Effect of low-fat, fermented milk enriched with plant sterols on serum lipid profile and oxidative stress in moderate hypercholesterolemia.

Hansel B., Nicolle C., Lalanne F. et al.

Study design

- Multicentre, parallel group, double-blind, controlled study
- At visit 0, 365 hypercholesterolemic subjects were screened and crossed consumption of soy phytosterol-enriched foods. After 2 weeks (Visit 1), the 3-week run-in period started, subjects took two pots a day of plain Taillefine® yoghurt. At visit 2, 209 subjects were randomly assigned to two 125g pots/day (one intake) of either control (plain fermented dairy product) or active product (fermented dairy product enriched with phytosterol esters to an equivalent of 0.8g of phytosterols per unit: Danacol®). The allocation was double-blind and lasted 6 weeks, with an intermediate visit after 3 weeks. Serum lipids were determined at screening, on D21 and on D42. Serum lipids, plasma phytosterols, β-carotene, C-reactive protein (CRP) and isoprostanes were determined five days before inclusion (D0) and on final visit (D42). Diet supervision (± questionnaire) was performed at all visits.

Study population

- Inclusion criteria:
  - Hypercholesterolemic subjects of both sexes, aged 18 to 75 years not treated with lipid-lowering drugs with the exception of monotherapy with one statin
  - Stable serum LDL-cholesterol levels: ≥ 130mg/dL and ≤ 190mg/dL (verified at V2)
  - Normal weight or overweight (BMI ≥ 19 and ≤ 30 kg/m2)
  - Assessed at V2: compliance to consumption of Taillefine® ≥ 80%
  - Lipid-lowering drug other than a statin
  - Diabetes; history of symptomatic cardiovascular disease in 6 months prior to the study
  - Triglyceride level ≥ 250mg/dL (verified at V2)
  - Intolerance to dairy products or refusal to consume
  - For females: pregnancy or breast-feeding
  - Assessed at V2: ß-sitosterol level > 10,000ng/mL, campesterol level > 10,000ng/mL

Key findings

- Results of the Hansel et al. trial highlight the beneficial effects of daily consumption of the sponnable, plant sterol-enriched, low fat, fermented milk product Danacol®.
- With a low dosage of plant sterols (1.6g/day), daily consumption of sponnable Danacol®:
  - Provides a clinically relevant LDL-cholesterol reduction: -9.5% at 3 weeks (p<0.001 vs control group) maintained throughout consumption period: -7.8% at 6 weeks (p<0.001 vs control group)
  - With an additive LDL-lowering effect in patients on stable statin therapy
  - Without impact on HDL-cholesterol or triglyceride levels
  - Without affecting two markers of oxidative stress
  - Is safe and well-tolerated, leading only to a moderate increase in ß-sitosterol (within the normal individual variability range)

Evaluation

- Main outcome criterion:
  - Evolution of serum LDL-cholesterol concentration
- Secondary outcome criteria:
  - Evolution of total serum cholesterol, HDL-cholesterol and triglyceride concentrations
- Safety evaluation:
  - Systematic recording of adverse events and vital signs
  - Changes in serum concentrations of ß-sitosterol, campesterol, and campesterol

"Thus, the consumption of Danacol® may represent a useful additive therapeutic measure to the classic hypocholesterolemic diet of the American Heart Association in hypercholesterolemic patients at high cardiovascular disease risk."

Pr. Eric Bruckert, main investigator of the study

Clinical considerations

Effects of daily intake of plant sterol-enriched fermented milk on:
- Blood lipid profile (especially LDL-cholesterol)
- Safety parameters
- Oxidative stress

Danacol®, the sponnable yoghurt, effects on lipids, sterols, and oxidative stress in patients with hypercholesterolaemia.
Effect of low-fat, fermented milk enriched with plant sterols on serum lipid profile and oxidative stress in moderate hypercholesterolemia.

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**Clinical trial**

**Clinical considerations**

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Danacol®, the spoonable yoghurt, effects on lipids, sterols, and oxidative stress in patients with hypercholesterolemia.
Daily consumption of Danacol® yoghurt significantly lowers cholesterol...

