# CVD risk factor

U6

## Cardiovascular risk

Documento di consenso
e raccomandazioni per la prevenzione
cardiovascolare in Italia
2018

Documento coordinato da *Massimo Volpe*,
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in collaborazione con:

**SIMI** Società Italiana di Medicina Interna

**SID** Società Italiana di Diabetologia

**SIIA** Società Italiana dell'Ipertensione Arteriosa

**SISA** Società Italiana per lo Studio dell'Aterosclerosi

**CNR** Consiglio Nazionale delle Ricerche

**FMSI** Federazione Medico Sportiva Italiana

**GICR- IACPR** Gruppo Italiano di Cardiologia Riabilitativa e Preventiva
Italian Association for Cardiovascular Prevention, Rehabilitation and Epidemiology

**SIF** Società Italiana di Farmacologia

**SItI** Società Italiana di Igiene Medicina Preventiva e Sanità Pubblica


**Figura 1.** Network per la promozione di "vita in salute".

# CVD risk factor

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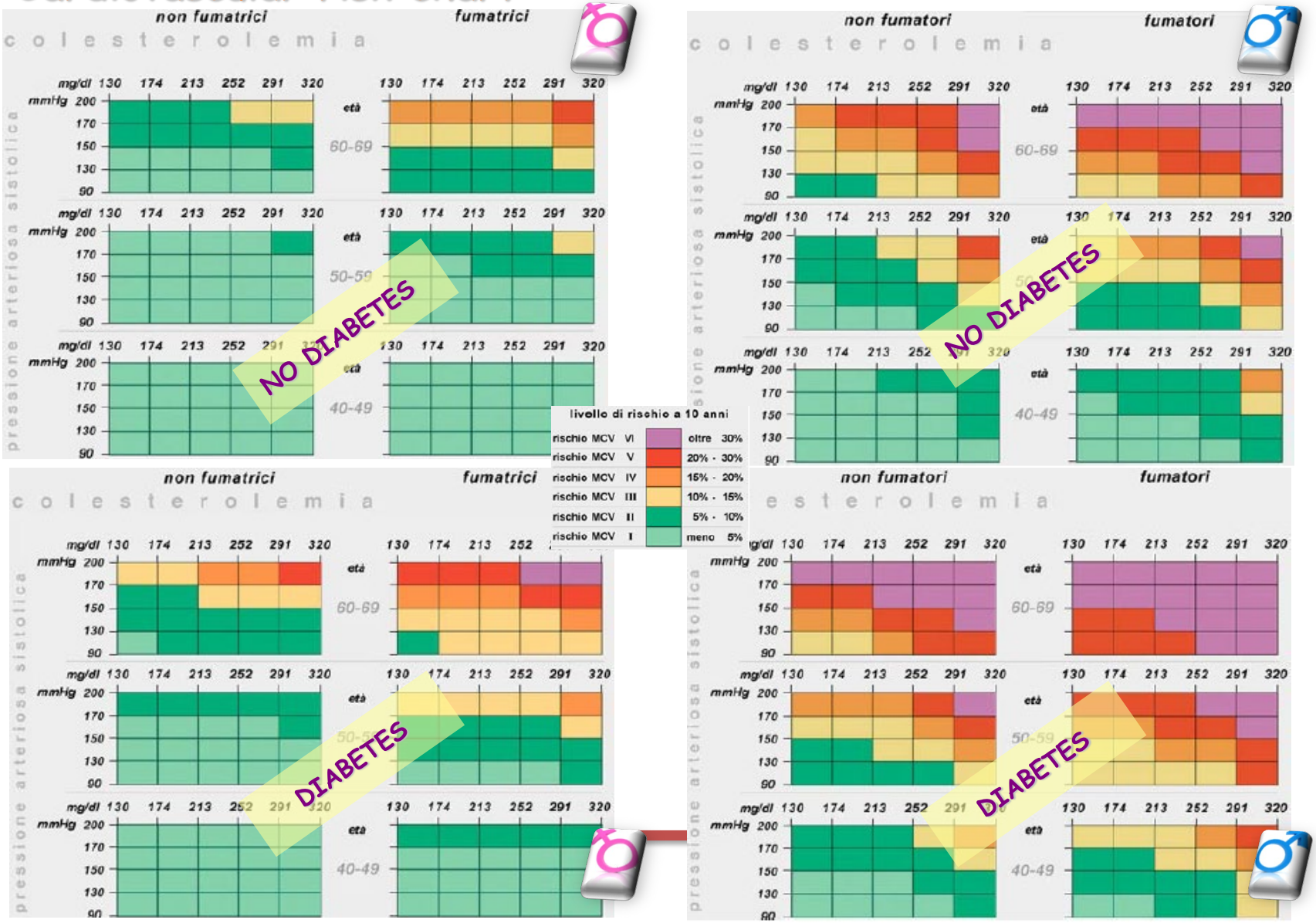
## Cardiovascular risk chart



# CVD risk factor

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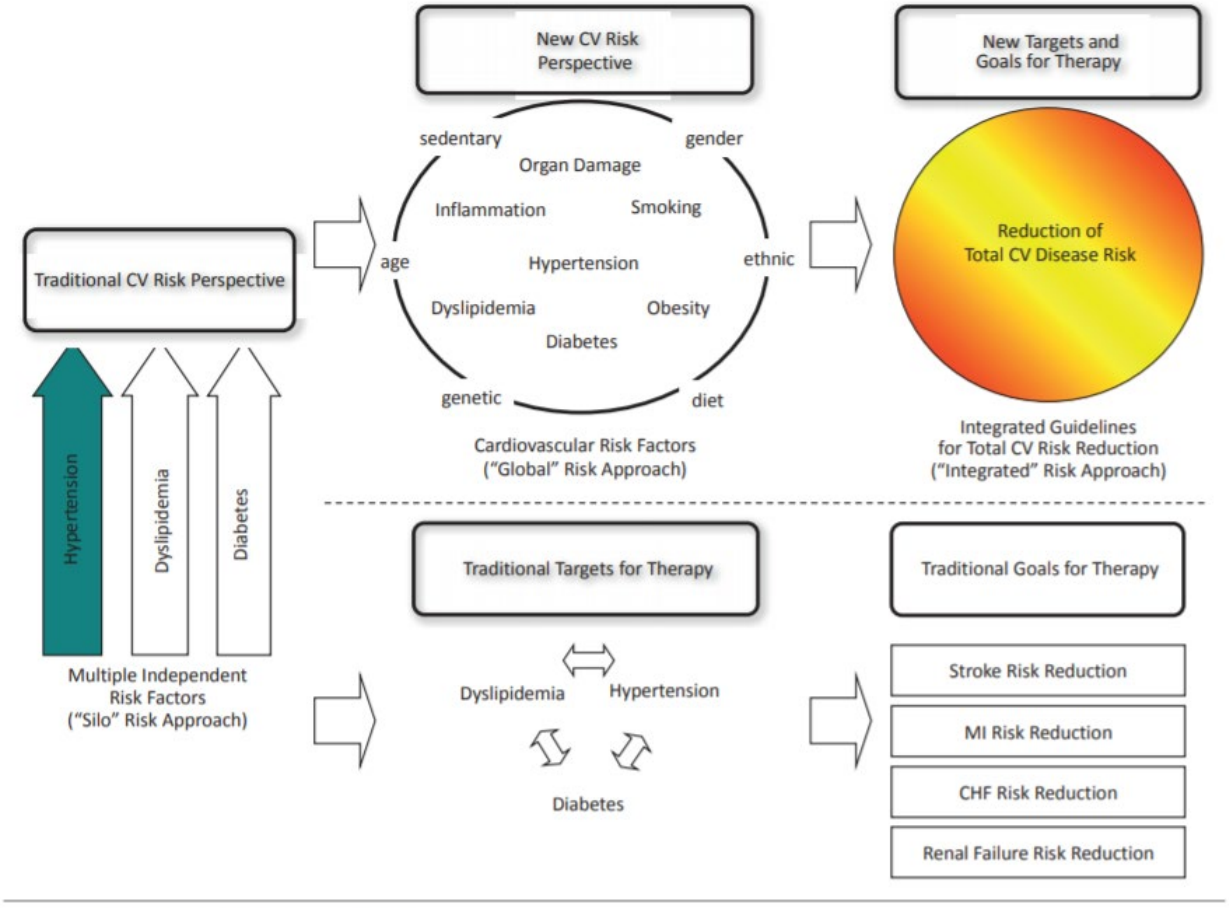


**Figura 5.** Prevenzione cardiovascolare integrata.
Modificata da Volpe et al.[14].

**Table 6** Lipid changes in some common conditions

| *Condition* | *Total cholesterol* | *HDL cholesterol* | *Triacylglycerol* |
|---|---|---|---|
| Diabetes mellitus | Normal or ↑ | ↓ | ↑ |
| Hypothyroidism | ↑ | ↑ | Can be ↑ |
| Chronic renal failure | Normal or ↑ | ↓ | ↑ |
| Nephrotic syndrome | ↑ | Often ↓ | Often ↑ |
| Cholestasis[a] | ↑ | ↓ | Can be ↑ |

[a]An abnormal lipoprotein called LpX is present.

# CVD risk factor

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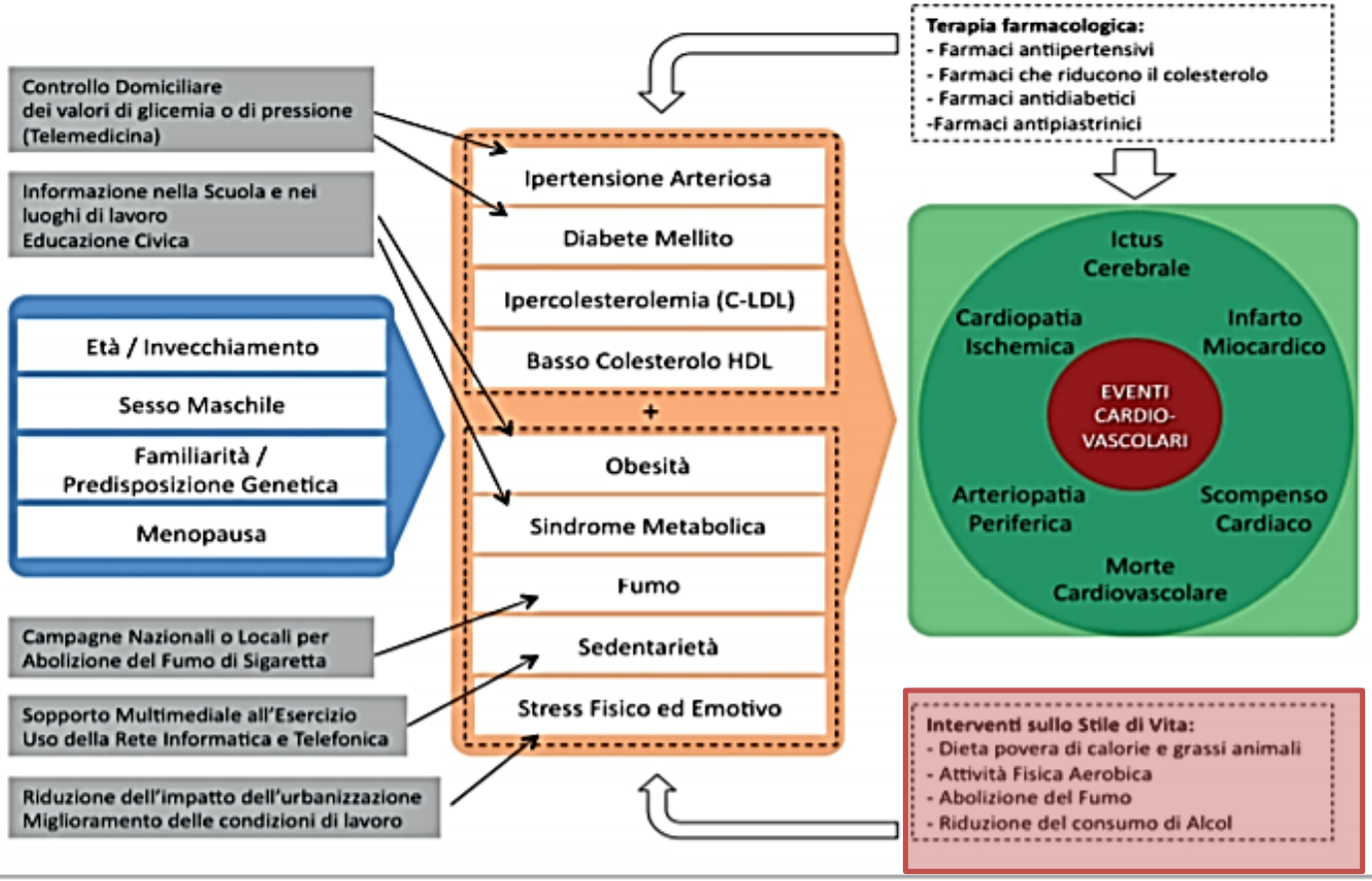


Nutraceutica

**Figura 6.** Possibili interventi farmacologici e non farmacologici per il trattamento e il controllo delle malattie cardiovascolari. C-LDL, colesterolo LDL.

# Phytosterols: example of overlapping food concepts

U6

Food based of phytosterols
as main active component
Enriched food…
Functional…Novel food…
Food supplement….? …..





**FOCUS ON NUTRACEUTICAL AND FUNCTINAL FOODS ON THE HYPERLIPIDEMIA**

**A RISK FACTOR OF CARDIOVASCULAR DESEASES**

# Phytosterols: example of overlapping food concepts

## HYPERLIPIDEMIA THE ROLE OF THE LIPOPROTEINS

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### Exogeneous pathway from diet

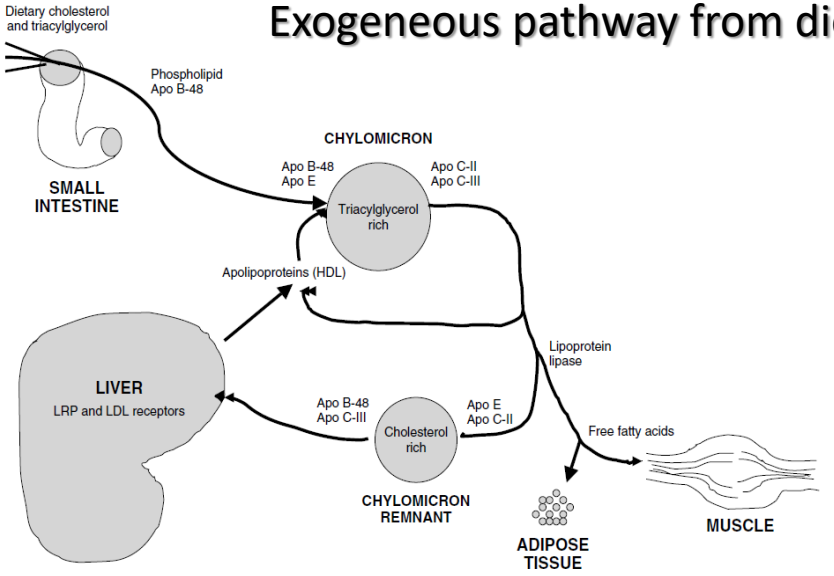



**Figure 3** Exogenous (dietary) lipid pathway. This shows the transport of dietary lipid from intestine to peripheral tissues and liver. Movement of apolipoprotein between high-density lipoprotein (HDL) and chylomicrons is shown. LRP, low-density lipoprol receptor-related protein.

### Endogeneous pathway from liver

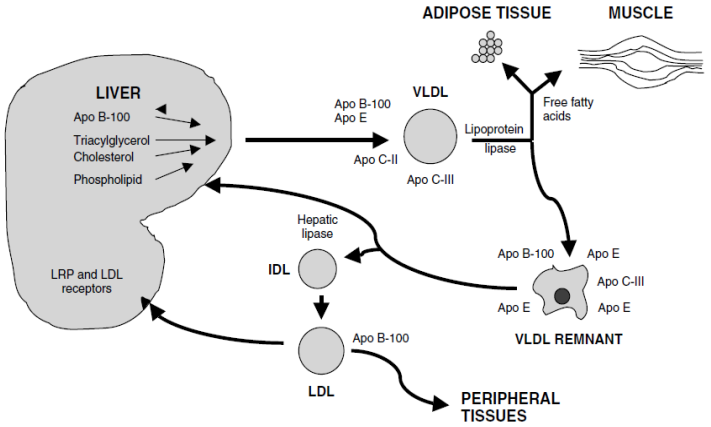



**Figure 4** Endogenous lipid pathway. This shows the formation of very low-density lipoprotein (VLDL) lipid particles ($VLDL_1$ and $VLDL_2$) in the liver with the interconversion, through the action of lipoprotein lipase, to VLDL remnant and through immediate-density lipoprotein (IDL) to LDL. Lipids are taken up from LDL both peripherally and in the liver. LRP, low-density lipoprotein receptor-related protein.

**Table 3** Fredrickson/WHO classification of hyperlipoproteinemia

| *Type* | *Lipids increased* | *Lipoprotein increased* |
|---|---|---|
| I | Triacylglycerol | Chylomicrons |
| II-a | Cholesterol | LDL |
| II-b | Cholesterol and triacylglycerol | LDL and VLDL |
| III | Cholesterol and triacylglycerol | Chylomicron remnants and IDL |
| IV | Triacylglycerol | VLDL |
| V | Cholesterol and triacylglycerol | Chylomicrons and VLDL |

### Reverse cholesterol transport

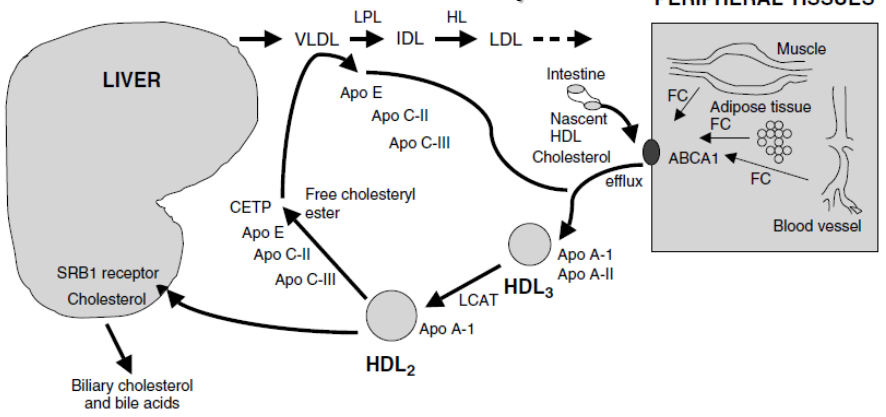
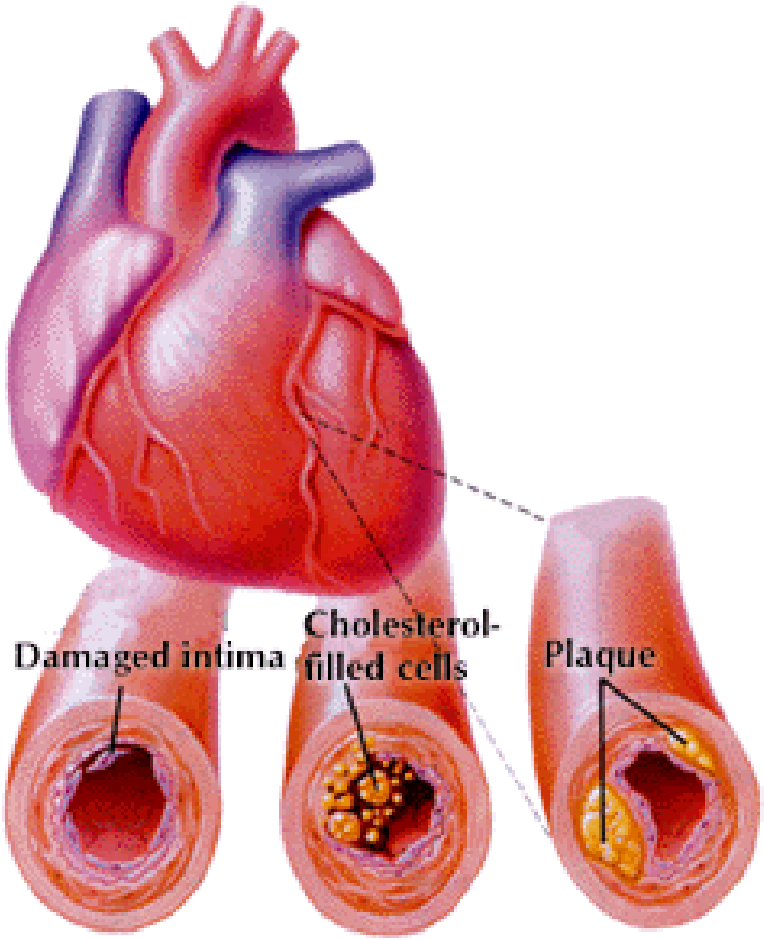



**Figure 5** Reverse cholesterol transport. Nascent high-density lipoprotein ($HDL_3$) picks up free cholesterol from the peripheries to become $HDL_2$, by a lecithin–cholesterol acyl transferase (LCAT)-mediated conversion. Cholesterol is then transported to the liver with uptake by the SRBI receptor. A second method of transport to the liver involves CETP-mediated esterification of HDL and conversion into immediate-density lipoprotein (IDL) and low-density lipoprotein (LDL), which is then taken up by the LDL receptor. This transfer of lipid between $HDL_2$ and VLDL/IDL maintains a cycle within HDL, and IDL/LDL deliver cholesterol from the peripheries to the liver. HDL may also deliver cholesterol directly to the liver. FC, free cholesterol.

