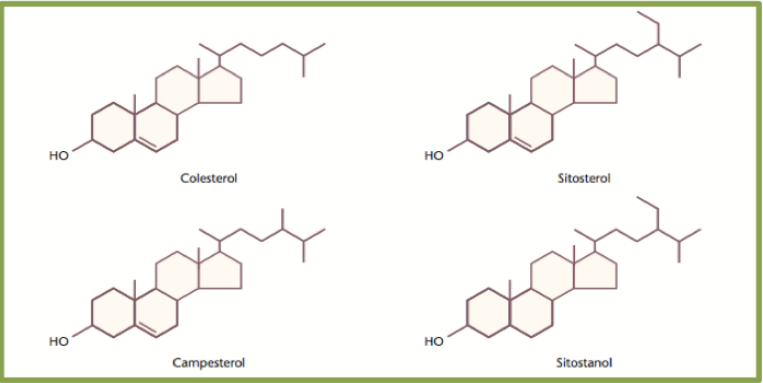
Nuclear receptors LXR α and β are involved in lipid metabolism. Recently it has been shown that activation of LXR increases the **expression of ABC G5/G8** (which are responsible for pumping cholesterol from the enterocyte to intestinal lumen). Plant sterols interact with LXR receptors causing activation and the subsequent expression of transporters ABCG5/G8.

4.

	Colesterol	Fitosteroles	Fitostanoles
Ingestión en la dieta (mg/día)	300-500	200-400	<10
Fuente dieta	Mantequilla, huevos, carne	Aceites vegetales, cereales	Aceite coco, otros aceites
Síntesis endógena	Colesterol biliar (800-1200 mg/día)	No	No
Tasa absorción (%)	40-60	<5	0,1-2
Concentración plasma (mg/dL)	140-320	0,3-1,7	0,3-0,6
Excreción (%)	40-60	>95	>98

4.

Chemical structure of cholesterol and main plant sterols:



6. Conclusions:

After long years of research, it has been concluded that an intake of at least 1.6 g / day of plant esters lowers blood cholesterol levels.

Danacol meets all the requirements necessary to cause the reduction of cholesterol levels in blood so it can be marketed as a **functional product** with this reducing capacity.

Personally, I think it would be a good idea to reinforce education in this field, starting in primary schools and teaching children **good diet habits** and a **healthy lifestyle**, avoiding exposing them to the factors of cardiovascular disease that are most extensive and devastating in our society.