- Significant reduction of LDL-cholesterol after just 3 weeks only in the phytosterol-enriched group (p<0.0001), maintained up to 6 weeks

97.7% of subjects were compliant at week 6 (consuming >80% of scheduled servings)

Nutritional composition of Danacol®

- Energy: 630kJ/255kcal
- Protein: 6.1g
- Carbohydrates: 8.0g (of which sugars 2.1g)
- Fat (excluding sterols): 0.4g (of which saturates 0.2g)
- Plant sterol (equivalent as free sterols): 0.3g
- Fibre: 0g
- Calcium: 194mg
- Sodium: 90mg

Further results on inflammation...

- No change in high-sensitivity C-reactive protein versus control group
- No significant change in plasma campesterol or in plasma lathosterol, a marker of endogenous cholesterol synthesis

To help hypercholesterolemia management:

- 67% of subjects showed a >5% decrease in LDL-cholesterol after consuming Danacol® for 6 weeks

Danacol® confers a similar benefit in patients on stable statin therapy.

- 8.0 ± 2.1% vs 8.4 ± 1.2% decrease in LDL-c in statin-treated and untreated subjects respectively, p=0.09

No significant change in HDL-cholesterol or triglycerides after consuming Danacol® for 6 weeks

- No adverse effect related to the consumption of Danacol®

Tolerance Data

- Increase of plasma β-sitosterol (35% compared to control group)
- No significant change in plasma campesterol or in plasma lathosterol, a marker of endogenous cholesterol synthesis

Danacol® Compliance

- 97.7% of subjects were compliant at week 6 (consuming >80% of scheduled servings)

"Compliance is obviously a key aspect of therapeutic strategies"

Spoonable Danacol® (plain*) per 125g serving

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… without affecting ‘good’ cholesterol

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… with no deleterious effects on markers of oxidative stress

- No significant change in:
  - serum β-carotene levels when normalised to LDL-cholesterol between the two groups
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No added sugar
Low in fat

Danacol® Compliance

- 97.7% of subjects were compliant at week 6 (consuming >80% of scheduled servings)

“Compliance is obviously a key aspect of therapeutic strategies”

Tolerance Data

- Increase of plasma β-sitosterol (35% compared to control group)
- No significant change in plasma campesterol or in plasma lathosterol, a marker of endogenous cholesterol synthesis

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Further results on inflammation...

No significant change in high-sensitivity C-reactive protein versus control group.

To help hypercholesterolaemia management:

Daily consumption of Danacol® yoghurt significantly lowers cholesterol…

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To help hypercholesterolaemia management:
Effect of low-fat, fermented milk enriched with plant sterols on serum lipid profile and oxidative stress in moderate hypercholesterolemia.


CLINICAL TRIAL

Study design

Multicentre, parallel group, double-blind, controlled study

At visit 0, 365 hypercholesterolaemic subjects were screened and ceased consumption of any phytosterol-enriched food. After 2 weeks (visit 1), the 3-month run-in period started, subjects took two pots a day of plain Taillefine® yoghurt. At visit 2, 298 subjects were randomly assigned to two 170g pots/day (one intake) of either control (plain fermented dairy product) or active product (fermented dairy product enriched with phytosterol esters in an equivalent of 0.8 grams of two phytosterols per unit: Danacol®). The allocation was double-blind and lasted 6 weeks, with an intermediate visit after 3 weeks. Serum lipids were determined at screening, on D21 and on D42. Serum lipids, plasma phytosterols, β-carotene, C-reactive protein (CRP) and isoprostanes were determined five days before inclusion (D0) and on final visit (D42). Blood sampling (via a questionnaire) was performed at all visits.