# CLASSIFICAZIONE (SU QUADRO CLINICO) DELLE DISLIPIDEMIE

- IPERCOLESTEROLEMIE
- IPERTRIGLICERIDEMIE
- IPERLIDEMIE COMBINATE

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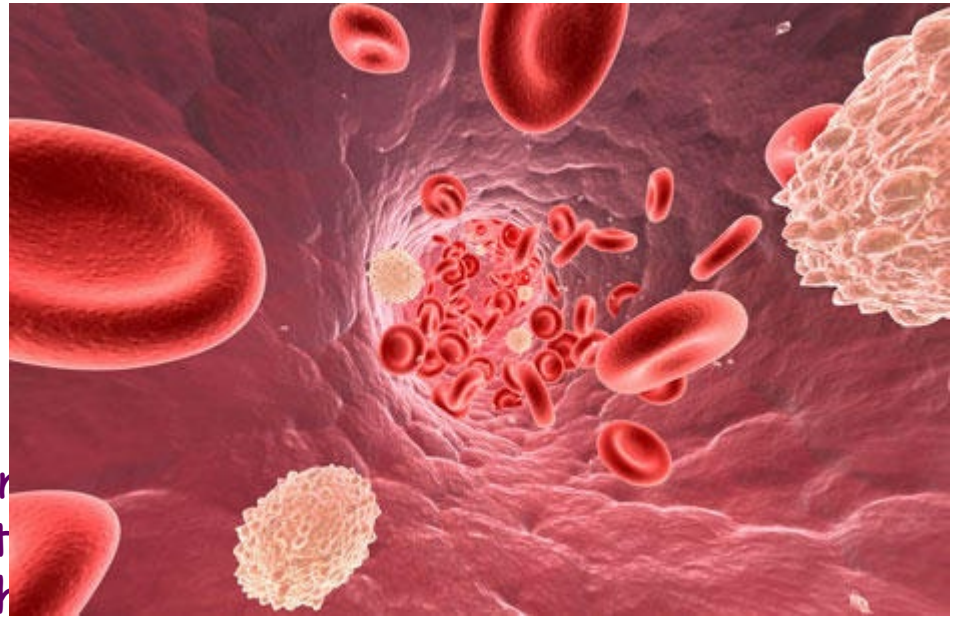
- IPERTRIGLICERIDEMIE



# Hypercolesterolemia a risk factor

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| National Cholesterol Education Program Cholesterol Guidelines | | | |
|---|---|---|---|
| | Desirable | Borderline High | High |
| Total Cholesterol | Less than 200 | 200 - 239 | 240 and higher |
| LDL Cholesterol (the "bad" cholesterol) | Less than 130 | 130 - 159 | 160 and higher |
| HDL Cholesterol (the "good" cholesterol) | 50 and higher | 40 - 49 | Less than 40 |
| Triglycerides | Less than 200 | 200 - 399 | 400 and higher |

COSTI SANITARI ANNUI
1,2 MILIARDI

**How to keep cholesterol and triglycerides at a favorable level**

Hypercholesterolemia is caused by unbalanced nutrition, smoking, physical inactivity, excess weight and diabetes; more rarely by a genetic alteration.

Healthy nutrition can reduce cholesterol level in the blood by 5% to 10%; a 10% reduction of cholesterolemia reduces the possibility of dying from a cardiovascular disease by 20%.

Therefore it is important to:
limit the consumption of fats in general replace saturated fats (butter, cheese, fatty meat, sausages) with poly-unsaturated (seed oil) and mono-unsaturated fats (olive oil) increase the consumption of fruit, vegetables and legumes reduce the consumption of desserts limit the consumption of alcohol.
It is also important to regularly do some **physical activity**, stop **smoking**, keep the **blood pressure** under control, and lose weight if you are **overweight**.

# Hyperlipidemia non pharma

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**Elimination of aggravating factors**
**Hyperlipoproteinemia may be aggravated by other pathological conditions (eg diabetes mellitus, alcoholism, hypothyroidism). It is necessary to reduce all risk factors that could accelerate the atherosclerotic process (hypertension, hyperglycemia, etc.).**

**-Diet**
**Low in saturated fats (animal origin); rich in fish, fruit, vegetables.**

**Phytosterols**
**PUFA polyunsaturated fatty acids**
**Soy Protein**
**Fermented red rice (monacoline)**
**Beta glucans**
**berberine**
**polycosanols**

# Hypercolesterolemia diet management

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**low in calories**
**Weight reduction**
**Increased physical activity**

**Tabella 4**
**Indicazioni dietetiche per soggetti con elevati valori di colesterolo plasmatico**

| Alimenti | Consigliati | Sconsigliati |
|---|---|---|
| Farinacei | Pasta normale o integrale, pane bianco o integrale, riso | Crackers, fette biscottate, pane all'olio, pasta all'uovo, biscotti, dolciumi |
| Carni | Manzo magro, coniglio, maiale magro, vitello magro, petto di tacchino, pollo senza pelle, bresaola, prosciutto crudo privato del grasso | Carni grasse e semigrasse come: oca, anatra, agnello, maiale, frattaglie, midollo, fegato, cervello |
| Pesci | Merluzzo, sogliola, palombo, trota, spigola, orata, salmone, cernia, tonno al naturale | Anguilla, capitone, pesci sott'olio, frutti di mare e crostacei |
| Latte e latticini | Latte scremato, yogurt magro, ricotta fresca | Latte intero, panna, formaggi grassi e semigrassi quali groviera, caciotta, fontina, pecorino, parmigiano, stracchino, provola, ricotta di pecora |
| Uova | | Tutti i cibi a base di uova |
| Verdura | Tutta | |
| Frutta | Frutta fresca | Frutta secca non a guscio quali i fichi e l'uva secchi; frutta conservata |
| Condimenti | Olio d'oliva, di mais, di soia, di girasole, di arachidi | Burro, lardo, strutto, margarina, salse troppo condite |
| Bevande | Caffè e tè non zuccherati | Bibite in genere e alcolici |
| Dolciumi | | Caramelle, cioccolato, zucchero, miele, pasticceria in genere |
| Tipi di cotture | Griglia, al vapore, al forno, bollito, al cartoccio, a microonde, allo spiedo | Frittura, arrosti conditi |

# Hypertrigliceridemies diet management

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Food sources of triglycerides are represented by carbohydrates, rather than by food fats, as the sugars do not have an effective storage system (just a little glycogen can be contained in the liver and muscles), while for lipids the storage is more adequate. For this reason the absorbed carbohydrates are transformed into triglycerides in the liver and then sent to the fat cells. In situations such as diabetes or insulin resistance this mechanism jams, therefore there is accumulation of triglycerides in fat cells (= hepatosteatosis) and excess of lipids in the blood (= hypertriglyceridemia).

**FOODS TO AVOID**:

· **Sugars in general**: white and cane sugar, honey, fructose and sweeteners based on fruit sugar, sweets, ice creams, sugary and non-sugary sugary drinks, jams and jams.

· **Fruit in large quantities**: fruit sugars increase triglycerides, so it should be limited to 2 fresh fruits per day. Pay attention to the fruit very rich in sugars (figs, persimmons, grapes, mandarins), which should be consumed occasionally. Avoid sugary dried fruit (= dried fruit).

· **Wine, bitters, digestives, aperitifs, beer**: alcohol determines the production of triglycerides by the liver, so the intake of drinks containing it must be eliminated. The inclusion of small doses of alcoholic beverages on an occasional basis must be agreed with the doctor and only in particular situations.

· **Sugary, non-carbonated and non-sugary drinks**: if you really can't avoid eating them, prefer light drinks or those sweetened with sweeteners other than fructose.

**FOODS TO BE USED WITH MODERATION**:

· **Bread, pasta, rice**: they should be consumed avoiding large portions, as the complex carbohydrates that compose them, once digested, release simple sugars. The same goes for potatoes.

· **Seasoning fats**: limit the consumption of raw used oil to 3-4 tablespoons per day, preferring the extra-virgin olive oil or monosemic seed oils (peanuts, sunflower, corn, soya, rice).

· **Mayonnaise**, various sauces: they are often high-calorie foods, to be used in a limited way.

FREE FOODS:

· Various vegetables: cooked or raw, they can be consumed freely, even in large quantities.

· Protein sources (meat, fish, eggs, legumes, milk and cheese): free intake of these foods, taking care to increase the consumption of fish (which contains fats from the omega-3 series, able to lower triglycerides).

· Unsweetened drinks: water, herbal tea, barley, tea, karkadè.

# Phytosterols

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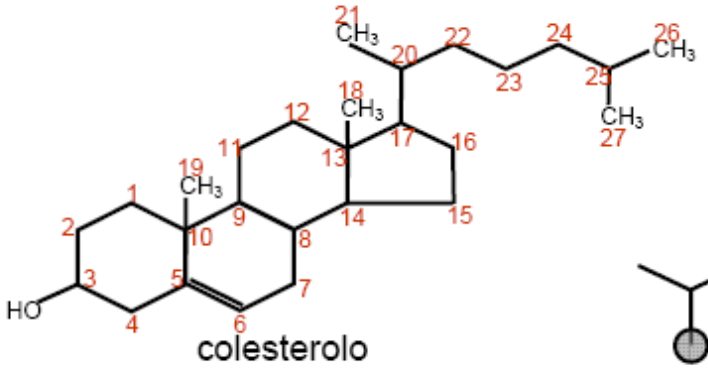
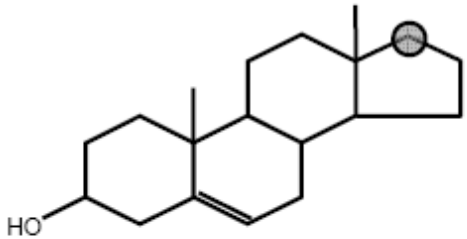
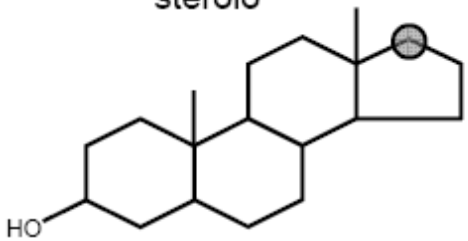


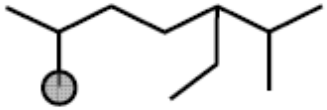

colesterolo



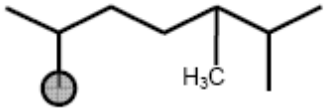

sterolo



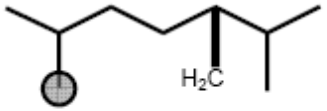

stanolo



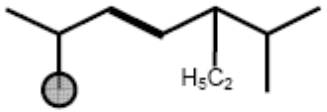
sitosterolo
sitostanolo




campesterolo
campestanolo




bressicasterolo
bressicastanol




stigmasterolo
stigmastanolo

Structural similarities
so
functional analogies?

Only partially

**Figura 1. Struttura chimica dei più comuni steroli e stanoli vegetali.**

# Phytosterols

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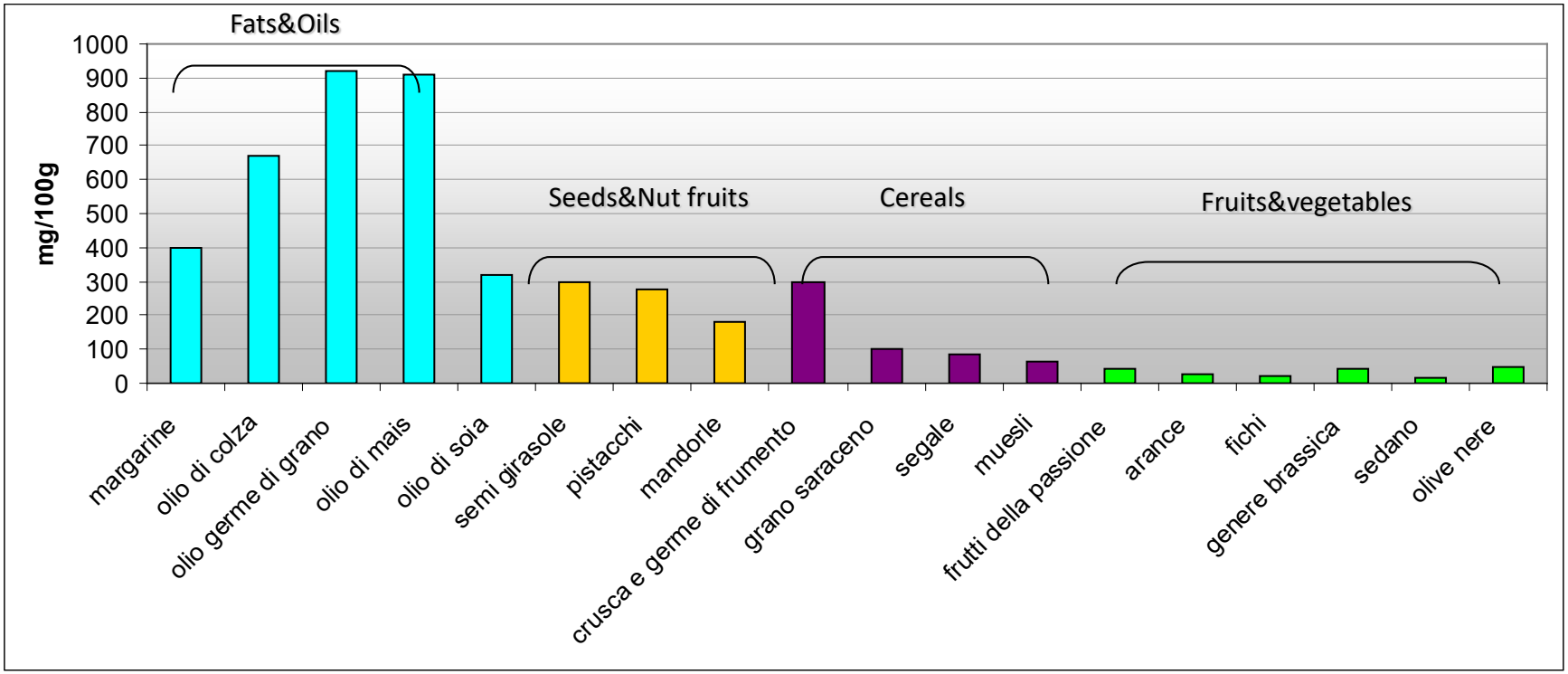
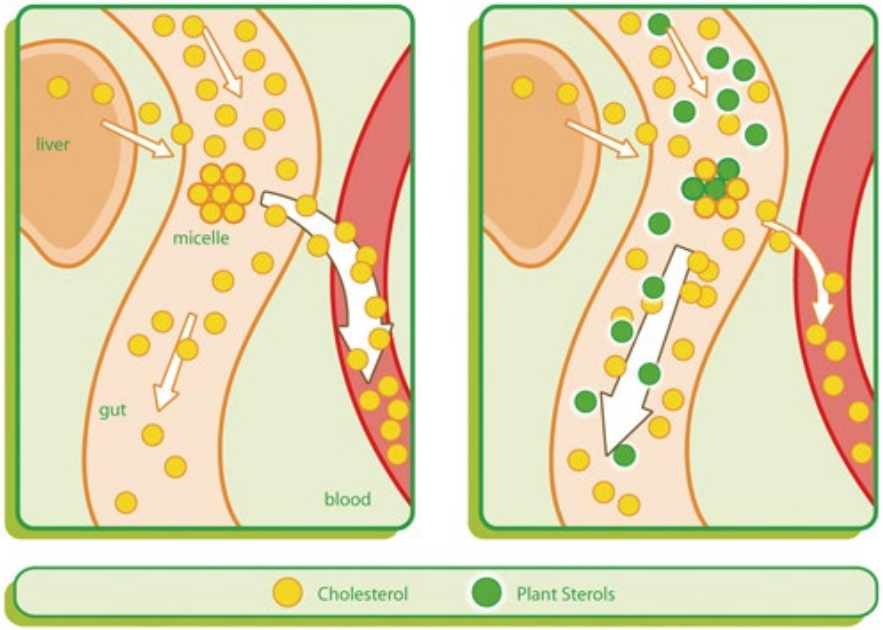



Natural foods with the highest vegetable sterols are vegetable oils, followed by nuts and cereals and their derivatives

# Phytosterols

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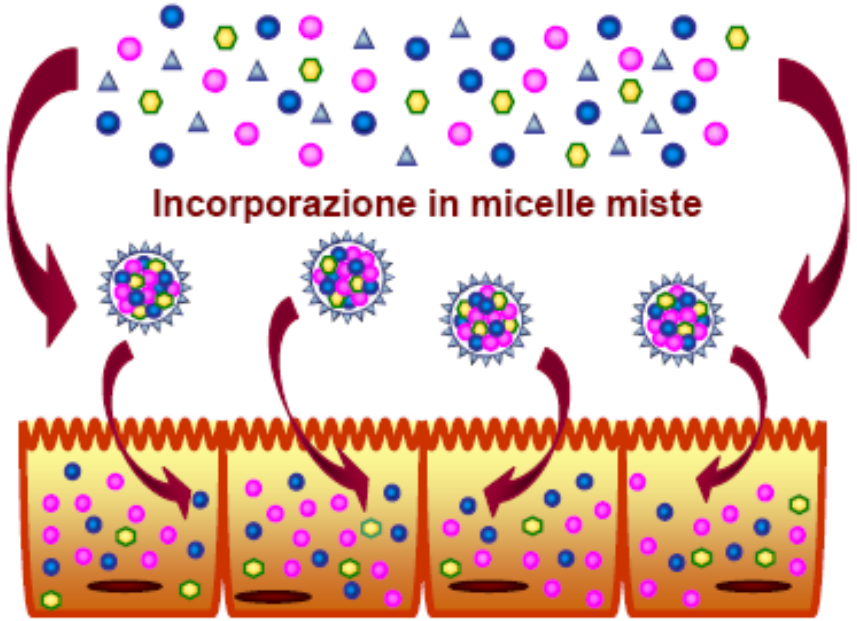
Ingestione con gli alimenti

BOCCA
STOMACO

INTESTINO



# Phytosterols: Cholesterol lowering mechanism

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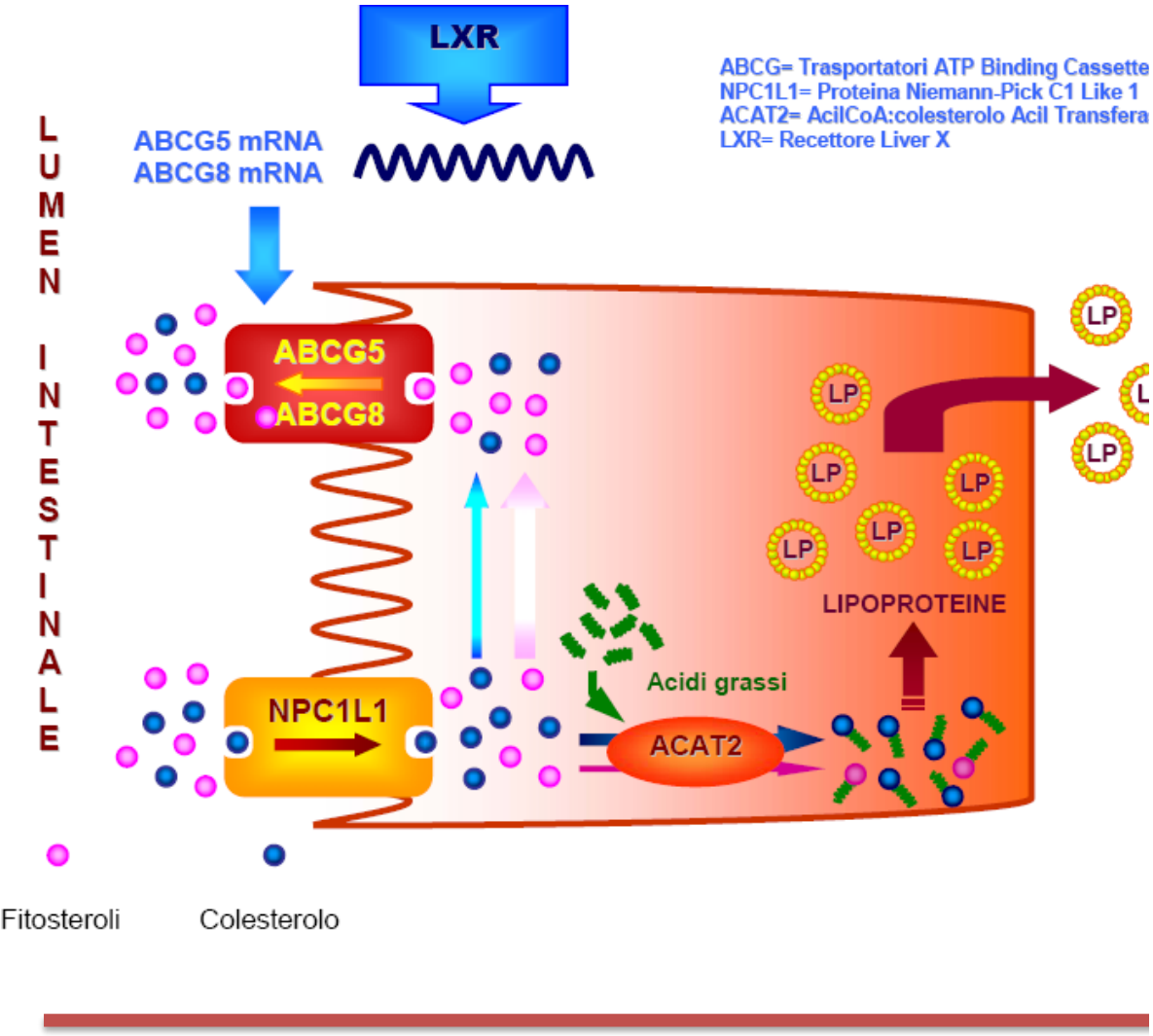