Study population

Inclusion criteria:
- Hypercholesterolaemic subjects of both sexes, aged 18 to 75 years not treated with lipid-lowering drugs with the exception of monotherapy with one statin
- Stable serum LDL-cholesterol levels: ≥ 130mg/dL and ≤ 190mg/dL (verified at V2)
- Normal weight or overweight (BMI ≥ 19 and ≤ 30kg/m2)
- Assessed at V2: compliance to consumption of Taillefine® ≥ 80%
- Lipid-lowering drug other than a statin
- Diabetes; history of symptomatic cardiovascular disease in 6 months prior to the study
- Triglyceride level ≥ 250mg/dL (verified at V2)
- Intolerance to dairy products or refusal to consume
- For females: pregnancy or breast-feeding
- Assessed at V2: β-sitosterol level > 10,000ng/mL, campesterol level > 10,000ng/mL

Evaluation

Main outcome criterion:
- Evolution of serum LDL-cholesterol concentration

Secondary outcome criteria:
- Evaluation of total serum cholesterol, HDL-cholesterol and triglyceride concentrations
- Safety evaluation:
  - Systematic recording of adverse events and vital signs
  - Changes in serum concentrations of 8-cis-retinol, CFU, 4-hydroxy- and 4-isoprostanes

Key findings

Results of the Hansel et al trial highlight the beneficial effects of daily consumption of the sponnable, plant sterol-enriched, low fat, fermented milk product Danacol®.

With a low dosage of plant sterols (1.6g/day), daily consumption of sponnable Danacol®:
- Provides a clinically relevant LDL-cholesterol reduction: -8.5% at 3 weeks (p<0.001 vs control group) maintained throughout consumption period: -7.8% at 6 weeks (p<0.001 vs control group)
- With an additive LDL-lowering effect in patients on stable statin therapy
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"Thus, the consumption of Danacol® may represent a useful additive therapeutic measure to the classic hypocholesterolemic diet of the American Heart Association in hypercholesterolemic patients at high cardiovascular disease risk."

Pr. Eric Bruckert, main investigator of the study

Clinical considerations

Effects of daily intake of plant sterol-enriched fermented milk on:
- Blood lipid profile (especially LDL-cholesterol)
- Safety parameters
- Oxidative stress

Danacol®, the sponnable yoghurt, effects on lipids, sterols, and oxidative stress in patients with hypercholesterolemia.

Catherine Nicolle
catherine.nicolle@danone.com
Carine Emsellem
carine.emsellem@danone.com
Effects of a phytosterol-enriched dairy product on lipids, sterols and 8-isoprostane in hypercholesterolemic patients: a multicenter Italian study.

Mannarino E., Pirro M., Cortese C. et al.

Nutrition, Metabolism & Cardiovascular Diseases (2008)

Study design

Multicentre, parallel group, double-blind study

CLINICAL TRIAL

Clinical considerations

Effects of daily intake of plant sterol-enriched fermented milk on:

> Plasma lipid profiles (especially LDL-cholesterol) and safety parameters
> A reliable marker of in vivo oxidation

Danacol®, the drinkable yoghurt, affects on lipids, sterols, and plasma isoprostanes in patients with hypercholesterolemia

Danacol®, 1 bottle of drinkable yoghurt Danacol® enriched with phytosterol esters to an amount equivalent to 1.6 grams of free phytosterols

Study population

Inclusion criteria:
- Hypercholesterolemic subjects of both sexes, aged 20-75 years, not treated with lipid lowering drugs with the exception of monotherapy with one statin (with blood analysis)
- LDL cholesterol ≥ 130 mg/dL and ≤ 190 mg/dL for over 3 months
- BMI ≥ 19 and ≤ 30 kg/m²

Exclusion criteria:
- Plasma triglyceride level ≥ 350 mg/dL
- Diabetes, previous cardiovascular event within the last 6 months
- Lipid lowering drug other than a statin
- Subject smoking more than 20 cigarettes/day
- Intolerance to dairy products or refusal to consume

Evaluation

Main outcome criteria:
- Evaluation of the concentration of serum LDL-cholesterol

Secondary outcome criteria and safety evaluation:
- Evaluation of the concentration of total serum cholesterol, HDL cholesterol and triglycerides
- Changes in serum concentration of β-carotene, lathosterol, and plasma 8-isoprostane levels
- Systemic recording of adverse events and vital signs

Key findings

Results of the Mannarino E. et al. trial highlight new evidence of the beneficial effects of daily consumption of the plant sterol-enriched low fat fermented milk product Danacol®.

Daily consumption of Danacol® provides:

- A significant reduction in LDL-cholesterol from 3 weeks: -10.5% (p<0.001 vs. control group) maintained through 6 weeks: -12% (p<0.001 vs. control group)
- With a trend to additional effect in patients with higher levels of baseline LDL-cholesterol
- Preliminary evidence of an equal decrease in patients on stable statin treatment

No effect on:
- HDL-cholesterol or triglycerides, consistent with most trials conducted with phytosterols
- Plasma β-sitosterols and campesterols levels
- Plasma β-carotene/LDL-cholesterol ratio

An anti-oxidative effect through a significant reduction of plasma 8-isoprostane, a reliable marker of in vivo oxidation

“The use of phytosterols may thus represent a simple and safe tool to reduce plasma cholesterol in patients with mild cholesterol elevations, thus enhancing the attainment of LDL-cholesterol goal in hypercholesterolemic patients.”

Dr. E. Mannarino, main investigator of the study

Blood sampling

Consumption of one low fat dairy product with a main meal

Danacol®, n=57

Control, n=53

V2 (screening) n=116

V3 (randomisation)

V0 (screening) n=116

V1 (randomisation)

V4 (final visit)

Evaluation

- Multicentre, parallel group, double-blind study
- One hundred and eighty five moderate hypercholesterolemic subjects were screened and had to cease consumption of any food enriched with phytosterols. After 2 weeks, the run-in period started, for 2 weeks during which the subject took 1 cup per day of plain Vitasnella®, a low fat yoghurt. Subjects were randomly assigned to 1 bottle (equivalent to 1.6 grams of free phytosterols) of Danacol® enriched with phytosterol esters or a control group enriched with 1 bottle of a dairy product with no amount equivalent to 1.6 grams of free phytosterols. The allocation lasted 6 weeks, with 8 interobserver visits after 3 weeks. Serum lipids were determined at inclusion (baseline), interim visits (V2 and final visit V4). Serum lipid profiles, apolipoproteins (A1, A1c), plasma phytosterols, beta carotene, C-reactive protein (as CRP) and serum were determined at baseline (V0) and on final visit (V4).

Study population

- Inclusion criteria:
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Effects of daily intake of plant sterol-enriched fermented milk product Danacol®.

Danacol®, the drinkable yoghurt, affects on lipids, sterols, and plasma isoprostanes in patients with hypercholesterolemia

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Mannarino E., Pirro M., Cortese C. et al.
Nutrition, Metabolism & Cardiovascular Diseases (2008)

Clinical trial

Clinical considerations

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Study design

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Evaluation

- Main outcome criterion:
  - Evaluation of the concentration of serum LDL-cholesterol
- Secondary outcome criteria and safety evaluation:
  - Evaluation of the concentration of total serum cholesterol, HDL-cholesterol and triglycerides
  - Changes in serum concentrations of β-carotene, β-sitosterol, lathosterol, and plasma 8-isoprostane levels
  - Systemic recording of adverse events and vital signs

Blood sampling

Consumption of one low fat dairy product with each meal:

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<tr>
<td>Danacol®, n=52</td>
<td>28</td>
<td>12</td>
<td>21</td>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control, n=49</td>
<td>28</td>
<td>12</td>
<td>21</td>
<td>40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Danacol®, the drinkable yoghurt, affects on lipids, sterols, and plasma isoprostane in patients with hypercholesterolaemia
Daily consumption of Danacol®, the drinkable yoghurt, significantly lowers cholesterol...

>>> Significant reduction of LDL-cholesterol after 3 weeks only in the phytosterol-enriched group (p<0.001) maintained up to 6 weeks

A similar benefit in patients on stable statin therapy,

% LDL-cholesterol decrease after 6 weeks of daily consumption of Danacol®: -10.9 +/-2% vs. -11.5 +/-1.8% for those patients not taking a statin before randomisation. (Preliminary analysis, n=27 patients in Danacol® group and control group respectively)

A 2-fold greater reduction of LDL-C/HDL-C ratio in the Danacol® group

"a good predictor of cardiovascular risk in hypercholesterolemic patients..."

... while providing an anti-oxidative effect through the reduction of plasma 8-isoprostane

>>> Significantly greater reduction of plasma 8-isoprostane in the phytosterol-enriched group.

Risk evaluation of oxidative burden with phytosterols with measurement of isoprostane

Plasma 8-Isoprostane... "extremely accurate measure of oxidant injury in vivo..."