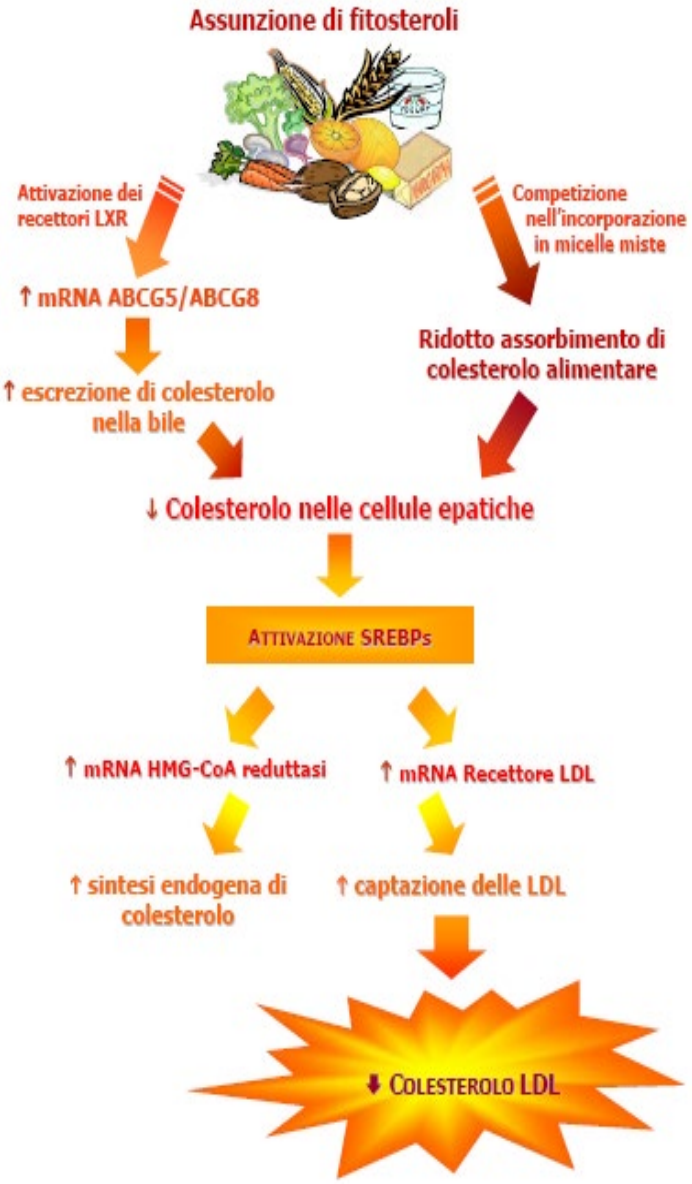

# Phytosterols: Efficacy&dose

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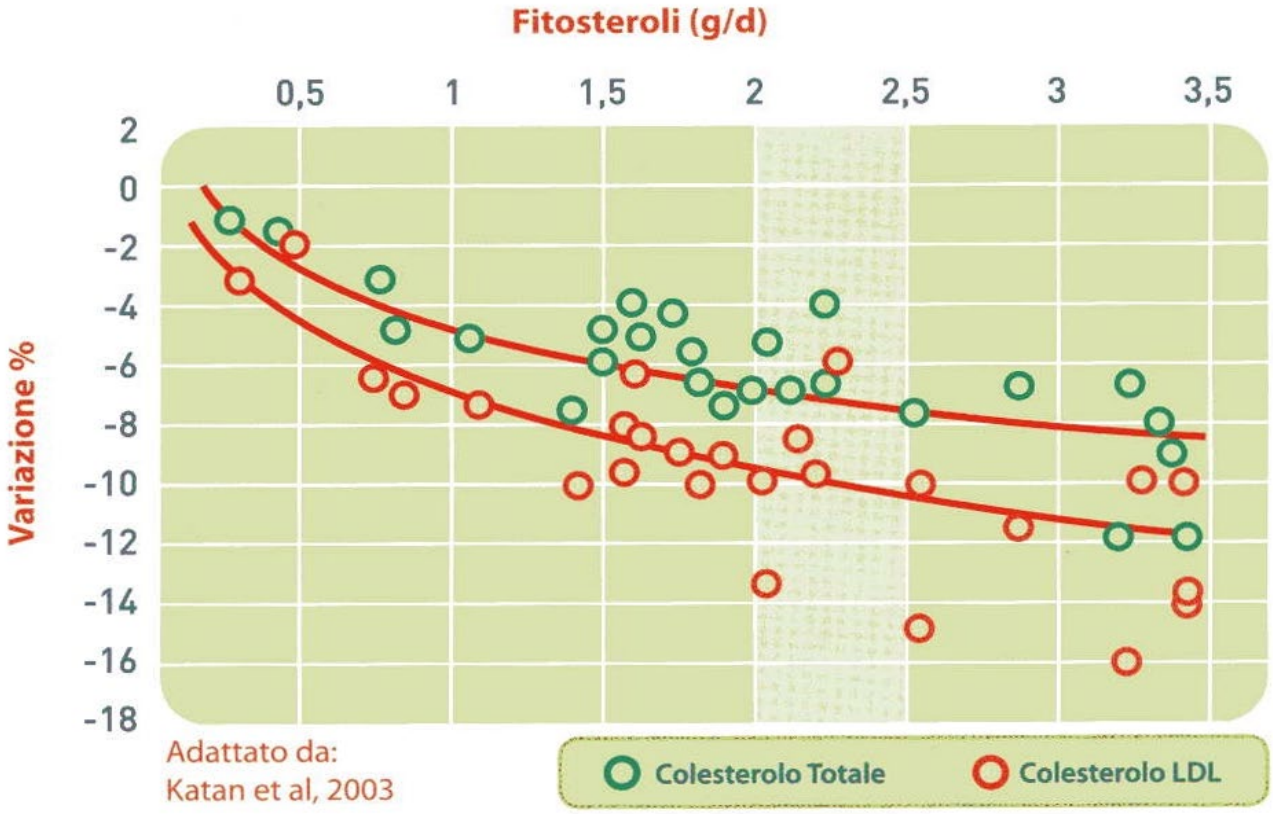
## dose-effect relationship




CVD reduction 20%

The intake of 2 to 2.5 g / day of plant sterols associated with a healthy, balanced diet rich in fruit and vegetables reduces the LDL cholesterol level without significant effects on HDL and triglycerides.

# Phytosterols: Efficacy&dose

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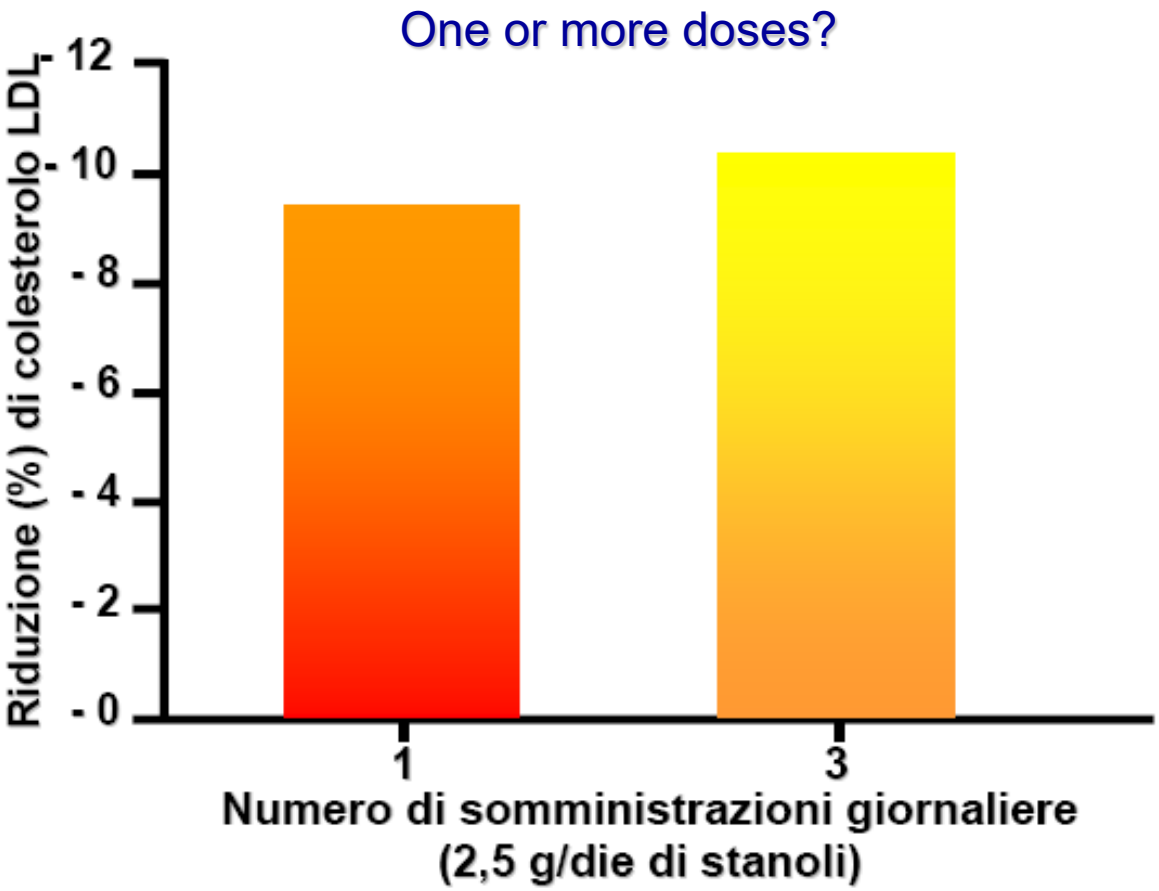


The intake of phytosterols in one meal or in multiple daily doses results in a reduction in comparable LDL cholesterol

# Phytosterols: way to administered

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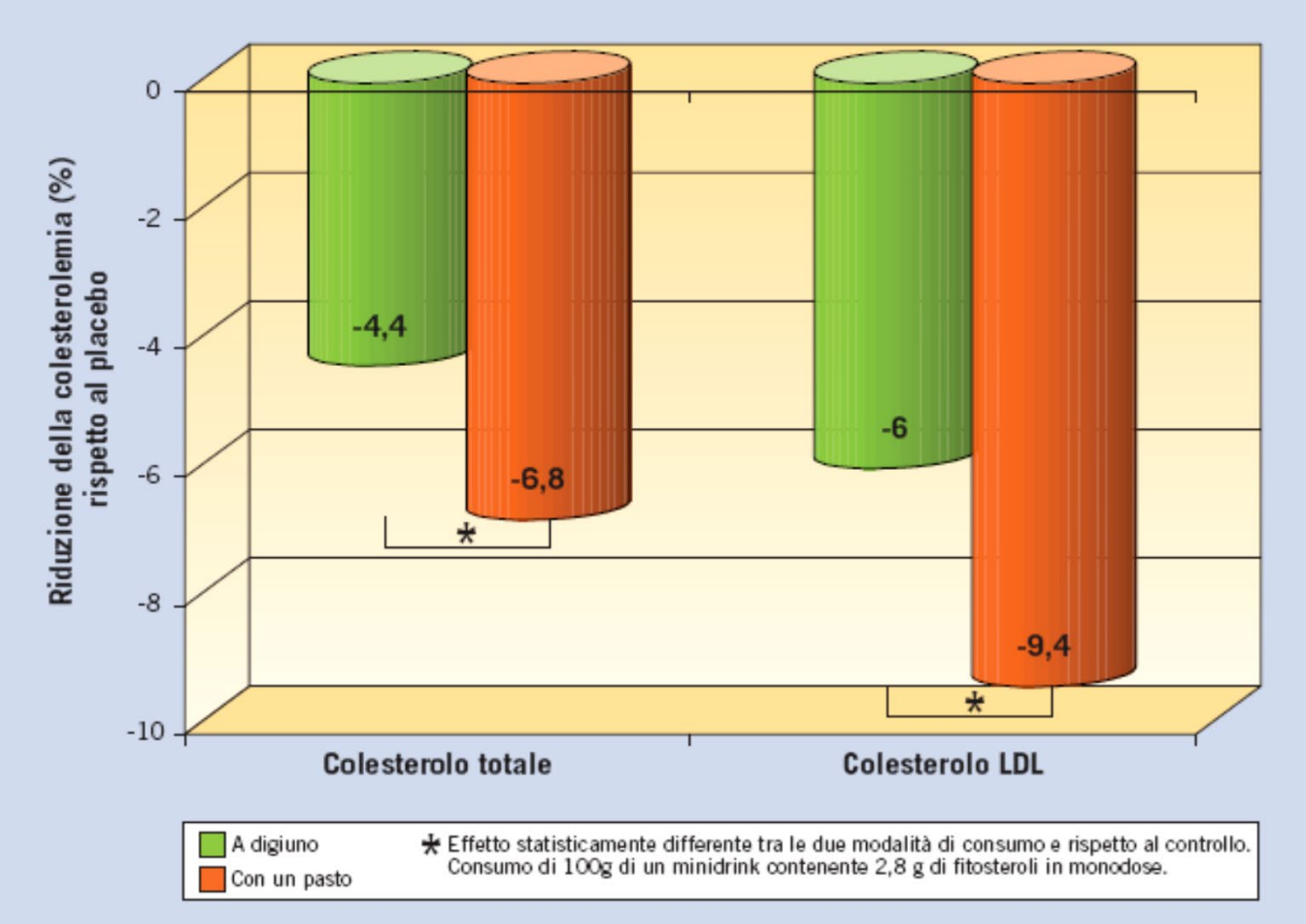


Effect of the use of a single dose of phytosterols on cholesterol. Consumption during a meal increases the effect on cholesterolemia compared with fasting.

# Phytosterols: which is the best?

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Condimenti -16%


Latte -15.9%
Yogurt -8.6%

Pane - 6.5%
Cereali - 5.4%

Integratori alimentari
- 4%÷ - 10%

# Phytosterols: which is the best?

U6

## Cholesterol lowering action in phytosterol trials using capsules or tablets

| Authors | Study size | Study design | Matrix | Type of phytosterol | Dose free phytosterol | Duration | ΔLDL (mmol/L)[a] |
|---|---|---|---|---|---|---|---|
| Acuff et al. [54] | $n = 16$ | Double-blind, placebo-controlled, sequential study | Capsule | Plant sterol ester | 0.8 g/day in 2 capsules | 4 wk | −0.34 |
| Carr et al. [55] | $n = 32$ | Randomized, double-blind, two-group parallel, placebo-controlled | Capsule | Plant sterol ester of stearate | 1.8 g/day in 3 capsules | 4 wk | −0.35 |
| Denke et al. 1994 | $n = 33$ | Sequential study, low cholesterol diet | Capsule | Free Sitostanol in oil | 3.0g/day in 12 capsules | 1 month | −0.15[b] |
| Earnest et al. [56] | $n = 54$ (25 active, 29 placebo) | Randomized, double-blinded, parallel, placebo-controlled | Capsule | Plant sterol ester | 1.56 g/day of ester in 4 capsules | 12 wk | −0.38 |
| Goldberg et al. [57] | $n = 26$ (13 per arm) | Double-blind, placebo-controlled, parallel clinical trial | Tablet | Plant stanol lecithin complex | 1.8 g/day in 8 tablets | 6 wk | −0.68 |
| McPherson et al. [53] | $n = 27$ per | Placebo-controlled, double-blind | Capsule time release >60 min | Aqueous stanol lecithin complex | 1.01 g/day in 8 capsules | 6 wk | −0.28 |
| McPherson et al. [53] | $n = 25$ | Placebo-controlled, double-blind | Tablet fast dissolve <10 min | Spray dried stanol lecithin complex | 1.26 g/day in 6 tablets | 6 wk | −0.68 |
| Woodgate et al. [58] | $n = 29$ (14 active, 15 control) | Randomized, double-blind, placebo-controlled | Softgel capsule | Stanol ester | 1.6 g/day in 3 capsules | 4 wk | −0.39 |

[a] In cross-over trials ΔLDL = mean LDL end of treatment − mean LDL end of control. In parallel trials ΔLDL = ΔLDL treatment − ΔLDL control.
[b] In Denke et al. mean LDL of preceding and subsequent step one diet phases used as LDL control.

# Phytosterols: which is the best?

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Currently ther are 10 permits concerning the following types of phytosterols, esters of phytosterols, phytostanols or phytostanols esters:

- Milk drinks
- Soy drinks
- Rice drinks?
- spreadable creams
- milk • fermented milk
- yogurt
- spreadable margarine
- rye bread
- sauces and seasonings

Frequently used by population aged> 45 years. Simulation studies show exposure to doses> 3g / day when using more than one .....

**Examples of phytosterols / stanols concentrations in some EU functional foods and recommended daily consumption.**

| Product category | Common packing size | Recommended consumption | Phytosterol concentration | Daily intake |
|---|---|---|---|---|
| Yellow fat spreads | 250 g | 3x8-10 g/day | 7.5-8 g/100 g | 2-2.3 g |
| Milk type products | 1000 ml | 2-3x250 ml/day | 0.3 g/100 ml | 1.5-2.4 g |
| Yoghurt type products | 65-125 ml | 1-2x65-125 ml/day | 0.6-3.1 g/100 ml | 1.5-2 g |
| Cheese type products | 125 g | 3x30 g/day | 2.2 g/100 g | 2.1 g |
| Cream cheese | 200 g | 40-60 g/day | 5.0 g/100 g | 2-3 g |
| Milk-based soft drink | 1000 ml | 350 ml/day | 0.5 g/ 100 ml | 1.8 g |
| Rye bread | 750 g | 3x80 g/day | 0.8 g/100 g | 2 g |

# Phytosterols: which is the best?

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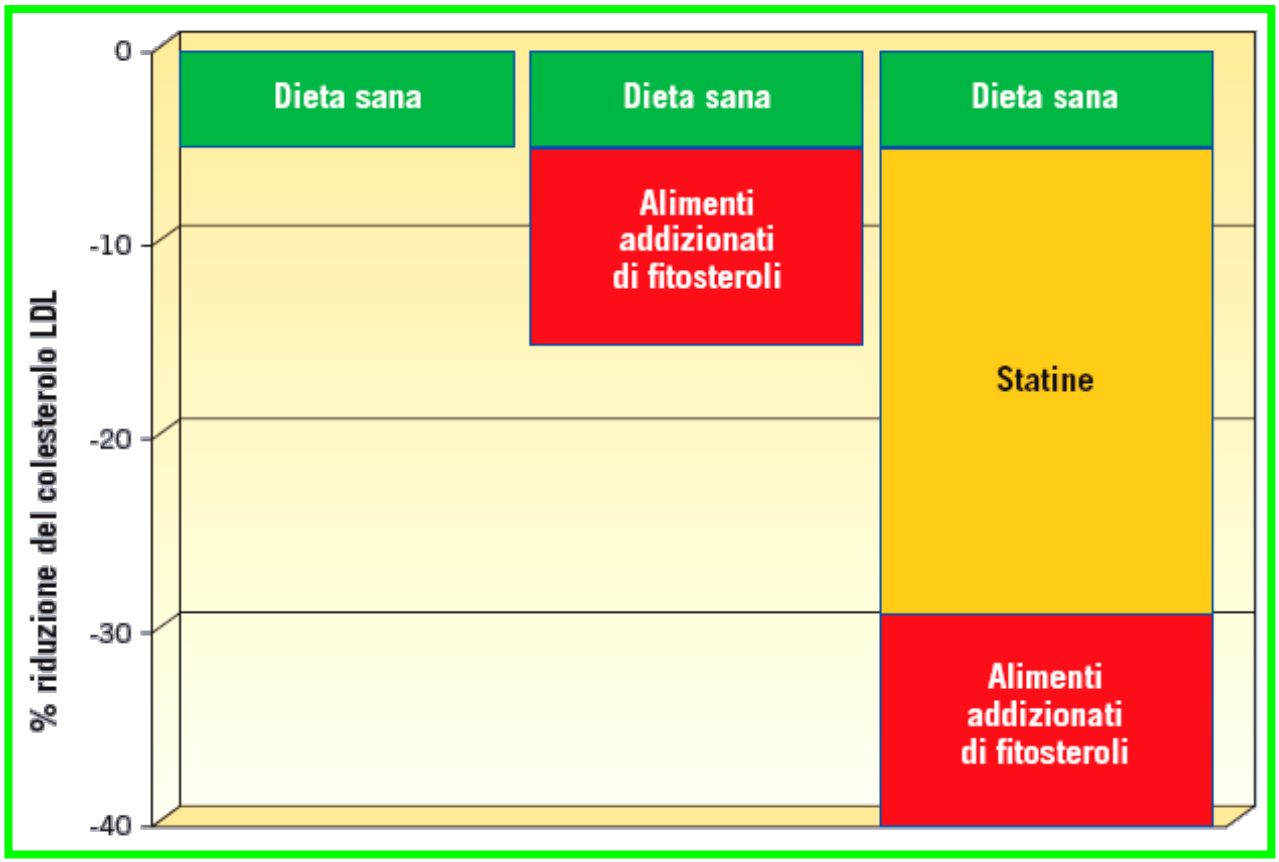


- Moderate-low RCV subjects (<10%)
- In non-pharmacological strategies
- Subjects already in statin therapy

# Phytosterols: additional labelling requirements

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INDICATIONS FOR CORRECT USE OF ADDITIVES WITH FITOSTEROLS

To provide consumers with the information they need for their correct use, all phytosterols added products must bear a label that, in addition to containing omitting data, must clearly specify that:

- The product is intended exclusively for people who intend to reduce their cholesterol levels in the bloodstream
- patients who undergo a cholesterol-lowering treatment should consume the product only under medical supervision
- the product may be inadequately nutritionally suitable for pregnant women, breastfeeding and children under the age of 5
- The product should be taken in the framework of a varied and balanced diet, which involves regular consumption of fruit and vegetables so as to counteract the reduction of carotenoids
- Intake over 3g / die of added sterols / stanols should be avoided.

(To facilitate this, the product should have a clear indication of what the standard portion to be consumed in g ml, and the indication of the phytosterol content contained in that portion)

# Phytosterols: safety of use

U6

- ✓ Interactions with other nutrients (carotenoids)
- ✓ Estrogenic effect
- ✓ Increase in plasma levels of phytosterols and induction of atherosclerosis
- ✓ Potential allergenicity?