Nutritional composition of Danacol®

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Drinkable Danacol® (plain*) per 100g serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>37 kcal/157 kJ</td>
</tr>
<tr>
<td>Protein</td>
<td>3.5 g</td>
</tr>
<tr>
<td>Carbohydrates:</td>
<td></td>
</tr>
<tr>
<td>of which sugars</td>
<td>4.7 g</td>
</tr>
<tr>
<td>Fat (excluding sterols):</td>
<td></td>
</tr>
<tr>
<td>of which saturates</td>
<td>0.6 g</td>
</tr>
<tr>
<td>Plant sterol</td>
<td>equivalent as free sterol</td>
</tr>
<tr>
<td>Fibre</td>
<td>0.7 g</td>
</tr>
<tr>
<td>Calcium</td>
<td>123 mg</td>
</tr>
<tr>
<td>Sodium</td>
<td>40 mg</td>
</tr>
</tbody>
</table>

* No added sugar
* Low in fat

Positive effects of Danacol® on lipid profile

>>> A trend towards a greater effect among patients with higher LDL cholesterol at baseline (p=0.08 between tertiles)

More than 1 in 2 patients experienced a LDL cholesterol reduction of over 10%
Daily consumption of Danacol®, the drinkable yoghurt, significantly lowers cholesterol...

- Significant reduction of LDL-cholesterol after 3 weeks only in the phytosterol-enriched group (*p* < 0.001) maintained up to 6 weeks

- Positive effects of Danacol® on lipid profile
  - A trend towards a greater effect among patients with higher LDL cholesterol at baseline (*p* < 0.08 between tertiles)
  - Significantly greater reduction of plasma 8-isoprostane in the phytosterol-enriched group.
  - More than 1 in 2 patients experienced a LDL cholesterol reduction of over 10%

- Nutritional composition of Danacol®
  - Energy: 37 kcal/157 kJ
  - Protein: 3.5 g
  - Carbohydrates: 4.4 g
    - of which sugars: 4.1 g
    - of which saturates: 0.6 g
    - Plant sterol (equivalent as free sterol): 1.0 g
  - Fat: 0.7 g
  - Calcium: 123 mg
  - Sodium: 40 mg

  - No added sugar
  - Low in fat

- To help hypercholesterolemia management:
  - A similar benefit in patients on stable statin therapy.
    - % LDL decrease after 6 weeks of daily consumption of Danacol®: -10.5 ±2.5% vs. -11.5 ±1.8% for those patients not taking a statin before randomisation.
    - (Preliminary analysis, *n* = 7 patients in Danacol® group and control group respectively)

- A 2-fold greater reduction of LDL-C/HDL-C ratio in the Danacol® group
  - "a good predictor of cardiovascular risk in hypercholesterolemic patients..."

- Risk evaluation of oxidative burden with phytosterols with measurement of isoprostane
  - Plasma 8-Isoprostane...
    - "extremely accurate measure of oxidant injury in vivo..."

- More than 1 in 2 patients experienced a LDL cholesterol reduction of over 10%

- Change of LDL-C (mg/dL) %

- Change in LDL-C concentrations after 3 and 6 weeks of Danacol® (1.6 g/d) or control fermented milk consumption

- *p* < 0.001 for between group comparisons

- Change in plasma 8-isoprostane concentrations after 6 weeks of Danacol® (1.6 g/d) or control fermented milk consumption

- *p* = 0.002

- Reduction of LDL-C according to baseline tertiles of LDL-C in subjects taking either Danacol® (1.6 g/d) or control product

- *p* < 0.01

- Reduction of 8-Isoprostene in tertiles of LDL-C in subjects taking either Danacol® (1.6 g/d) or control product

- *p* < 0.05 vs. control

- Reduction of LDL-C/HDL-C ratio in subjects taking either Danacol® (1.6 g/d) or control product
Effects of a phytosterol-enriched dairy product on lipids, sterols and 8-isoprostane in hypercholesterolemic patients: a multicenter Italian study.

Mannarino E., Pirro M., Cortese C. et al.

Nutrition, Metabolism & Cardiovascular Diseases (2008)

CLINICAL TRIAL

Clinical considerations
Effects of daily intake of plant sterol-enriched fermented milk on:

- Plasma lipid profiles (especially LDL-cholesterol) and safety parameters
- A reliable marker of in vivo oxidation

Danacol®, the drinkable yoghurt, affects on lipids, sterols, and plasma isoprostanes in patients with hypercholesterolemia

Key findings
Results of the Mannarino E. et al trial highlight new evidence of the beneficial effects of daily consumption of the plant sterol-enriched low fat fermented milk product Danacol®.

Daily consumption of Danacol® provides:

- A significant reduction in LDL-cholesterol from 3 weeks: -10.5% (p<0.001 vs. control group) maintained through 6 weeks: -12% (p<0.001 vs. control group)
- With a trend to additional effect in patients with higher levels of baseline LDL-cholesterol
- Preliminary evidence of an equal decrease in patients on stable statin treatment
- No effect on: HDL-cholesterol or triglycerides, consistent with most trials conducted with phytosterols
- Plasma β-sitosterols and campesterol levels
- Plasma β-carotene/LDL-cholesterol ratio

- An anti-oxidative effect through a significant reduction of plasma 8-isoprostane, a reliable marker of in vivo oxidation

“The use of phytosterols may thus represent a simple and safe tool to reduce plasma cholesterol in patients with mild cholesterol elevations, thus enhancing the attainment of LDL-cholesterol goal in hypercholesterolemic patients.”

Dr. E. Mannarino, main investigator of the study
Plant sterol-enriched fermented milk enhances the attainment of LDL-cholesterol goal in hypercholesterolemic subjects.

Key findings
Reports from the Plana et al. trial highlight the beneficial effects of daily consumption of the drinkable, plant sterol-enriched, low fat, fermented milk product Danacol®.

With a low dosage of plant sterols (1.6g/day), daily consumption of drinkable Danacol®, ensures:

- A significant reduction in LDL-cholesterol:
  - From 3 weeks: -12.2% (p<0.001 vs. control group) maintained through 6 weeks: -10.6% (p<0.001 vs. control group)
- An additive effect was observed in patients on stable statin therapy at baseline
- Without affecting HDL-cholesterol or triglycerides
- 2- to 3-fold more people attain their target cholesterol levels (21/43 vs. 8/40 for the control group).

“...by taking a daily dose of the product [Danacol®], the mean relative [CVD] risk reduction would be about 10%.”

Dr. Luis Masana, main investigator of the study

Study design
- Multicentre, randomised, double-blind, placebo-controlled, parallel group study

Eighty-four hypercholesterolemic subjects were screened and followed a standard Mediterranean diet plus 1 low-fat drinkable yoghurt per day during the 4-week run-in period.
- At Visit 1, subjects were randomly assigned to 100 mL/day of either control (liquid yoghurt: milk fermented with S. thermophilus and L. bulgaricus), or active product 1 (liquid yoghurt Danacol® milk fermented with S. thermophilus and L. bulgaricus enriched with plant sterols to an equivalent of 1.6 grams of free phytosterols per day).
- The allocation was double blind and lasted 6 weeks, with an intermediate visit at 3 weeks.
- Serum lipids, vitamin A and ß-carotene were determined at screening, randomisation, follow-up and final visits (D-28, D0, D21 and D42).
- Measurements at D2 and D4 were performed in duplicate, with a separation of 2 to 3 days.

Study population
- Inclusion criteria:
  - Hypercholesterolemic subjects of both sexes, aged 18 to 75 years
  - Serum LDL-cholesterol levels: > 130 mg/dL if 10-year cardiovascular (CV) risk ≤ 20% and no ischemic heart disease,
    > 100 mg/dL if 10-year CV risk > 20% or ischemic heart disease
- Exclusion criteria:
  - Treated with lipid lowering drugs with the exception of monotherapy with a statin

Evaluation
- Main outcome criterion:
  - Change from D0 to D42 of the concentration of serum LDL-cholesterol
- Secondary outcome criteria:
  - Change from D0 to D42 of the concentration of serum total cholesterol, HDL-cholesterol and triglycerides
  - Proportion of subjects who reach their target LDL-cholesterol levels according to respective risk at D21 and D42
- Safety evaluation:
  - Systematic recording of adverse events and vital signs
  - Changes in serum concentrations of ß-carotene, ß-carotene adjusted by LDL-cholesterol, vitamin A, C-reactive protein (CRP), ß-sitosterol, campesterol and lathosterol

Clinical considerations
Effects of daily intake of plant sterol-enriched fermented milk on:
- Blood LDL-cholesterol levels
- Percentage of patients attaining their therapeutic targets

Danacol®, the drinkable yoghurt, effects on lipids, sterols, in patients with hypercholesterolemia

Danacol® - December 2008.