"3 g/day of phytosterols/stanols help to reduce cholesterol" the minimum duration required to achieve the maximum effect of plant sterols and stanols on LDL-cholesterol lowering is two to three weeks. Plant sterols added to foods such as margarine-type spreads, mayonnaise, salad dressings, and dairy products have been shown consistently to lower blood LDL-cholesterol concentrations in a large number of studies, the effective dose of plant sterols (as powder diluted in water) needed to achieve a given magnitude of effect in a given timeframe cannot be established with the data provided (6 weeks 2g/day).

# Phytosterols: example of overlapping food concepts

U6


Bevanda lattea fermentata alla frutta addizionata di steroli vegetali e dolcificata con edulcoranti

- atte scremato e latte scremato in polvere
- Steroli vegetali (1,6%)
- Ananas (1%)
- Fibra alimentare (oligofruttosio)
- Addensanti (amido modificato di mais, pectina, gomma di guar)
- Aromi
- Correttori di acidità (acido citrico, citrato di calcio, citrato di sodio)
- Edulcoranti (acesulfame K, sucralosio)
- Streptococcus thermophilus
- Lactobacillus bulgaricus

Riduce il colesterolo Fino a -10% in tre settimane grazie agli steroli vegetali

non è destinato alle persone che non hanno bisogno di controllare il colesterolo nel sangue. Potrebbe non essere adatto alle donne in gravidanza, durante l'allattamento e per i bambini di età inferiore ai 5 anni. Nel caso si stia seguendo una cura per la riduzione del colesterolo consumare il prodotto solo sotto controllo medico. Si raccomanda il consumo di una bottiglietta di al giorno (1,6 g di steroli vegetali). deve essere consumato nel quadro di una dieta varia e bilanciata che comporti il consumo regolare di frutta e verdura così da contribuire a mantenere i livelli di carotenoidi. Evitare il consumo di più di 3 g di steroli vegetali al giorno, poiché una quantità maggiore non apporta benefici addizionali. Le malattie cardiovascolari sono dovute a molteplici fattori. Intervenire su uno solo di questi può anche non avere effetti benefici. **L'effetto benefico si ottiene con l'assunzione quotidiana di almeno 1,5-3g di steroli/stanoli vegetali. Agitare prima dell'uso

# Phytosterols: example of overlapping food concepts

U6


100% Vegetale Soia con Steroli Vegetali Melograno 6 x 90 g
100% VEGETALE
Bevanda vegetale a base di soia con fermenti vivi con melograno e con aggiunta di steroli vegetali

Composizione: **Estratto di soia 73%** (acqua, semi di soia decorticati (7%)),Preparazione di frutta (melograno 9%, zucchero, acqua, **fitosteroli 1,1%,** amido modificato di tapioca; coloranti: succo concentrato di barbabietola rossa, succo concentrato di carota nera; antiossidanti: acido ascorbico, vitamina E; aromi naturali),Fibra alimentare,Fermenti

Aiuta a mantenere livelli normali di colesterolo - Fonte di proteine vegetali - A basso contenuto di grassi saturi. Addizionato di steroli vegetali che aiutano a mantenere livelli normali di colesterolo Questo prodotto è destinato esclusivamente alle persone che vogliono mantenere livelli normali di colesterolo nel sangue. Nel caso si stia seguendo un trattamento ipocolesterolemizzante, consumare il prodotto solo sotto controllo medico. Potrebbe essere inadeguato alle donne in gravidanza, durante l'allattamento e per i bambini di età inferiore ai 5 anni. Il prodotto deve essere consumato nel quadro di una dieta varia e bilanciata che comporti il consumo regolare di frutta e verdura così da contribuire a mantenere livelli di carotenoidi. Evitare il consumo di più di 3g di steroli vegetali al giorno, poiché una quantità maggiore non apporta benefici addizionali. Una bottiglietta da 90 g contiene 1,0 g di fitosteroli

# Phytosterols: example of overlapping food concepts

U6

## Benecol® Original Spread:

**Nutrition Facts**
Serving size 1 Tbsp (14g)
Servings. About 16

| Amount/Serving | |
|---|---|
| **Calories** 70 | Fat Cal.70 |
| | % DV* |
| **Total Fat** 8g | 10% |
| Sat Fat 1g | 5% |
| Trans Fat 0g | |
| Polyunsaturated Fat 2g | |
| Monounsaturated Fat 4.5g | |
| **Cholesterol** 0mg | 0% |
| **Sodium** 105mg | 5% |
| **Total Carbohydrate** 0g | 0% |
| **Protein** 0g | 0% |

Vitamin A 20% • Vitamin E 20%

Not a significant source of dietary fiber sugars, vitamin C, calcium and iron.

*Percent Daily Values (DV) are based on a 2,000 calorie diet.

**INGREDIENTS:** CANOLA OIL, WATER, PALM AND PALM KERNEL OIL, PLANT STANOL ESTER, LESS THAN 2 PERCENT OF SALT, BUTTERMILK, VEGETABLE MONOGLYCERIDES (EMULSIFIER), POTASSIUM SORBATE, CITRIC ACID, AND CALCIUM DISODIUM EDTA(TO PROTECT FRESHNESS), ARTIFICIAL FLAVOR, DL-ALPHA TOCOPHEROL ACETATE (VITAMIN E), VITAMIN A PALMITATE, BETA-CAROTENE (COLOR).

**Contains: Milk Gluten Free**


## Benecol® Light Spread:

**Nutrition Facts**
Serving size 1 Tbsp (14g)
Servings. About 16

| Amount/Serving | |
|---|---|
| **Calories** 50 | Fat Cal.50 |
| | % DV* |
| **Total Fat** 5g | 6% |
| Sat Fat 1g | 5% |
| Trans Fat 0g | |
| Polyunsaturated Fat 1.5g | |
| Monounsaturated Fat 3g | |
| **Cholesterol** 0mg | 0% |
| **Sodium** 95mg | 4% |
| **Total Carbohydrate** 0g | 0% |
| **Protein** 0g | 0% |

Vitamin A 20% • Vitamin E 20%

Not a significant source of dietary fiber sugars, vitamin C, calcium and iron.

*Percent Daily Values (DV) are based on a 2,000 calorie diet.

**INGREDIENTS:** WATER, CANOLA OIL, PLANT STANOL ESTER, PALM FRUIT AND PALM KERNEL OIL, LESS THAN 2 PERCENT OF SALT, POLYGLYCEROL POLYRICINOLEATE (PGPR) AND VEGETABLE MONOGLYCERIDE (EMULSIFIER), WHEY(MILK), POTASSIUM SORBATE, CITRIC ACID AND CALCIUM DISODIUM EDTA (TO PROTECT FRESHNESS), ARTIFICIAL FLAVOR, DL-ALPHA TOCOPHEROL ACETATE (VITAMIN E), VITAMIN A PALMITATE, BETA-CAROTENE (COLOR)

**Contains: Milk Gluten Free**


***4 cioccolatini morbidi al giorno ti danno 2 grammi di stanoli vegetali!***

# Phytosterols: example of overlapping food concepts

U6


**INGREDIENTI:**
Steroli vegetali tit. 68% (con maltodestrine, esteri di saccarosio degli acidi grassi, inulina); agente antiagglomerante: biossido di silicio.

16 Bustine monodose da sciogliere in acqua o altri alimenti: bevande, latte, yogurt, minestre.

Naturalmente privo di lattosio. Senza glutine, conservanti, coloranti, aromi.

# Phytosterols: example of overlapping food concepts

U6

## EU Register on nutrition and health claims

The search tool only allows searches for health claims*, and not nutrition claims.

* **Health claims for which protection of proprietary data is granted** (and for which the right of use of the claim is restricted to the benefit of the applicant) are **only** listed here.

You can also download the complete dataset of nutrition and health claims in the following formats: (1.14 Mb) (2.22 Mb)

EU Register | Search

Showing 1 to 3 of 3 entries (filtered from 2,337 total entries) 10 records per page

‹ 1 ›

| Claim type | Nutrient, substance, food or food category | Claim | Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation | Health relationship | EFSA opinion reference / Journal reference | Commission Regulation | Status | Entry ID |
|---|---|---|---|---|---|---|---|---|
| Art.14(1)(a) | Plant stanol esters | Plant stanol esters have been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease. | Information to the consumer that the beneficial effect is obtained with a daily intake of 1,5-3 g plant stanols. Reference to the magnitude of the effect may only be made for foods within the following categories: yellow fat spreads, dairy products, mayonnaise and salad dressings. When referring to the magnitude of the effect, the range "7 % to 10 %" for foods that provide a daily intake of 1,5-2,4 g plant stanols or the range "10 %-12,5 %" for foods that provide a daily intake of 2,5-3 g plant stanols and the duration to obtain the effect "in 2 to 3 weeks" must be communicated to the consumer. | | Q-2008-118, Q-2009-00530 & Q-2009-00718, Q-2011-00851, Q-2011-01241 | Commission Regulation (EC) 983/2009 of 21/10/2009, Amended by Commission Regulation (EC) 376/2010 of 03/05/2010, Amended by Commission Regulation (EU) No 686/2014 of 20/06/2014 | Authorised | N/A |
| Art.13(1) | Plant sterols and plant stanols | Plant sterols/stanols contribute to the maintenance of normal blood cholesterol levels | In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of at least 0.8 g of plant sterols/stanols. | maintenance of normal blood cholesterol concentrations | 2010;8(10):1813, 2011;9(6):2203 | Commission Regulation (EU) 432/2012 of 16/05/2012 | Authorised | 549, 550, 567, 568, 713, 1234, 1235, 1466, 1634, 1984, 2909, 3140 |
| Art.14(1)(a) | Plant sterols/Plant stanol esters | 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. | Information to the consumer that the beneficial effect is obtained with a daily intake of 1,5-3 g plant sterols/stanols. Reference to the magnitude of the effect may only be made for foods within the following categories: yellow fat spreads, dairy products, mayonnaise | | Q-2008-779, Q-2009-00530 & Q-2009-00718, Q-2011-01241 | Commission Regulation (EU) 384/2010 of | Authorised | N/A |

# Phytosterols: example of overlapping food concepts

Food based of phytosterols
as main active component
Enriched food…
Functional…Novel food…
Food supplement….? …..





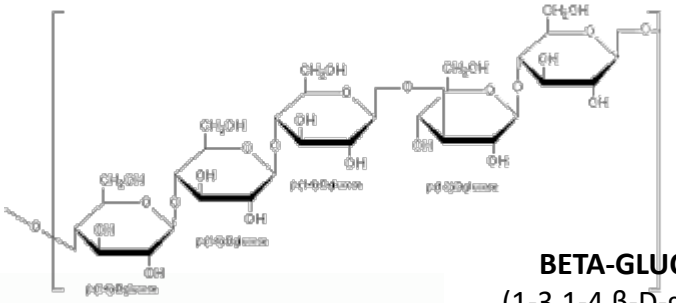
**FOCUS ON NUTRACEUTICAL AND FUNCTINAL FOODS ON THE HYPERLIPIDEMIA**

**A RISK FACTOR OF CARDIOVASCULAR DESEASES**

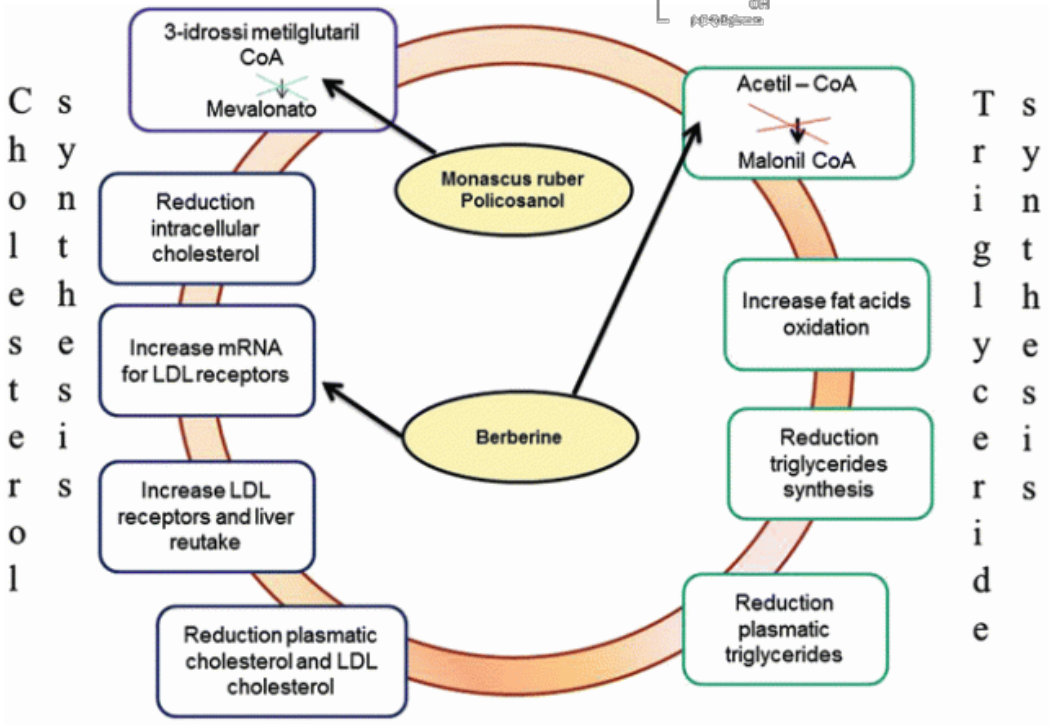
# Phytosterols&....synergistic effects of combinations

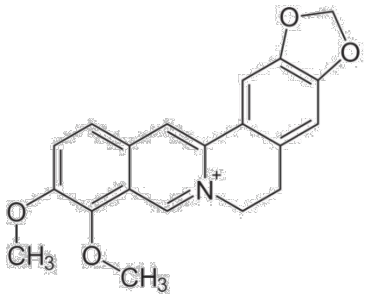
U6

**OCTACOSANOLO**



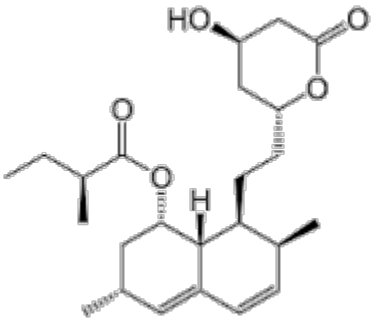
**BETA-GLUCANO**
(1-3,1-4 β-D-glucano)



**BERBERINA**

**SOY&Legumes proteins**



**MONACOLINA k**

# Fiber

U6


Nutrition, Metabolism & Cardiovascular Diseases (2017) 27, 2–17

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

ELSEVIER

REVIEW

Joint position statement on "Nutraceuticals for the treatment of hypercholesterolemia" of the Italian Society of Diabetology (SID) and of the Italian Society for the Study of Arteriosclerosis (SISA)

M. Pirro [a,b], C. Vetrani [c,d], C. Bianchi [d,e], M.R. Mannarino [a,b], F. Bernini [b,f], A.A. Rivellese [c,d,*]

From a functional point of view, dietary fiber is grouped into 4 classes :

1. insoluble, non-fermentable fiber (bran). It is an insoluble fiber that is poorly fermented in the intestine; it can exert mechanical laxative effects;

2. soluble, non-viscous, fermentable fiber (inulin, dextrin, oligosaccharides). It is quickly and easily fermented in the intestine. It does not cause increased viscosity and it is rapidly and completely fermented by the intestinal microbiota. It may have a prebiotic effect, but it does not exert laxative effects;

3. soluble, viscous, fermentable fiber (b-glucan, guar gum, pectin, glucomannan). It is quickly fermented and forms a viscous gel in water, increasing chime viscosity and reducing nutrient absorption. It is rapidly fermented in the intestine, thus losing its laxative effects;

4. soluble, viscous, non-fermentable fiber (psyllium, methylcellulose). It reduces the absorption of nutrients due to its viscosity and exerts laxative effects.

A regular intake of fiber, mostly the type with higher viscosity, reduces LDL cholesterol concentrations. When an adequate intake of fiber with diet alone is not feasible, the use of fiber-containing supplements can be an effective strategy to safely reduce cholesterol levels and possibly cardiovascular risk. Side effects related to excessive intake of fiber are unusual , except for symptoms of intestinal discomfort with higher doses (bloating, flatulence, meteorism) . Overall, the use of added fiber may be advised when people are unable to increase their intake of dietary fiber with natural foods: 1) in the general population; 2) in patients with mild hypercholesterolemia and low to moderate cardiovascular risk; 3) in patients with mild hypercholesterolemia and/or metabolic syndrome

# Fiber

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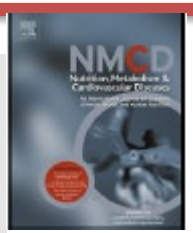



**Table 1** Meta-analyses and randomized controlled trials in humans on the lipid-lowering effects of different types of fiber.

| Fiber | Type of study | Subjects (number, type) | Average dose (range) | Mean duration (range) | Observed effects | Ref. |
|---|---|---|---|---|---|---|
| β-Glucan (oats) | Meta-analysis of 25 RCT | n:1600<br>Healthy subjects<br>Hypercholesterolemia<br>Diabetes mellitus | 5.0 g/day (2–30 g/day) | 6 weeks (2–12 weeks) | ↓ LDL-C: −6.2 mg/dl<br>No effect on TG and HDL-C | [28] |
| | Meta-analysis of 28 RCT | n:2529<br>Healthy subjects<br>Hypercholesterolemia<br>Type 2 Diabetes | (3–12.4 g/day) | 2–12 weeks | ↓ LDL-C: −9.6 mg/dl<br>No effect on TG and HDL-C | [29] |
| *Psyllium* | Meta-analysis of 17 RCT | n:757<br>Healthy subjects<br>Hypercholesterolemia | 9.1 g/day (2–30 g/day) | 7 weeks (2–56 weeks) | ↓ LDL-C: −10 mg/dl<br>No effect on TG and HDL-C | [28] |
| | Meta-analysis of 21 RCT | n: 1717<br>Hypercholesterolemia | (3–20 g/day) | (2–26 weeks) | ↓ LDL-C: −11 mg/dl<br>No effect on TG | [30] |
| | RCT | n:187<br>Hypercholesterolemia on pharmacological treatment | 14 g/day | 8 weeks | ↓ LDL-C: −11 mg/dl (−6%)<br>↓ TG: −20 mg/dl (−17%)<br>No effect on HDL-C | [31] |
| Pectin | Meta-analysis of 7 RCT | n: 277<br>Healthy subjects<br>Hypercholesterolemia<br>Diabetes mellitus | 4.7 g/day (2–30 g/day) | 5 weeks (4–6 weeks) | ↓ LDL-C: −9.9 mg/dl<br>No effect on TG and HDL-C | [28] |
| Guar gum | Meta-analysis of 18 RCT | n: 356<br>Healthy subjects<br>Hypercholesterolemia<br>Diabetes mellitus | 17.5 g/day (2–30 g/day) | 66 days (4–24 weeks) | ↓ LDL-C: −22 mg/dl<br>No effect on TG and HDL-C | [28] |
| Chitosan | Meta-analysis of 9 RCT | n:1219<br>Healthy subjects | 3.7 g/day (0.24–15 g/day) | 8.3 weeks (4–24 weeks) | ↓ LDL-C: −6.2 mg/dl<br>↑ HDL-C: 1.2 mg/dl<br>↓ TG: −11 mg/dl | [32] |
| Glucomannan | Meta-analysis of 14 RCT | n: 531<br>Healthy subjects<br>Hypercholesterolemia<br>Diabetes mellitus | (1.2–15.1 g/day) | (3–16 weeks) | ↓ LDL-C: −16 mg/dl<br>↓ TG: −11 mg/dl<br>No effect on HDL-C | [33] |
| HPMC | RCT | n:52<br>Hypercholesterolemia | A: 5 g/day<br>B: 15 g/day | 8 weeks | A: ↓ LDL-C: −14 mg/dl<br>No effect on TG and HDL-C<br>B: ↓ LDL-C: −14 mg/dl<br>No effect on TG and HDL-C | [34] |
| | RCT | n:13<br>Hypercholesterolemia on pharmacological treatment | 5 g/day | 4 weeks | ↓ LDL-C: (−10%)<br>No effect on TG and HDL-C | [35] |

↑: increase, ↓: reduction, HDL-C: HDL-cholesterol, LDL-C: LDL-cholesterol, HPMC: hydroxypropyl-methylcellulose, TG: triglycerides, RCT: randomized controlled trials.