V0 V1 V2 V3

D -28 Control, n=40
D 0 Danacol®, n=44
D 21
D 42

Blood sampling
Danacol®, n=44
Control, n=40

V0 V3 V2

Study design

Study population

Evaluation

Clinical considerations
Plant sterol-enriched fermented milk enhances the attainment of LDL-cholesterol goal in hypercholesterolemic subjects.

Plana N., Nicolle C., Ferre R. et al.

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Daily consumption of Danacol® yoghurt lowers LDL-cholesterol by more than 10% on average... Significant reduction of LDL-cholesterol after just 3 weeks only in the phytosterol enriched group (p<0.001), maintained up to 6 weeks

Nutritional composition of Danacol®

- No significant change in the β-carotene/LDL cholesterol ratio

Tolerance data

- Increase of plasma sitosterol and campesterol concentrations by 26.7% and 38.8% respectively
- In accordance to the product composition
- Final values of plasma phytosterol within normal ranges

To help hypercholesterolemia management:

... helping patients to meet their cholesterol targets

- Over twice as many subjects receiving Danacol® achieved predefined LDL-cholesterol targets compared to the control group

With Danacol®, about 50% of patients attained recommended LDL-c target values, compared to 20% for the control group

About 70% (n=4) of patients at high cardiovascular risk on target

No adverse effect related to the consumption of Danacol®

Action of Danacol® on fat-soluble compound

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Providing the appropriate diet food can minimise or compensate carotenoid-lowering effect

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  - Change from D0 to D42 of the concentration of serum LDL-cholesterol
- **Secondary outcome criteria:**
  - Change from D0 to D42 of the concentration of serum total cholesterol, HDL-cholesterol and triglycerides
  - Change from D0 to D21 of the concentration of serum total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides
  - Proportion of subjects who reach their target LDL-cholesterol levels according to respective risk at D21 and D42
- **Safety evaluation:**
  - Systematic recording of adverse events and vital signs
  - Changes in serum concentrations of 5-carnitine, 8-carnitine adjusted by LDL-cholesterol, vitamin A, C-reactive protein (CRP), HDL-cholesterol, proteinuria and albuminuria

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  - $\%$ LDL decrease after 6 weeks of daily consumption of Danacol® - $10.5 \pm 2\%$ vs. $11.5 \pm 1\%$ for those patients not taking a statin before randomisation. (Preliminary analysis: $n=27$ patients in Danacol® group and control group respectively)

Nutritional composition of Danacol®

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Danacol® (g/d)</th>
<th>Control (g/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>37kcal/157kJ</td>
<td>37kcal/157kJ</td>
</tr>
<tr>
<td>Protein</td>
<td>3.5g</td>
<td>3.5g</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>4.4g</td>
<td>4.4g</td>
</tr>
<tr>
<td>of which sugars</td>
<td>4.1g</td>
<td>4.1g</td>
</tr>
<tr>
<td>Fat (excluding sterols)</td>
<td>0.6g</td>
<td>0.6g</td>
</tr>
<tr>
<td>of which saturated</td>
<td>0.6g</td>
<td>0.6g</td>
</tr>
<tr>
<td>Plant sterol (equivalent as free sterols)</td>
<td>1.6g</td>
<td>1.6g</td>
</tr>
<tr>
<td>Fibre</td>
<td>0.7g</td>
<td>0.7g</td>
</tr>
<tr>
<td>Calcium</td>
<td>123mg</td>
<td>123mg</td>
</tr>
<tr>
<td>Sodium</td>
<td>40mg</td>
<td>40mg</td>
</tr>
</tbody>
</table>

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