# SOY

U6

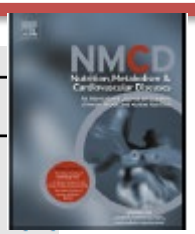



**Table 5** Meta-analyses of randomized controlled trials in humans on the lipid-lowering effects of soy.

| Type of study | Subjects (number, type) | Average dose (range) | Mean duration (range) | Observed effect | |
|---|---|---|---|---|---|
| Meta-analysis of 38 RCT | n: 743<br>Healthy subjects<br>Hypercholesterolemia | Soy proteins<br>47 g/day (18–124 g/day) | – | ↓ LDL-C: −12.9%<br>↓ TG: −10.5%<br>↑ HDL-C: 2.4% | |
| Meta-analysis of 10 RCT | n: 959<br>Healthy subjects<br>Hypercholesterolemia | Soy proteins (19–60 g/day)<br>Isoflavones (1–95 mg/day) | At least 14 days | ↓ LDL-C: −6.56 mg/dl<br>↑ HDL-C: 1.16 mg/dl | |
| Meta-analysis of 8 RCT | n: 639<br>Healthy subjects<br>Hypercholesterolemia | Soy proteins (25–100 g/day)<br>Isoflavones (3–132 mg/day) | – | ↓ LDL-C: −5.79 mg/dl | [70] |
| Meta-analysis of 23 RCT | n:1833<br>Healthy subjects<br>Hypercholesterolemia | Isoflavones (3–185 mg/day) | (4–26 weeks) | ↓ LDL-C: −5.25%<br>↓ TG: −7.27%<br>↑ HDL-C: 3.03% | [71] |
| Meta-analysis of 41 RCT | n: 1756<br>Healthy subjects<br>Hypercholesterolemia | Soy proteins (20–106.2 g/day)<br>Isoflavones (2–192.4 mg/day) | (3–52 weeks) | ↓ LDL-C −4.25 mg/dl<br>↓ TG: −6.26 mg/dl<br>↑ HDL-C: 0.77 mg/dl | [72] |
| Meta-analysis of 11 RCT | n: 430<br>Healthy subjects<br>Hypercholesterolemia | Soy proteins (25–133 g/day)<br>Isoflavones (0–317.9 mg/day) | (3–14 weeks) | ↓ LDL-C: −4.98%<br>↓ TG: −0.69%<br>↑ HDL-C: 3.00% | [73] |
| Meta-analysis of 30 RCT | n: 2913<br>Healthy<br>Hypercholesterolemia | Soy proteins 26.9 g/day<br>(15–40 g/day) | (4–52 weeks) | ↓ LDL-C: −8.88 mg/dl (~6%)<br>↓ TG: −7.70 mg/dl<br>↑ HDL-C: 2.74 mg/dl | [74] |
| Meta-analysis of 43 RCT | Healthy subjects<br>Hypercholesterolemia | Soy proteins <65 g/day | (4–18 weeks) | ↓ LDL-C: from −4.2 to −5.5%<br>↓ TG: −10.7%<br>↑ HDL-C: 3.2% | [75] |
| Meta-analysis of 8 RCT | n: 183<br>Type 2 diabetes mellitus | Soy proteins (30–111 g/day)<br>Isoflavones (0–132 mg/day) | (6–208 weeks) | ↓ LDL-C: −11.6 mg/dl<br>↓ TG: −19.5 mg/dl<br>↑ HDL-C: 1.9 mg/dl | [76] |
| Meta-analysis of 14 RCT | Familial hypercholesterolemia | – | – | ↓ LDL-C: 4.6 mg/dl<br>↓ TG: −22 mg/dl<br>↑ HDL-C: 2.7 mg/dl | [51] |

↑: increase, ↓: reduction, HDL-C: HDL cholesterol, LDL-C: LDL cholesterol, TG: triglycerides, RCT: randomized controlled trials.

FDA to release a claim in 1999 stating that dietary intake of 25 g/day of soy protein can reduce cardiovascular risk

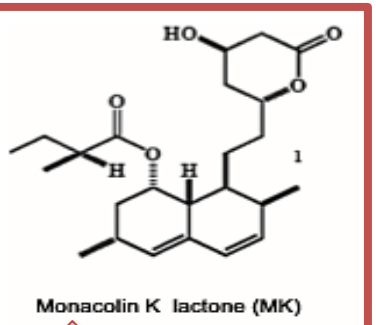
Soy (*Glycine max*) is an East Asian native leguminous plant, rich in proteins (36e46%, depending on the variety), lipids (18%), soluble carbohydrates (15%) and fiber (15%). The high content of essential amino acids is a particular feature of soy compared to other legumes. Soy contains also several micronutrients such as lecithin (0.5%), sterols (0.3%), isoflavones (0.1%), tocopherols (0.02%) and low levels of tocotrienols, lignans and sphingolipids.

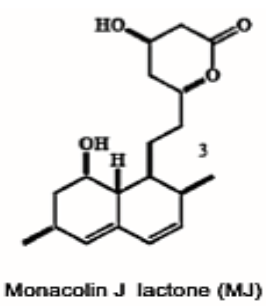
The cholesterol-lowering effect of soy may be related also to its content in lecithin, phytosterols and bglucan, which are able to reduce intestinal cholesterol absorption. Moreover, soy proteins including bconglycinin (7S globulin) and glycinin (11S globulin), and peptides obtained by their intestinal hydrolysis may exert cholesterol-lowering effects by promoting LDL-receptor (LDLR) expression. 3 di-peptides, Lys-Ala, Val-Lys, and Ser-Tyr, were reported to reduce TG synthesis, while Ser- Tyr additionally reduced apoB secretion in HepG2 cells

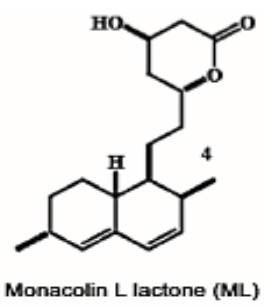
# RED YEAST RICE EXTRACTS

U6

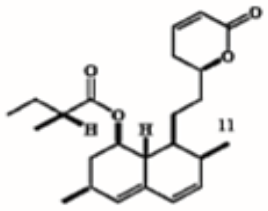
The composition is not yet well characterized due to secondary monacolins competing with the Monacolina K

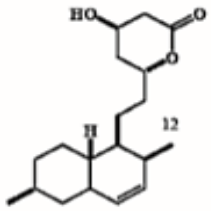


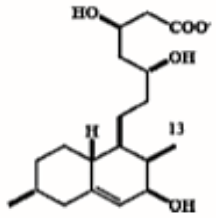



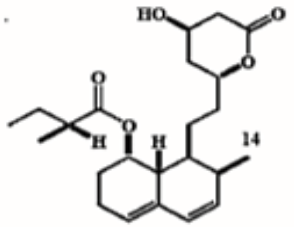





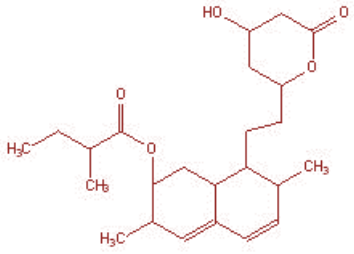




**Max level in food supplements 3 mg from July 2022**



LOVASTATINA

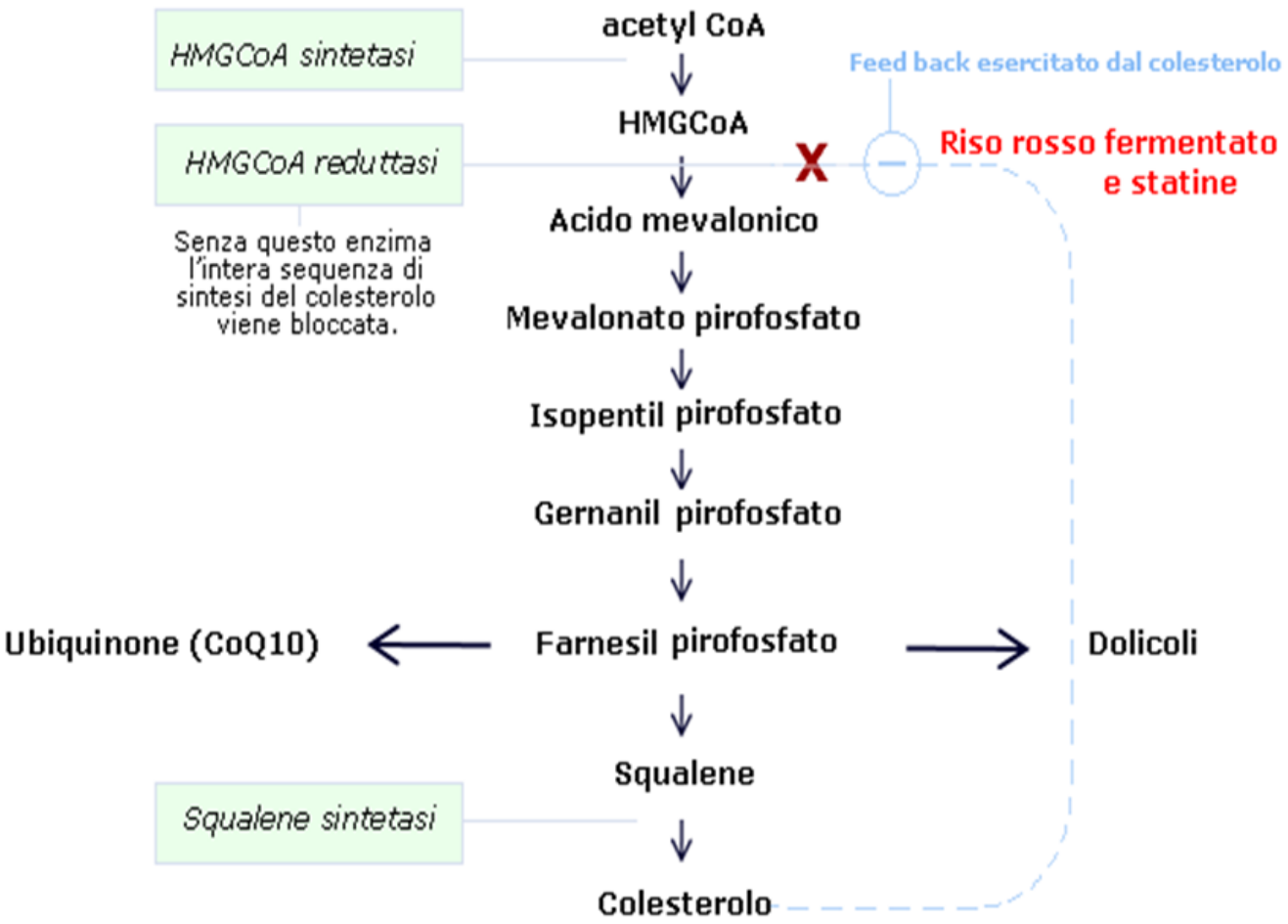
Functional Health claim

Monacolin K from red yeast rice contri… the maintenance of normal blood cho… levels

# RED YEAST RICE EXTRACTS

U6

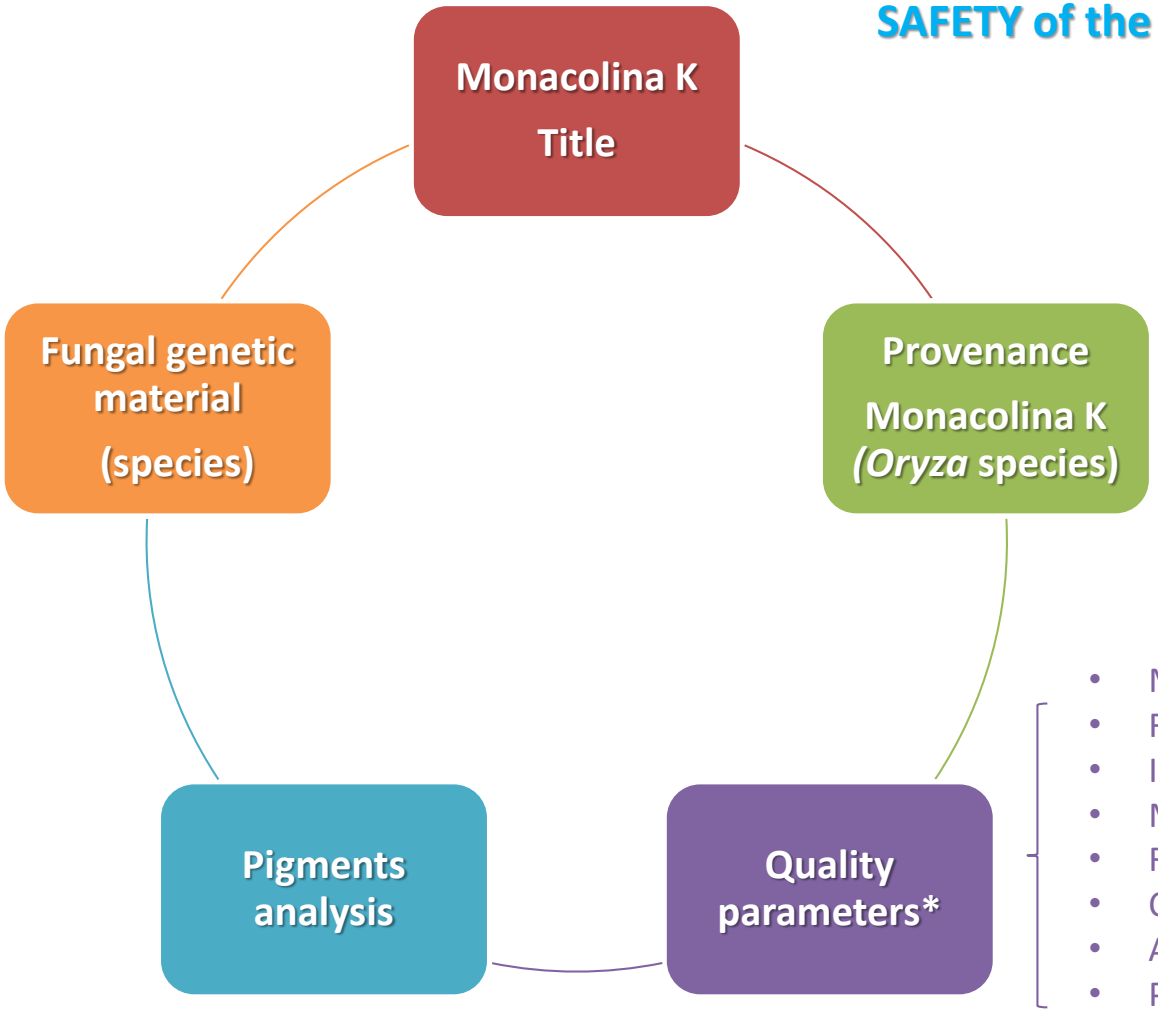
## BIOSINTESI DEL COLESTEROLO



# RED YEAST RICE EXTRACTS

U6

## SAFETY of the EXTRACTS RED FERMENTED RICE




- Microbiological parameters
- Radioactivity
- Irradiation
- Metals
- Redisual solvents
- Citrinine
- Aflatoxines
- Pesticides
- Allergenes

*Parameters setted by EFSA (Scientific opinion on the safety of monacolins in red yeast rice
EFSA Journal 2018;16(8):5368)

# RED YEAST RICE EXTRACTS

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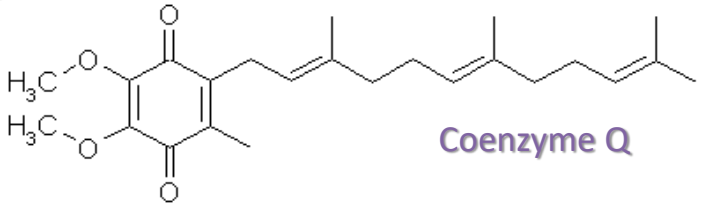
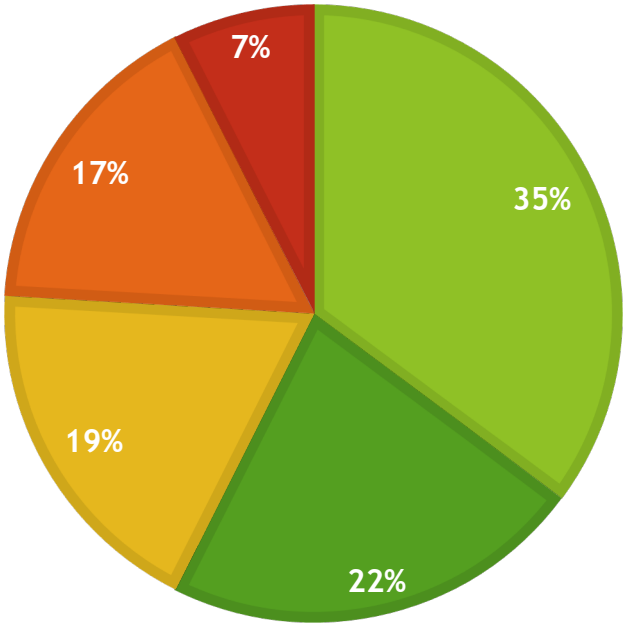
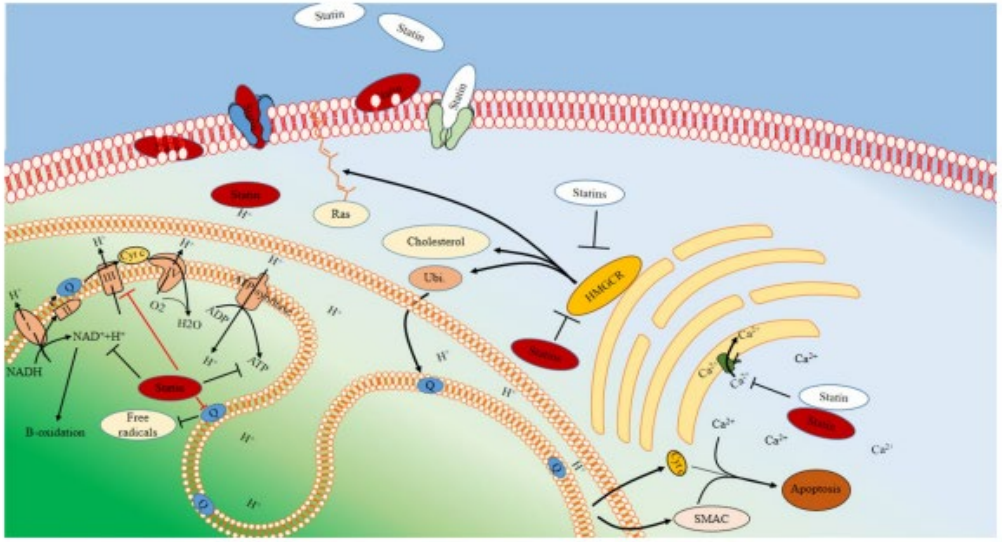
## ADVERSE EFFECTS of the EXTRACTS RED FERMENTED RICE



Coenzyme Q




Effect of statins in mitochondria. Statins through the inhibition of complex III and ubiquinone synthesis interrupt the transport of electrons and the consequent oxidation of NADH in NAD +

- mialgia e/o aumento CK
- reazioni gastrointestinali
- reazioni a livello epatico
- reazioni cutanee
- altro

Y.Ahmadi et al. Oxidative stress as a possible mechanism of statin-induced myopathy. Inflammopharmacology, 2018, 26, pp 667–674

# Advantages, disadvantages and possible indications of cholesterol-lowering nutraceuticals.

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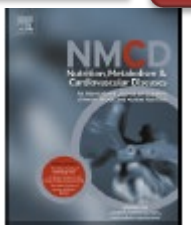
| | Advantage | Disadvantages | Possible indication |
|---|---|---|---|
| Fiber | - LDL-C reduction by 4–14%<br>- Effect on other CV risk factors<br>- Relatively low-cost | Intestinal discomfort for excessive doses | - General population that fails to increase fiber intake with diet alone<br>- Patients with mild hypercholesterolemia and low to moderate cardiovascular risk[a]<br>- Patients with mild hypercholesterolemia and metabolic syndrome |
| Phytosterols | - LDL-C reduction by 8–10%<br>- No interaction with lipid-lowering drugs | - Self purchasing by patients and risk of no medical supervision<br>- Possible excessive intake with the risk of reduced absorption of fat soluble vitamins<br>- High cost | - Patients with mild hypercholesterolemia and low to moderate cardiovascular risk[a]<br>- Patients with intolerance to multiple statins<br>- In addition to drug therapy for patients who do not reach optimal levels of LDL-C |
| Soy products | - LDL-C reduction by 4–13% | - Self purchasing by the patient<br>- Risk of allergies<br>- High cost | - General population<br>- Patients with mild hypercholesterolemia and low to moderate cardiovascular risk[a] |
| Red yeast rice | - LDL-C reduction by 16–25%<br>- Good safety profile<br>- Reduction of cardiovascular risk | - Variability of composition and purity of OTC products<br>- Self purchasing by patients and risk of no medical supervision<br>- Higher cost compared to generic statins<br>- Possible side effects at high doses | - Patients with mild to moderate hypercholesterolemia and low to moderate cardiovascular risk[b] |
| Berberine[d] | - LDL-C reduction by 20%<br>- Better safety profile in patients with intolerance to multiple statins<br>- Favorable effect on TG, HDL-C and blood glucose | - Variability of intestinal absorption<br>- Self purchasing by patients and risk of no medical supervision<br>- Higher cost compared to generic statins | - Patients with mild to moderate hypercholesterolemia and low to moderate CV risk[c]<br>- Patients with mild hypercholesterolemia and metabolic syndrome[e]<br>- Patients with intolerance to multiple statins<br>- In addition to drug therapy for patients who do not reach optimal levels of LDL-C |

HDL-C: HDL cholesterol, LDL-C: LDL cholesterol, CV: cardiovascular; TG: triglycerides; OTC: over the counter.

[a] Patients requiring a reduction of LDL cholesterol by up to 10–15%.
[b] Patients requiring a reduction of LDL cholesterol by up to 20–25%.
[c] Patients requiring a reduction of LDL cholesterol by up to 20%.
[d] Studies performed almost exclusively in Asian populations and therefore not easily transferable to other populations.
[e] Even in combination with a statin, in patients with modest increase in serum triglycerides and/or blood glucose.




A cholesterol level of 200 to 239 mg/dl

# Phytosterols&….synergistic effects of combinations

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## ASSEMBLED PRODUCTS RATIONAL

There are various reasons why it might be preferable to commercialize products of this kind:
a) legal restrictions (e.g. you cannot use more than 10 mg of monacolins/dose by law),
b) side effects (e.g., doses of berberine exceeding than 500 mg/day are more likely to cause gastrointestinal problems), and
c) economic reasons (a more complex formulation allows competitive differentiation and a possible saving on raw material).

Sometimes this phenomenon leads to the creation of products where there is no real rational association and the active substances are under-dosed in relation to the lipid-lowering effect sought. Therefore, before prescribing these nutraceuticals, it would be desirable to investigate

1. the reliability of the origins of the raw materials,
2. dosage compatibility of the individual components with the desired effectiveness,
3. the rationality of the synergy in relation to the action mechanism of the various formulations of substances, and
4. the existence of studies to confirm the effectiveness of the association.

One of the **most tested associations is between monacolins (3 mg) and polycosanol (10 mg)**, which has the rationale of combining an inhibitor of the synthesis of the hydroxymethyl-glutaryl-coenzyme A reductase (polycosanol) with an inhibitor of the activity (monacolin). This association would apparently produce a reduction of LDL cholesterol of about 15% .
Another preconceived association with a **rational formulation combines berberine with cholesterol synthesis inhibitors which facilitates the disposal of circulating cholesterol** . This kind of addition increases the cholesterol-lowering efficacy (up to 25% reduction of LDL cholesterol), also acting on triglycerides (−20%).

# Phytosterols&....synergistic effects of combinations

U6

## ASSEMBLED PRODUCTS RATIONAL

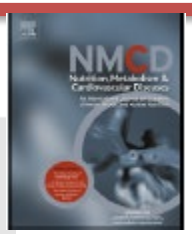


**Table 9** LDL-C reduction, levels of evidence and strength of recommendation for different cholesterol-lowering nutraceuticals.

| | Degree of LDL cholesterol reduction | Level of evidence | Strength of recommendation |
|---|---|---|---|
| Fiber | + | I | A |
| Phytosterols | + | I | A |
| Soy derivatives | +/− | II | C |
| Policosanol | − | VI | D |
| Red yeast rice | ++ | I | A |
| Berberin | ++ | [a] | [a] |

Levels of evidence and strength of recommendation according to the Italian standard of care for diabetes [153]: Levels of evidence: I: evidence obtained from multiple randomized controlled trials and/or from systematic reviews of randomized controlled trials; II: evidence obtained from one randomized trial; VI: *consensus* of experts. Strength of recommendation: A: strongly recommended; C: basic uncertainty; D: no recommendation.

[a] The level of evidence would be I, because supported by meta-analysis of interventional studies, and strength of recommendation A; however, because these studies were conducted almost exclusively in Asian populations, the data are not easily transferable to other ethnic groups.

The cholesterol-lowering effect of some nutraceuticals (fiber, phytosterols, RYR) is consistent and supported by a good level of scientific evidence. Therefore, their use may be advised in some particular categories of patients. With regard to BBR, there is sufficient evidence showing significant cholesterol-lowering effects, although these effects emerged from interventional studies carried out almost exclusively in Asian populations, thus making these results difficult to be generalized to other ethnic groups . Data on the cholesterol-lowering effects of soy are conflicting and, therefore, the strength of the recommendation is quite low, whereas the scientific evidence is inconclusive for PCS.

1) On the basis of the data present in the literature some nutraceuticals (added fiber, phytosterols, red yeast rice) may help control hypercholesterolemia;

2) Of course, the above nutraceuticals may be of help only in subjects who do not yet need pharmaceutical treatments, or in addition to drug therapy.

# Claims of foods properties

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**Table 2** Claims released by EFSA and FDA on nutraceuticals with cholesterol-lowering activity.

| Nutraceutical | Effective dose evaluated in the claim | EFSA | FDA |
|---|---|---|---|
| Fiber: | | | |
| β-Glucan[a] | ≥3 g/day | Reduction of LDL-C | Reduction del LDL-C Reduction of CHD risk |
| Chitosan | 3 g/day | Maintenance of normal levels of LDL-C | – |
| Glucomannan | 4 g/day | Maintenance of normal levels of LDL-C | – |
| Guar gum | 10 g/day | Maintenance of normal levels of LDL-C | – |
| HPMC | 5 g/day | Maintenance of normal levels of LDL-C | – |
| Pectin | 6 g/day | Maintenance of normal levels of LDL-C | – |
| *Psyllium* | ≥7 g/day | – | Reduction of LDL-C |
| Phytosterols | 3 g/day | Reduction of LDL-C | Reduction of LDL-C |
| Soy derivatives | 25 g/day | – | Reduction of CV risk |
| Policosanol | – | – | – |
| Red yeast rice | 10 mg/day of monacolin K | Maintenance of normal levels of LDL-C | Monacolin K has the same restrictions to which is subjected lovastatin |
| Berberine | – | – | – |

CHD: coronary heart disease, LDL-C: LDL cholesterol, CV: cardiovascular, HPMC: hydroxypropylmethylcellulose.
[a] From oats and barley.

| | | |
|---|---|---|
| Red Yest rice extracts (Monacolin K) | 10 mg/die | Monacolin K from red yeast rice contributes to the maintenance of normal blood cholesterol levels |
| Linoleic and alpha-linolenic acids | 10 g/die 2g/die | Maintenance of normal blood cholesterol levels |
| PUFA (EPA&DHA) | 2g/die | Maintenance of normal blood triglycerides levels |

# Physiological effects from traditional use

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Ministero della Salute

Il documento riporta:

>> l'Allegato 1 al DM 10 agosto 2018 sulla disciplina dell'impiego negli integratori alimentari di Sostanze e preparati vegetali come aggiornato con Decreto 9 gennaio 2019;

>> nell'ultima colonna le "Linee guida ministeriali di riferimento per gli effetti fisiologici" che non fanno parte integrante del predetto DM. Tali effetti, impiegabili in attesa della definizione dei claims sui botanicals, sono volti ad ottimizzare le funzioni dell'organismo nell'ambito dell'omeostasi secondo il modello definito dal Consiglio d'Europa (Homeostasis, a model to distinguish between food, including food supplements, and medicinal products, 07/02/2008).

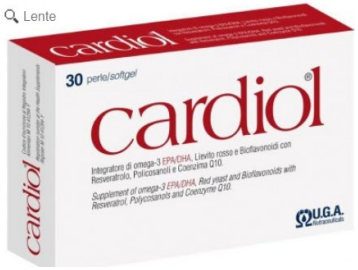
**Tabella 2: Ingrediente presente nella lista delle "Sostanze e preparati vegetali ammessi" del Ministero della Salute**

| AREA CARDIO-METABOLICA | |
|---|---|
| INGREDIENTE | EFFETTO FISIOLOGICO DI CUI ALL'ALLEGATO 1 DM 9 LUGLIO 2012 aggiornato il 27 marzo 2014 "Sostanze e preparati vegetali ammessi" |
| *Cynara cardunculus subsp. flavescens Wiklund* | Foglie: Metabolismo dei lipidi |

*Nota: la tabella sopra non è esaustiva delle sostanze a cui è associato un effetto fisiologico ammesso dalla lista ministeriale per la specifica area di riferimento.*


1 compressa contiene:
Berberis aristata e.s. 588mg equivalennte a Berberina 500mg.
Riso rosso fermentato 200mg equivalente a Monacolina 3mg.
Microalghe(Haematococcus pluvialis 20g equivalente a Astaxantina 0,5mg.
Policosanolo 10mg.
Acido folico 200mg.
Coenzima Q10 2,0mg.


Fitosteroli; agente di carica: cellulosa microcristallina; Riso Rosso fermentato da Monascus purpureus tit. al 3% in monacolina K; agente di carica: carbossimetilcellulosa sodica reticolata; agenti antiagglomeranti: biossido di silicio, sali di magnesio degli acidi grassi; agenti di rivestimento: idrossipropilmetilcellulosa, talco, polietilenglicole; coloranti: biossido di titanio, ossidi di ferro e idrossidi di ferro




Olio di pesce purificato per distillazione molecolare multipla e standardizzato al 75% in acidi grassi Omega-3 (min. 63% di EPA e DHA), Riso (Oryza sativa L.) fermentato con lievito Monascus purpureus e.s. titolato al 3% in monacolina K, Citrus reticulata L. frutto e.s. titolato al 40% in flavonoidi polimetossitati Tangeretina e Nobiletina (Bioflavonoidi) Polygonum cuspidatum radice e.s. standardizzato al 50% in resveratrolo, Oryza sativa L. frutto (crusca) e.s. titolato al 95% in policosanoli, Coenzima Q10, Acido folico, Vitamine B3, B6 e B12, Vitamina E come miscela di tocotrienoli e tocoferoli da palma (Elaeis guineensis Jacq.), Lignani di sesamo (Sesamum indicum L.) semi e.s. titolato al 60% in sesamina, Pepe nero (Piper nigrum L.) frutti e.s. titolato all'85%in piperina, Emulsionanti: lecitina di girasole, glicerinmonostearato, Involucro: gelatina, Agente di resistenza: glicerolo vegetale.
Coloranti: caramello,estratto di paprika, titanio diossido.
Prodotto senza glutine.

# Diabetes

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| Classification | Definition |
|---|---|
| Type 1 DM | Type 1 diabetes mellitus encompasses the majority of cases that are primarily due to pancreatic islet beta-cell destruction, attributable either to an autoimmune process or to an unknown cause (idiopathic). These patients are prone to ketoacidosis and require insulin injections for survival. It does not include cases with beta-cell destruction or failure to which specific causes can be assigned (e.g., cystic fibrosis, mitochondrial defects, etc.) |
| Type 2 DM | Type 2 is the most common form of diabetes mellitus. It is characterised by disorders of insulin action and insulin secretion, either of which may be the predominant feature. Both are usually present at the time that this form of diabetes manifests clinically. By definition, the specific reasons for the development of these abnormalities are not yet known. |
| Gestational DM | Gestational diabetes is carbohydrate intolerance resulting in hyperglycaemia of variable severity, with onset or first recognition during pregnancy. It does not exclude the possibility that the glucose intolerance may antedate pregnancy but had been previously unrecognised. The definition applies irrespective of whether or not insulin is used for treatment or whether the condition persists after pregnancy. Gestational DM usually resolves after pregnancy, but mothers and babies both have a higher risk of developing type 2 DM later in life. |

*Adapted from World Health Organization.[5]
DM = diabetes mellitus.

it affects young population that needs insulin because the pancreas does not produce insulin

it affects a predominantly elderly population, often characterized by excess weight, treated with oral anti-diabetics and diet

SINTOMATOLOGIA

⇧ della sete
⇧ della fame
⇧ minzione
stanchezza
chetoacidosi

acuta

nefropatie
cecita'
impotenza
malattie CV

cronica

# Diabetes

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Can J Diabetes 42 (2018) S64–S79

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

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2018 Clinical Practice Guidelines

Nutrition Therapy

Diabetes Canada Clinical Practice Guidelines Expert Committee

John L. Sievenpiper MD, PhD, FRCPC, Catherine B. Chan PhD, Paula D. Dworatzek PhD, RD, Catherine Freeze MEd, RD, CDE, Sandra L. Williams MEd, RD, CDE

Nutrition therapy and counselling are an integral part of the treatment and self-management of diabetes. The goals of nutrition therapy are to maintain or improve quality of life and nutritional and physiological health; and to prevent and treat acute- and longterm complications of diabetes, associated comorbid conditions and concomitant disorders.

It is well documented that nutrition therapy can improve glycemic control by reducing glycated hemoglobin (A1C) by 1.0% to 2.0% and, when used with other components of diabetes care, can further improve clinical and metabolic outcomes, resulting in reduced hospitalization rates.

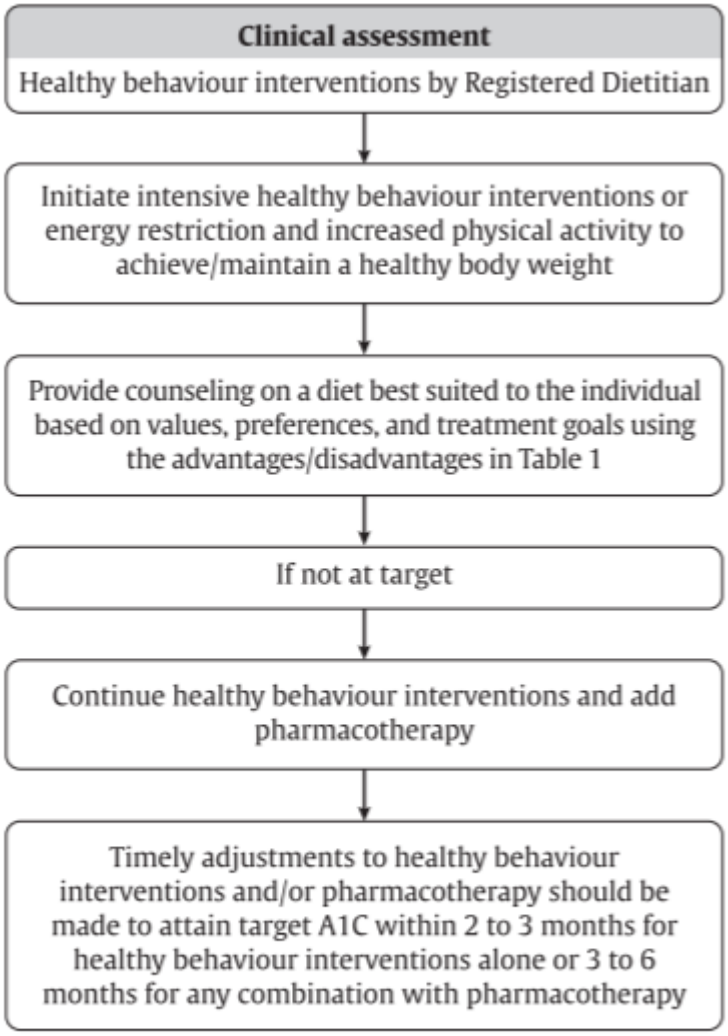


**Figure 1.** Nutritional management of hyperglycemia in type 2 diabetes. *A1C*, glycated hemoglobin.

# Diabetes

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DIABETES CANADA

CJD

ELSEVIER

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The glycated hemoglobin - or glycosylated, if you prefer - allows you to broadly evaluate the average blood sugar level in the last two or three months.

It is therefore a very useful test to evaluate the adequacy of the glycemic control of the diabetic patient, recently re-evaluated also in the diagnosis of the disease.

Glycation is the non-enzymatic biological process whereby sugars can bind covalently to proteins. The most abundant blood sugar, glucose, can therefore irreversibly bind to a specific part of hemoglobin, forming HbA1c or glycated hemoglobin. The higher the blood glucose concertation, the greater the percentage of glycated hemoglobin (HbA1c or A1C).

Why do you measure?

Given the irreversibility of the glycation, the glycosylated hemoglobin contained in the red blood cells (avid of glucose) circulates in the blood for the whole duration of their life (on average 90/120 days). Within certain limits, this is an absolutely normal process, which does not entail any danger to the patient's health, given that glycated hemoglobin continues to perform its function normally. The problems, rather, are related to the high blood glucose levels that go with it.

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| *$HbA_{1c}$ (%)* | *$HbA_{1c}$ (mmol/mol)* | *Utilizzo* |
|---|---|---|
| 4.0 | 20 | Limite inferiore in soggetti non diabetici |
| 5.4 | 36 | Limite superiore in gravidanza (1° e 2° trimestre) |
| 5.7 | 39 | Diagnosi di prediabete |
| 6.5 | 48 | Diagnosi di diabete |
| 7.0 | 53 | Obiettivo terapeutico primario |

| EMOGLOBINA GLICATA (%) | GLICEMIA MEDIA (MG/DL) |
|---|---|
| 5 | 97 (76–120) |
| 6 | 126 (100–152) |
| 7 | 154 (123–185) |
| 8 | 183 (147–217) |
| 9 | 212 (170–249) |
| 10 | 240 (193–282) |
| 11 | 269 (217–314) |
| 12 | 298 (240–347) |
| 13 | 326 (260-380) |
| 14 | 355 (290-410) |
| 15 | 384 (310-440) |
| 16 | 413 (330-480) |

# Diabetes

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Properties of dietary interventions*,†,‡

Properties of dietary interventions (listed in the order they are presented in the text)

| Dietary interventions | A1C | CV benefit | Other advantages | Disadvantages |
|---|---|---|---|---|
| Macronutrient-based approaches | | | | |
| Low-glycemic-index diets | ↓ (32,44,46,47) | ↓CVD (52) | ↓LDL-C, ↓CRP, ↓hypoglycemia, ↓diabetes Rx | None |
| High-fibre diets | ↓ (viscous fibre) (57) | ↓CVD (69) | ↓LDL-C, ↓non-HDL-C, ↓apo B (viscous fibre) (54,57,59) | GI side effects (transient) |
| High-MUFA diets | ↔ | ↓CVD | ↓Weight, ↓TG, ↓BP | None |
| Low-carbohydrate diets | ↔ | - | ↓TG | ↓Micronutrients, ↑renal load |
| High-protein diets | ↓ | - | ↓TG, ↓BP, preserve lean mass | ↓Micronutrients, ↑renal load |
| Mediterranean dietary pattern | ↓ (50,139) | ↓CVD (143) | ↓retinopathy (144), ↓BP, ↓CRP, ↑HDL-C (139,140) | None |
| Alternate dietary patterns | | | | |
| Vegetarian | ↓ (145,251) | ↓CHD (152) | ↓Weight (148), ↓LDL-C (149) | ↓vitamin B12 |
| DASH | ↓ (159) | ↓CHD (161) | ↓Weight (159), ↓LDL-C (159), ↓BP (159), ↓CRP (160) | None |
| Portfolio | - | ↓CVD (162,163) | ↓LDL-C (162,163), ↓CRP (162), ↓BP (163) | None |
| Nordic | - | - | ↓LDL-C+, ↓non-HDL-C (169–171) | None |
| Popular weight loss diets | | | | |
| Atkins | ↔ | - | ↓Weight, ↓TG, ↑HDL-C, ↓CRP | ↑LDL-C, ↓micronutrients, ↓adherence |
| Protein Power Plan | ↓ | - | ↓Weight, ↓TG, ↑HDL-C | ↓Micronutrients, ↓adherence, ↑renal load |
| Ornish | - | - | ↓Weight, ↓LDL-C, ↓CRP | ↔ FPG, ↓adherence |
| Weight Watchers | - | - | ↓Weight, ↓LDL-C, ↑HDL-C, ↓CRP | ↔ FPG, ↓adherence |
| Zone | - | - | ↓Weight, ↓LDL-C, ↓TG, ↑HDL-C | ↔ FPG, ↓adherence |
| Dietary patterns of specific foods | | | | |
| Dietary pulses/legumes | ↓ (176) | ↓CVD (181) | ↓Weight (179), ↓LDL-C (177), ↓BP (178) | GI side effects (transient) |
| Fruit and vegetables | ↓ (183,184) | ↓CVD (79) | ↓BP (186,187) | None |
| Nuts | ↓ (188) | ↓CVD (143,181) | ↓LDL-C (190), ↓TG, ↓FPG (189) | Nut allergies (some individuals) |
| Whole grains | ↓ (oats) (194) | ↓CHD (99) | ↓LDL-C, FPG (oats, barley) (57,193) | GI side effects (transient) |
| Dairy | ↔ | ↓CVD (199,200) | ↓BP, ↓TG (when replacing SSBs) (197) | Lactose intolerance (some individuals) |
| Meal replacements | ↓ | - | ↓Weight | Temporary intervention |

* ↓ = <1% decrease in A1C.

† Adjusted for medication changes.

‡ References are for the evidence used to support accompanying recommendations.

*A1C*, glycated hemoglobin; *apo B*, apolipoprotein B; *BMI*, body mass index; *BP*, blood pressure; *CHD*, coronary heart disease; *CHO*, carbohydrate; *CRP*, C reactive protein; *CV*, cardiovascular; *CVD*, cardiovascular disease; *DASH*, Dietary Approaches to Stop Hypertension; *FPG*, fasting plasma glucose; *GI*, gastrointestinal; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *MUFA*, monounsaturated fatty acid; *SSBs*, sugar-sweetened beverages; *TC*, total cholesterol; *TG*, triglycerides.

# Diabetes

U6

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**Stage-Targeted Nutrition and Other Healthy Behaviour Intervention Strategies for Type 2 Diabetes**

**Prediabetes**

- Weight loss or maintenance*
- Portion control
- Guidance to include low-GI CHO and reduce refined CHO
- Physical activity

**Early type 2 diabetes**

- Weight loss or maintenance*
- Portion control
- Low-GI CHO
- High fibre
- CHO distribution
- Dietary pattern of choice†
- Physical activity

**Type 2 diabetes not on insulin**

- Weight loss or maintenance*
- Portion control
- CHO distribution
- Low-GI CHO
- High fibre
- Dietary pattern of choice†
- Physical activity

**Type 2 diabetes on basal insulin only**

- Portion control
- Weight loss or maintenance*
- CHO consistency
- Low-GI CHO
- High fibre
- Dietary pattern of choice†
- Physical activity

**Type 2 diabetes on basal-bolus therapy**

- Portion control
- Weight loss or maintenance*
- CHO consistency initially then learn CHO counting
- Low-GI CHO
- High fibre
- Dietary pattern of choice†
- Physical activity

*As appropriate.
†Dietary patterns include Mediterranean, vegetarian, DASH, Portfolio, and Nordic dietary patterns, as well as diets emphasizing specific foods (i.e., dietary pulses, fruit and vegetables, nuts, whole grains and dairy products) which have evidence of benefit for people with diabetes.

**Figure 2.** Stage-targeted nutrition and other healthy behaviour strategies for people with type 2 diabetes. *CHO*, carbohydrate; *GI*, glycemic index; *NPH*, neutral protamine Hagedorn.

# Diabetes

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**Text Box 2:**

## NUTRITION RECOMMENDATIONS FOR THE MANAGEMENT OF DIABETES CHO IN DIABETES MANAGEMENT

(with the evidence-based review grade level)* See Text Box 1.

### Recommendations:

- A dietary pattern that includes CHO from fruits, vegetables, whole grains, legumes, and low-fat milk is encouraged for good health. (Level B)
- Monitoring CHO, whether by CHO counting, exchanges, or experienced-based estimation remains a key strategy in achieving glycemic control. (Level A)
- **The use of GI and load may provide a modest additional benefit over that observed when total CHO is considered alone. (Level B)**
- Sucrose-containing foods can be substituted for other CHOs in the meal plan or, if added to the meal plan, covered with insulin or other glucose-lowering medications. Care should be taken to avoid excess energy intake. (Level A)
- As for the general population, people with diabetes are encouraged to consume a variety of fiber-containing foods. However, evidence is lacking to recommend a higher fiber intake for people with diabetes than for the population as a whole. (Level B)

Sugar alcohols and nonnutritive sweeteners are safe when consumed within the daily intake levels established by the Food and Drug Administration (FDA). (Level A)

# Diabetes

U6

**Indirizzi dietetici per il DM tipo I e tipo II**

| Indirizzo dietetico | DM tipo I | DM tipo II |
|---|---|---|
| *Diminuzione delle calorie* | No | *Generalmente sì* |
| Maggior frazionamento dei pasti | Sì | Non sempre |
| *Assunzione costante, giorno per giorno, di calorie, glicidi, protidi e grassi* | *Molto importante* | *Non necessaria, se l'apporto medio di calorie rimane nei limiti bassi* |
| Rapporti costanti, giorno per giorno, fra glucidi, protidi e grassi ad ogni pasto | Consigliabile | Non necessario |
| *Regolarità degli orari dei pasti* | *Molto importante* | *Non necessario* |
| Cibo extra per un'insolita attività fisica | Indicato di regola | Non indicato di regola |
| *Ricorso al cibo per prevenire o curare l'ipoglicemia* | *Importante* | *Non necessario* |

## Alcune raccomandazioni dietetiche

**Alimenti contenenti carboidrati da includere o meno nella dieta dei soggetti diabetici**

| | Permessi | Da utilizzare in quantità moderata | Sconsigliati |
|---|---|---|---|
| **Cereali per colazione** | All-bran, Weetabix, grano e avena soffiati, müesli non zuccherati | Cornflakes, Rice Krispies, Special K, porridge (pappa di fiocchi di avena) | Cereali ricoperti di zucchero. |
| **Farina, pane** | Farina integrale, pane integrale, dolci fatti con farina integrale, pane di segale | Farina bianca, pane bianco o nero, dolci fatti con farina bianca | Farina gialla |
| **Riso, pasta** | Riso integrale, pasta integrale | Riso brillato, pasta non integrale | Semolino, tapioca |
| **Frutta** | Frutta fresca, frutta a guscio, frutta cotta dolcificata con dolcificanti artificiali, frutta in scatola in succo naturale | Succo di frutta senza zucchero aggiunto | Succhi di frutta zuccherati, frutta sciroppata |
| **Verdura** | Tutta la verdura e legumi | Patate | |
| **Prodotti caseari** | Latte scremato, yogurt al naturale | Latte intero, yogurt non al naturale | Latte condensato |
| **Dolci, biscotti e merendine** | Biscotti integrali | Biscotti comuni, dolci fatti con farina bianca, torte di frutta, biscotti secchi | Biscotti e torte molto zuccherati |
| **Zucchero e cibi dolci** | | Marmellate, confetture e altri prodotti ipocalorici | Zucchero, marmellate e confetture comuni, miele, melassa, sciroppi, bevande zuccherate, caramelle, cioccolato |

# Diabetes

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| Tipologia di prodotto | Alimenti disponibili |
|---|---|
| **Pane e similari** (arricchiti in fibra, con amido meno biodisponibile, etc.) | Cracker<br>Fette biscottate<br>Grissini<br>Pane<br>Pasta |
| **Biscotti ipoglicidici** (prodotti con sorbitolo o fruttosio) | Biscotti vari (frollini, petit four, petit beurre, soave, con marmellata, wafer, ecc.)<br>Pasticcini |
| **Dolci** (prodotti con sorbitolo o fruttosio) | Colomba<br>Plum-cake<br>Pandoro<br>Panettone<br>Torte (al limone, nocciole, ecc.) |
| **Marmellate e confetture** (prodotte con fruttosio o sorbitolo) | Confetture varie (albicocca, ciliegia, fragola, pesca, ecc.)<br>Marmellata di arancia |
| **Caramelle e dolciumi** (prodotti con edulcoranti naturali e di sintesi) | Bubble gum<br>Caramelle dure e gommose<br>Cioccolatini vari<br>Cioccolato fondente, al latte e bianco<br>Gelatine di frutta<br>Torroni |
| **Prodotti vari** | Base crostata<br>Budini<br>Creme (cacao, vaniglia, ecc.)<br>Müesli<br>Pan di Spagna<br>Preparati per budini<br>Preparati per torte |


L'uso di ques :ompliance
dietetica, se dogli di
consumare u

# Diabetes

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**Table II.** Nutraceutical supplements

| Nutraceutics | Action |
|---|---|
| L-carnitine | Promotion of insulin sensitivity and hypolipidemic actions |
| α-Lipoic acid | Treatment of diabetic neuropathy and degenerative neuronal disease |
| Berberine | Hypoglycemic and hypolipidemic actions |
| ω-3 | Anti-arrhythmic effect and decrease of triglycerides |

**Table I** Plants and their action of mechanism

| Name of the plant | Reported mechanism of action |
|---|---|
| *Acacia arabica (Lam.) Muhl.*<br>Common name: Babul<br>[Family: *Fabaceae*] | Acts through release of insulin from pancreatic beta cells, which accounts for the hypoglycaemic activity (Singh, 1975; Wadood, 1989) |
| *Aegle marmelos (L.) Correa*<br>Common name: Wood apple<br>[Family: *Rutaceae*] | Increases utilization of glucose; either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion<br>and also decreases the elevated glucose and glycosylated haemoglobin levels (Kamalakkanan, 2003) |
| *Allium cepa L.*<br>Common name: onion<br>[Family: *Liliaceae*] | Lowers blood glucose level and has potent<br>antioxidant activity, which may account for the hypoglycaemic potential (Augusti, 1973) |
| *Allium sativum L.*<br>Common name: garlic<br>[Family: *Alliaceae*] | Has strong antioxidant activity and rapid reactivity with thiol containing proteins responsible for the hypoglycaemic property (Rabinkov, 1998) |
| *Aloe vera (L.) Burm.f.*<br>Common name: Aloe<br>[Family: *Aloaceae*] | Maintains glucose homeostasis by controlling the carbohydrate metabolizing enzymes<br>and stimulates insulin release from pancreatic beta cells (Ajabnoor, 1990) |
| *Annona squamosa L.*<br>Common name: Sugar apple<br>[Family: *Annonaceae*] | Lowers blood glucose level (Shirwaikar, 2004) |

# Diabetes

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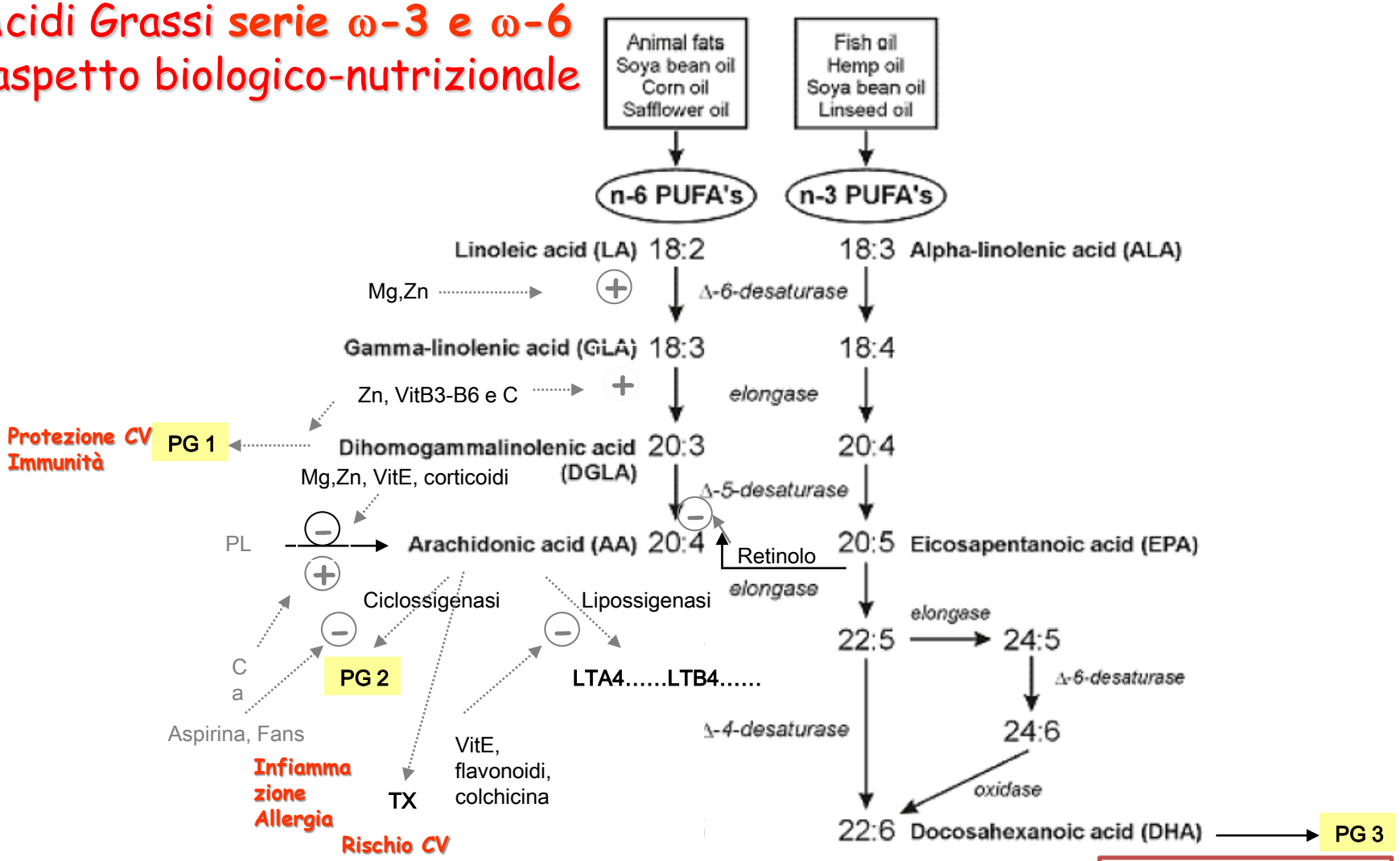
## Acidi Grassi serie ω-3 e ω-6 aspetto biologico-nutrizionale



# Diabetes

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Benefits of fish oil supplementation : a systematic review and meta-analysis. GD, Eslick, et al., et al. 2012, p. 67-76.
https://google/images/ndgdqx

# Diabetes

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| Alimento | | | EPA | DHA | ALA |
|---|---|---|---|---|---|
| Pesce | Pesce gatto | | Tracce | 0,2 | 0,1 |
| | Merluzzo | | Tracce | 0,1 | Tracce |
| | Sgombro | | 0,9 | 1,4 | 0,2 |
| | Salmone | Allevato | 0,6 | 1,3 | Tracce |
| | | Pescato | 0,3 | 1,1 | 0,3 |
| | | In scatola | 0,9 | 0,8 | Tracce |
| | Salmone Chinook | | 1,0 | 0,9 | Tracce |
| | Pesce spada | | 0,1 | 0,5 | 0,2 |
| | Tonno rosso | | 0,3 | 0,9 | – |
| | Tonnetto striato | Sott'olio | Tracce | 0,1 | Tracce |
| | | Al naturale | Tracce | 0,2 | Tracce |
| | Tonno ala lunga | Sott'olio | Tracce | 0,2 | 0,2 |
| | | Al naturale | 0,2 | 0,6 | Tracce |
| Molluschi e crostacei | Aragosta | | – | – | – |
| | Cozze | | 0,2 | 0,3 | Tracce |
| | Gamberetti | | 0,3 | 0,2 | Tracce |
| Frutta a guscio e semi | Burro di frutta secca | | – | – | 8,7 |
| | Semi di lino | | – | – | 18,1 |
| | Noci | | – | – | 9,1 |
| Oli vegetali | Colza | | – | – | 9,3 |
| | Semi di lino | | – | – | 53,3 |

The original source of EPA + DHA is plankton

The richest species in ω-3 are salmon, the category of blue fish.

Linseed oil and walnuts are the richest vegetable sources

Enriched foods in ω-3.

C. Berdanier, L. Berdanier. Adavenced in nutrition (2015) CrC Press

# Diabetes

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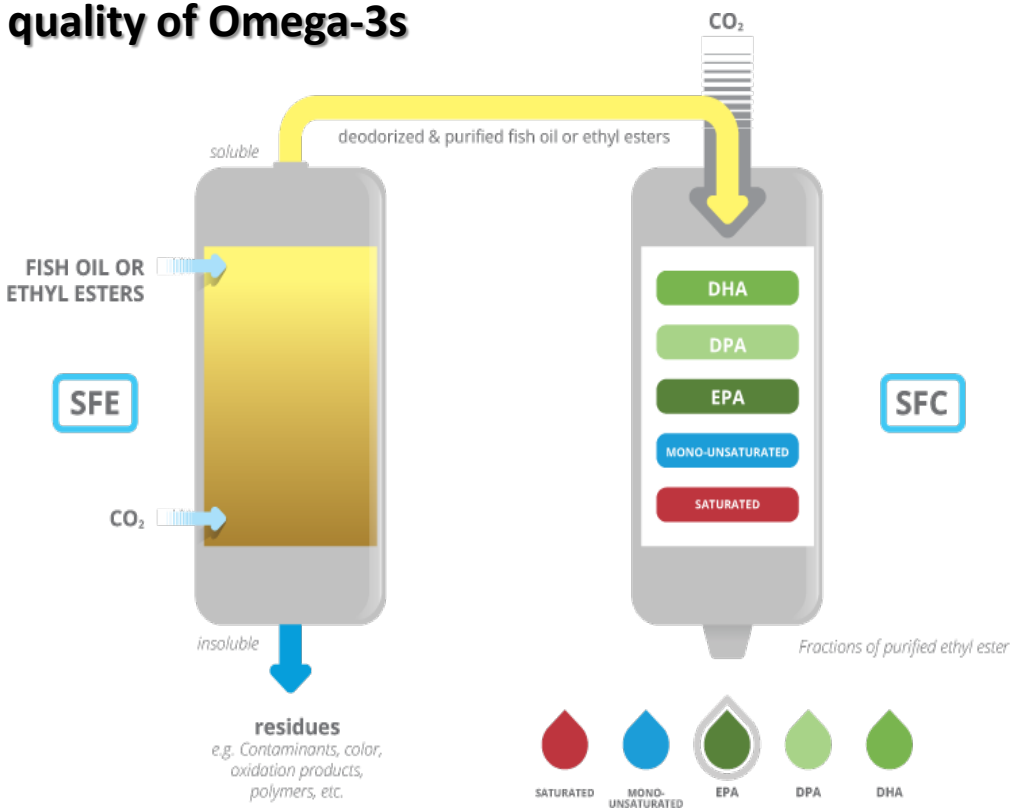
## Extraction and quality of Omega-3s

The extraction process used to obtain oils rich in Omega-3 determines the quality of the final product
The highest quality supplements, as well as the drugs, are obtained by extraction and fractionation with supercritical fluids
The purity of fish oil is given by the concentration of EPA and DHA, levels of contaminants and oxidation of the product

Quality certification is the IFOS (International Fish Oil Standards) certification




**Formulations:**
Pearls
Oils
Concetrated solutions

IFOS™ THE INTERNATIONAL FISH OIL STANDARDS PROGRAM

N, Rubio-Rodriguez, SM, De Diego e S, Beltran. s.l. : J Food ENG, 2012, p. 238-248.

# Diabetes

U6


Cromo picolinato, vitamina B1, vitamina B2, vitamina B6


Composizione PSYLLOGEL® Fibra Arance Rosse 20 Bustine Monodose: Fibra di Psyllium (84,40%) (Plantago Ovata) Pura Al 99%, Acidificante Acido Citrico, Estratto di Sambuco, Emulsionante: Lecitina Di Soia, Aroma Arance Rosse, Edulcorante: Aspartame (1%), Colorante: Beta Carotene, Antiagglomerante: Biossido di Silicio.


Olio di pesce contenente: Acido docosaesanoico (DHA), Acido eicosapentaenoico (EPA); Gelatina, Umidificante: E422; CoEnzima Q10; Acqua; Olio vegetale (Canola e Girasole); Aroma; Caratteristiche nutrizionali  per due mini perle EPA150 mg DHA300 mg CoQ1030 mg Valore Energetico8,54 kcal - 0,03 kJ Proteine0,24 g Carboidrati0,07 g Grassi0,81 g Formato 60 mini perle.


Berberis (Berberis aristata DC, cellulosa microcristallina, amido) corteccia estratto secco 85% berberina; Riso rosso fermentato (Oryza sativa L.) semi polvere 1,5% monacolina K; gelso bianco (Morus alba L.) foglie estratto secco 2% DNJ; agenti di carica: idrossipropilcellulosa [silice (nano)] e sodio carbossimetilcellulosa; agenti antiagglomeranti: stearato di magnesio vegetale e

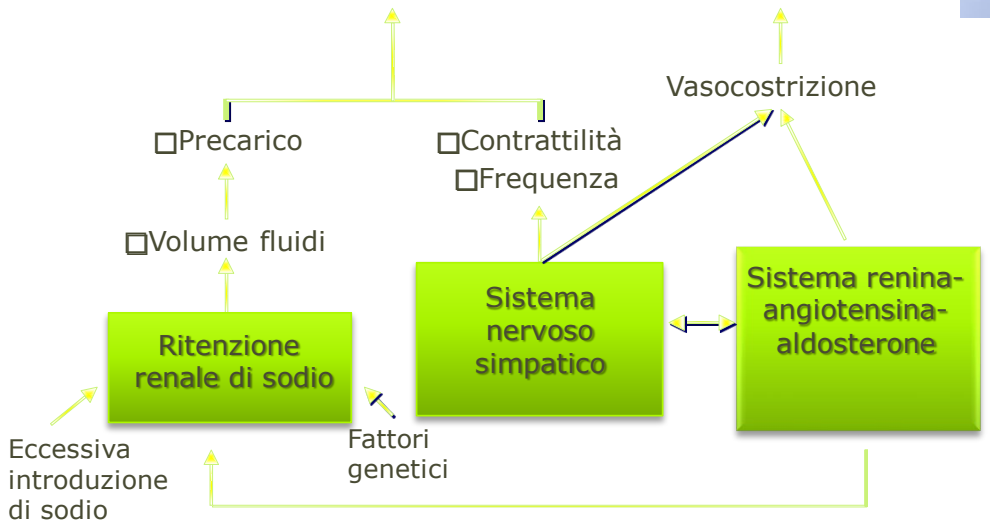
# Hypertension

U6

Arterial pressure is the blood pressure exerted by the heart on the artery wall during the phases of cardiac activity, represented by the contraction of the left ventricle (systole) and its relaxation (diastole).
In the systolic phase the maximum value of pressure is detected (systolic or maximum pressure, SBP), while in diastole the minimum value (diastolic or minimum pressure, DBP)

Pressione arteriosa = Gittata cardiaca x Resistenze periferiche (RP)

Ipertensione = Aumento gittata cardiaca e/o Aumento RP




| Blood Pressure | SBP | DBP |
|---|---|---|
| Classification | mmHg | mmHg |
| **Normal** | <120 | and <80 |
| **Prehypertension** | 120–139 | or 80–89 |
| **Stage 1 Hypertension** | 140–159 | or 90–99 |
| **Stage 2 Hypertension** | ≥160 | or ≥100 |
| **Ipotension** | <90 | <60 |

# Hypertension

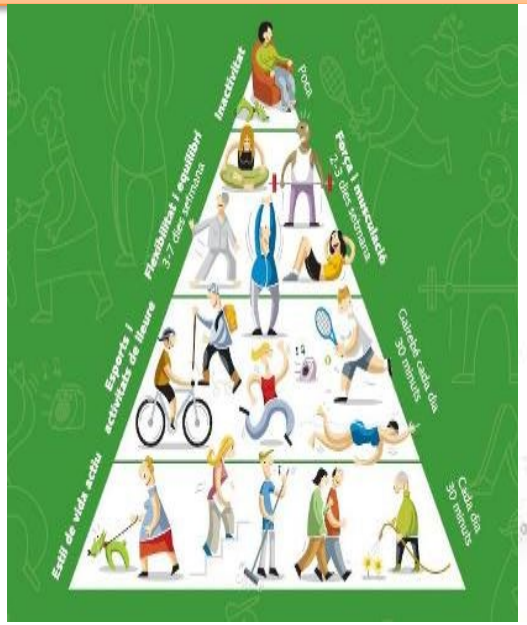
U6

Problems linked to hypertension

- heart rhythm disorders
- cardiac ischemia (angina or infarction)
- heart failure (the heart dilates and loses efficiency)
- transient brain disorders, permanent damage (stroke) to brain cells that do not receive enough blood and oxygen
- loss of memory, attention and orientation in space and time
- progressive reduction of renal function, to the point of causing chronic renal failure

Drug therapy is effective only if it is changed lifestyle:

Diet
Weight reduction
Physical activity
No smoke
No excess alcohol




# Hypertension

U6

- reduce body weight by at least 5 kg in hypertensive patients with overweight> 10% (low-calorie diet and moderate aerobic exercise)
- limit alcohol consumption to 30 ml of ethanol / day (and suspend cigarette smoking)
- reduce sodium consumption to no more than 100 mmol (<2.3 g of sodium or <6 g of sodium chloride),
- DIETARY PRODUCTS
  Low salt salts of Na content between 20-30%, the remainder K
  Na-free asodic salts only K salts
- increase the consumption of fruit and vegetables, which also ensure a adequate dietary intake of potassium, calcium and magnesium
- Milk and vegetable protein sources such as soy and lupine contain hypotensive tripeptides (Val-Pro-Pro and ile-pro-pro) due to antagonist effect blocking the conversion from angiotensin I to II
- reduce the consumption of cholesterol and saturated fat, to be replaced with mono or polyunsaturated fats. It also reduces the caloric intake important for weight control


Composizione:
Potassio Cloruro, Sodio Cloruro (35%), Potassio Citrato, Magnesio Solfato, Magnesio Carbonato, Calcio Carbonato.


Componenti:
potassio cloruro, sodio cloruro, sodio glutammato, destrosio, verdure disidratate (sedano, cipolla, carota, prezzemolo proteine vegetali idrolizzate, magnesio carbonato, caramello, esaltatore di sapidità: disodio inosinato guanilato.),

# Hypertension

U6

ANN MED

Taylor & Francis
Taylor & Francis Group

*Annals of Medicine*, 2015; Early Online: 1–10

ISSN 0785-3890 print /ISSN 1365-2060 online
DOI: 10.3109/07853890.2015.1078905

REVIEW ARTICLE

## Nutraceuticals for blood pressure control

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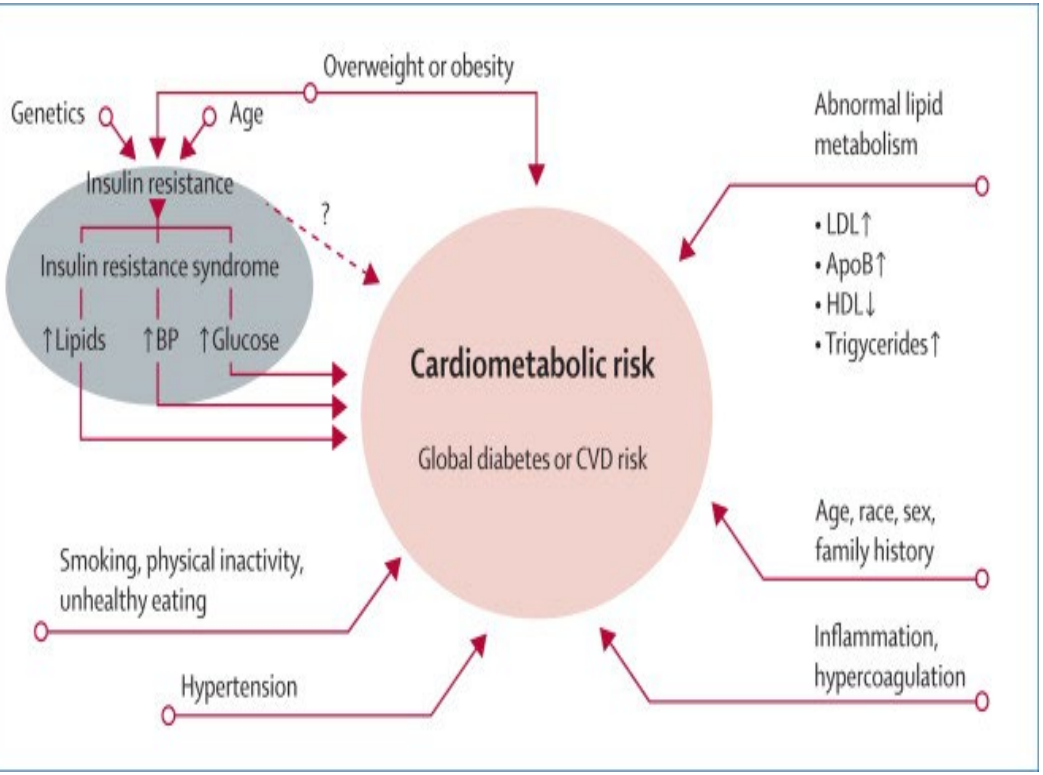
### Key messages

- A large number of nutraceuticals have shown blood pressure-lowering activity.
- They range from commonly used dietary components, such as chocolate and beetroot juice, to vitamins, minerals, probiotics, coenzyme Q10, melatonin, dried garlic, and several others.
- The long-term intake of these products, associated with an improved life-style, may reduce the number of subjects assigned to pharmacological treatment.

*L-arginine*
*Mg+ and k+*
*Cocoa flavanols*
*Beetroot juice*
*Aged dry garlic extract*
*Melatonin*

# Metabolic syndrome




Metabolic syndrome refers to a cluster of diseases that confer a cumulative risk for heart attack and stroke, providing health professionals with the ability to focus on prevention.

The original WHO definition of metabolic syndrome, also known as “syndrome X,” “insulin resistance syndrome” and “the deadly quartet,” required the patient to have one of the following: [2]

- Diabetes
- Impaired glucose tolerance
- Impaired fasting glucose >110 mg/dl
- Insulin resistance

Plus two of the following:

- ✓ A waist-to-hip ratio greater than 0.9 in men, 0.85 in women and/or a BMI greater than 30.
- ✓ Dyslipidaemia (abnormal levels of fat/cholesterol in the blood) HDL<35M a 39F; TG>115mg/dl
- ✓ Blood pressure of 140/90mmHg or higher
- ✓ Microalbuminuria (increased levels of the protein albumin) albumin/creatinin>20mg/g

# Metabolic syndrome&nutraceutical for

U6

The World Health Organization (WHO) for some years has been focusing on what is now commonly referred to as an "epidemic of obesity and diabetes" ("diabesity"): behind this outbreak, there are several risk factors grouped in what is called "metabolic syndrome" (MetS). The basis of this "epidemic" is either a diet too often characterized by excessive consumption of saturated and trans-esterified fatty acids, simple sugars and salt, either a sedentary lifestyle.

Treatment strategies for MetS include pharmacologic and non-pharmacologic options, with varying degrees of success rate. The first is indicated for patients with high cardiovascular risk, while the second one is the most cost-effective preventive approach for subjects with borderline parameters and for patients intolerant to pharmacological therapy. MetS non-pharmacological treatments could involve the use of nutraceuticals, most of which has plant origins (phytochemicals), associated with lifestyle improvement. Some nutraceuticals, when adequately dosed, should improve a number of the MetS components

**Primary intervention**
recommends that primary management for the metabolic syndrome is a healthy lifestyle. This includes: moderate calorie restriction (to achieve a 5–10 per cent loss of body weight in the first year) moderate increase in physical activity change in dietary composition. Nutraceuticals

**Secondary intervention**
In people for whom lifestyle change is not enough and who are considered to be at high risk for CVD, drug therapy may be required to treat the metabolic syndrome.

Contents lists available at ScienceDirect

Phytomedicine

journal homepage: www.elsevier.com/locate/phymed


## Role of phytochemicals in the management of metabolic syndrome

Arrigo F.G. Cicero*, Alessandro Colletti

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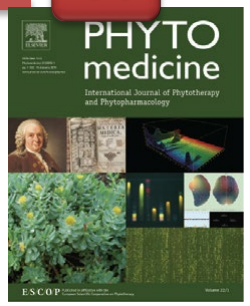
# Fiber-Metabolic syndrome&nutraceutical for

U5


Psyllium husk has maybe the largest scientific evidence of efficacy. Although true psyllium comes from *Plantago psyllium* , the husks and seeds of *Plantago ovata* ( *Plantaginaceae* ) are commonly referred to as psyllium.
Psyllium is one of the most widely used fibre supplements because it is reasonably cheap and is better tolerated than other fibre supplements.

**Effects**:

- ✓ Psyllium has mild lipid-lowering, anti-obesity, anti-diabetic and anti-hypertensive effects in humans .
- ✓ Psyllium husk and other soluble fibres have also a positive global impact on post-prandial glycaemia and other insulin-resistance re- lated parameters.
- ✓ has significant beneficial effects on both systolic and diastolic blood pressures with doses of 3.5 g t.i.d. taken 20 mins before two main meals.
- ✓ improve vascular function measured through augmentation.

**Side effects**
All the available trials and meta-analysis conclude for an overall safety of psyllium supplements. However, it could have transient gastrointestinal side effects which are usually not severe and only mildly decrease compliance to treatment, especially when micronized fibre is used. Entire seeds, used for the treatment of constipation, did not demonstrate a lipid-lowering action and they could exacerbate diverticulitis in patients affected by chronic diverticulosis.

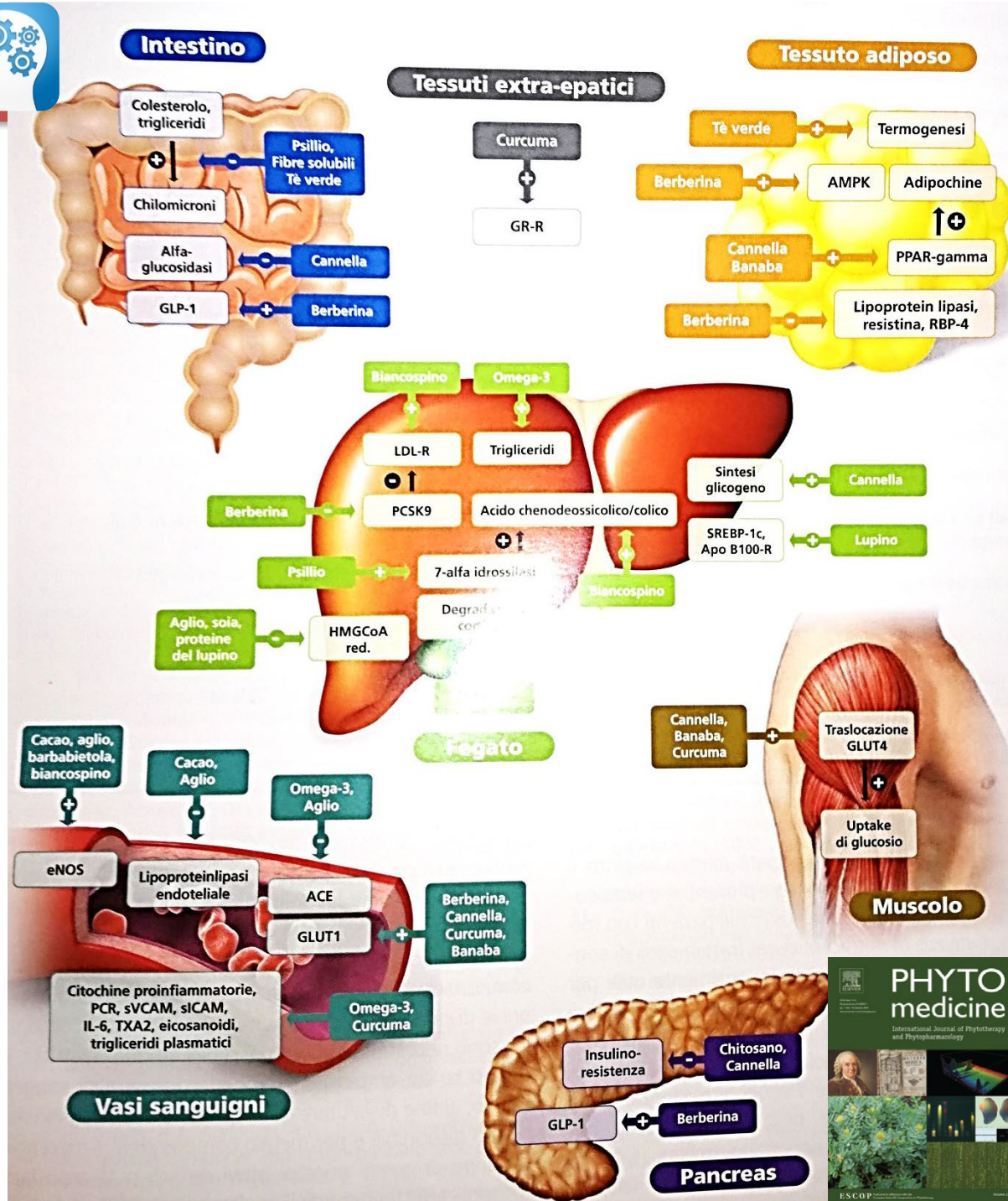
A main safety concern about soluble fibres use as cholesterol-lowering agents is the risk of drug interaction that regards oral antidiabetic drug, digoxin, warfarin, lithium, iron, oral steroids, tricyclic antidepressants, carbamazepine and other molecules

Other soluble fibes with positive effects on more than one MetS component are guar gum, fenugreek, chitosan and glucomannan

# .....nutraceutical for

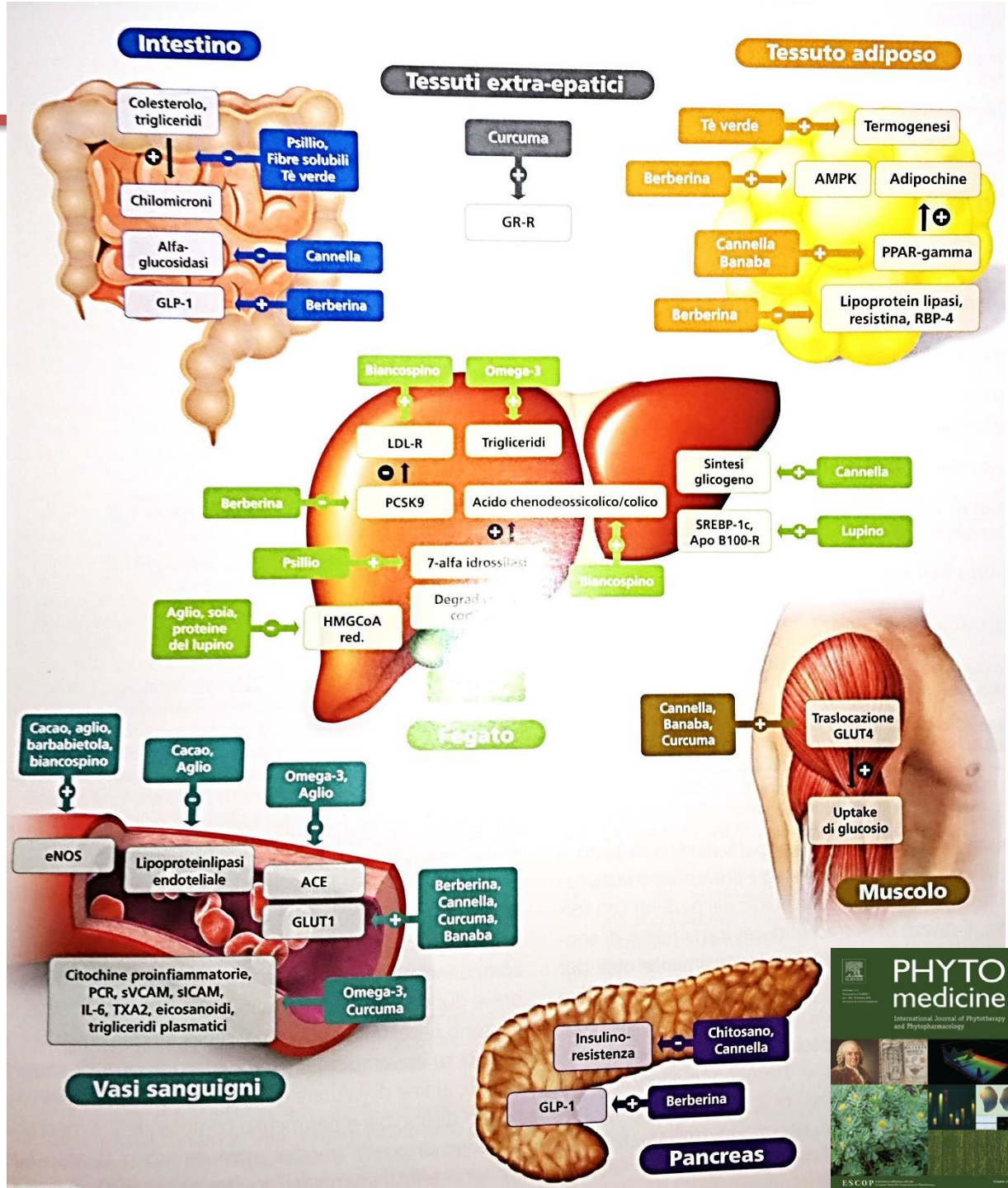
Patients with mixed hyperlipidaemia treated with berberine experienced a mean reduction of 25% in LDL and TG levels, by using doses of 500–1500 mg daily. Berberine has also an insulin-sensitizer effect comparable to that of metformin, through a mechanism involving retinol binding protein-4 (RBP-4) and GLUT-1 and an insulinotropic effect. Moreover it increases the levels of glucagon like peptide-1 (GLP-1), acting directly on pancreas .

Standard doses of berberine (50 0–10 0 0 mg/day) are usually well tolerated more than 1000 mg/day have been associated to arterial hypotension, constipation and cardiac damage. Berberine displaces bilirubin from albumin thus it should be avoided in jaundiced infants and pregnant women.Berberine also displaces warfarin, thiopental increasing their plasma levels. Meanwhile, it can markedly increase the blood levels of cyclosporine A by the inhibition of the cytochrome P450 in the liver and of the P-glycoprotein in the gut thus causing its increased bioavailability and reduced metabolism



# ……nutraceutical for

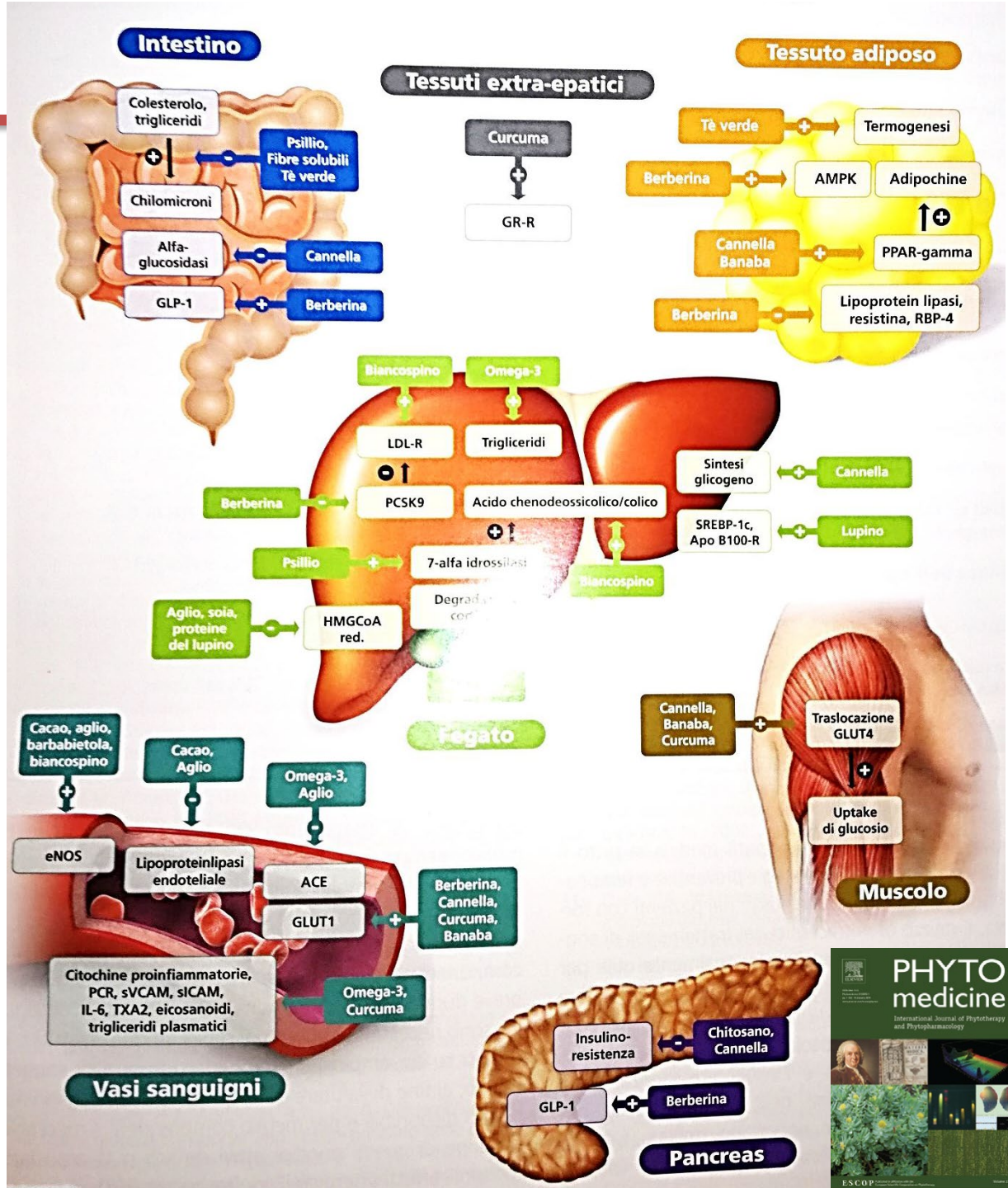
*Lagerstroemia speciosa* L., in Philippines folk medicine known as "banaba", seems to have anti-diabetic and anti-obesity effects. Although its mechanism of action is still not clear, the increase of cellular uptake of glucose, the inhibition of the hydrolysis of sucrose and starches, the decreased gluconeogenesis and the regulation of lipid metabolism, mediated by PPAR, MAPK. The main active components of banaba extract may be corosolic acid, ellagitannins, tannic acid and penta-O-galloyl-glucopyranose



# ……nutraceutical for

*Cinnamomum aromaticum* (Cassia) and *Cinnamomum zeylanicum* have been subjected to extensive research. Cinnamaldehyde administration to diabetic rats for 2 months significantly improves muscle and hepatic glycogen content; moreover it increases glucose uptake through GLUT-4 translocation in peripheral tissues. Several phenolic compounds, such as catechin, epicatechin, and procyanidin B2, and phenol polymers identified from the subfraftions of aqueous cinnamon extract has shown significant inhibitory effects on the formation of advanced glycation end-products, suggesting a potential in the prevention of diabetes complications .

Positive effects of cinnamon on fasting TG and HDL cholesterol, and postprandial hypertriglyceridemia have also been confirmed in animal models and diabetic patients.



# ……nutraceutical for

Consumption of green tea as well as cocoa can be beneficial in patients with MetS. In fact these nutraceuticals are rich in phytochemicals, including catechins and phenols, which have significant antioxidant properties with clear benefits for cardiovascular health.

Animal studies have shown that green tea lowers blood pressure by suppressing the activity of NADPH oxidase and reducing the reactive oxygen species.

A meta-analysis of 20 randomized clinical trials, with a total of 1536 participants who received green tea regularly, has shown a slight decrease in systolic blood pressure.

The flavonoids of cocoa are the most studied in the clinical field: in particular it has been shown that the flavonols content in some types of cocoa, improves the endothelial function in healthy subjects and in hyperglycaemic or hypertensive patients with or without glucose intolerance, increasing the flow-mediated vasodilation.