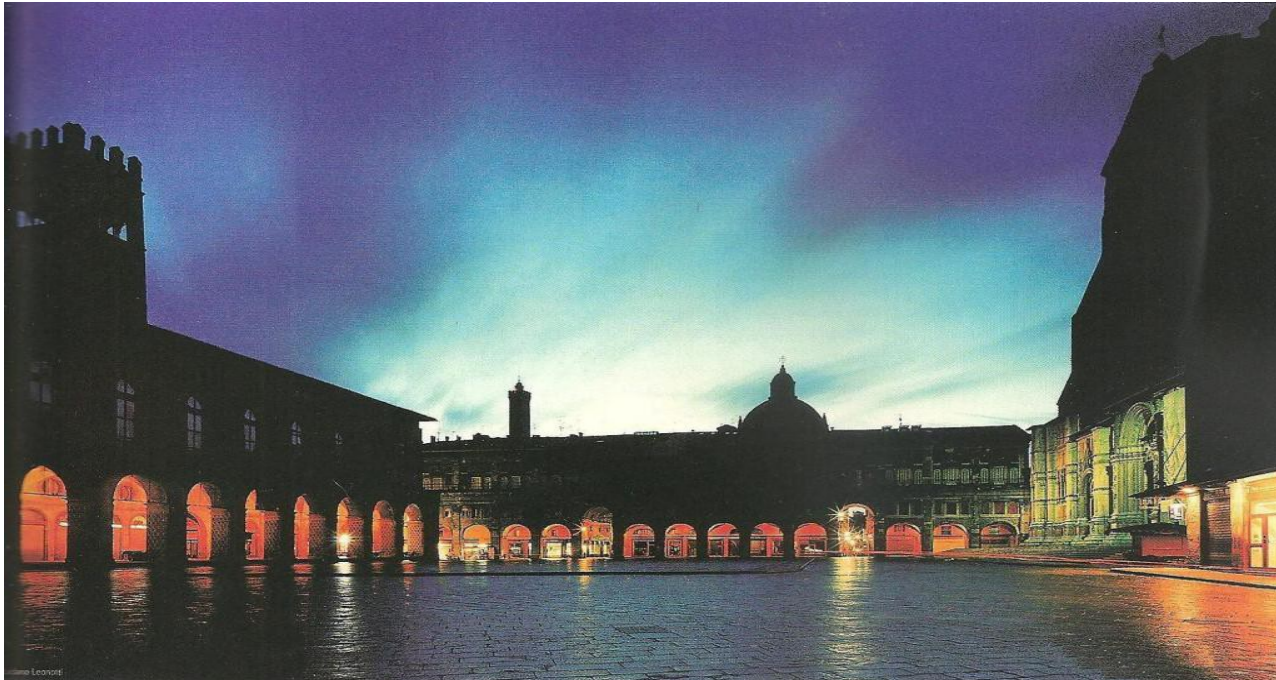


Nutraceutica e correzione del rischio cardiovascolare



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Dipartimento Cardio-Toraco-Vascolare
Università degli Studi di Bologna

COSA SONO I NUTRACEUTICI?

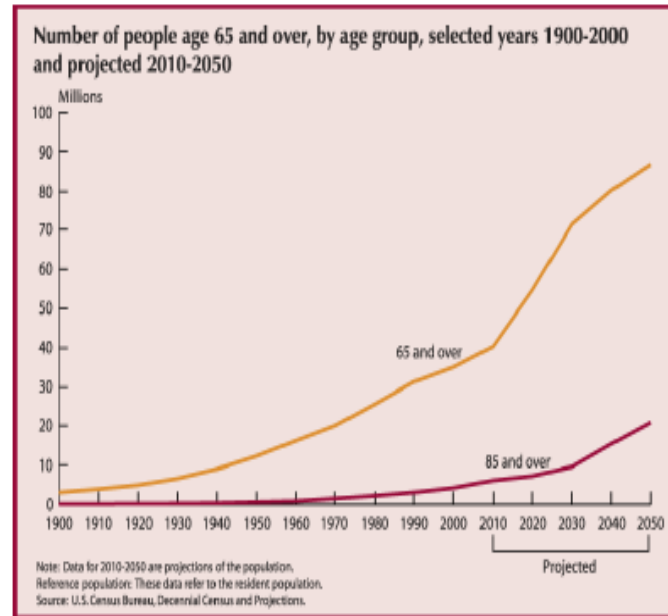
Neologismo originato dalle parole: **nutrizione** e **farmaceutico**

“Componente alimentare o principio attivo presente negli alimenti e che ha effetti positivi per il benessere e la salute, ivi inclusi la prevenzione e il trattamento delle malattie”



Perché fare prevenzione ?

L'aspettativa di vita a 65 anni è di 17 e a 80 anni di altri 8 anni

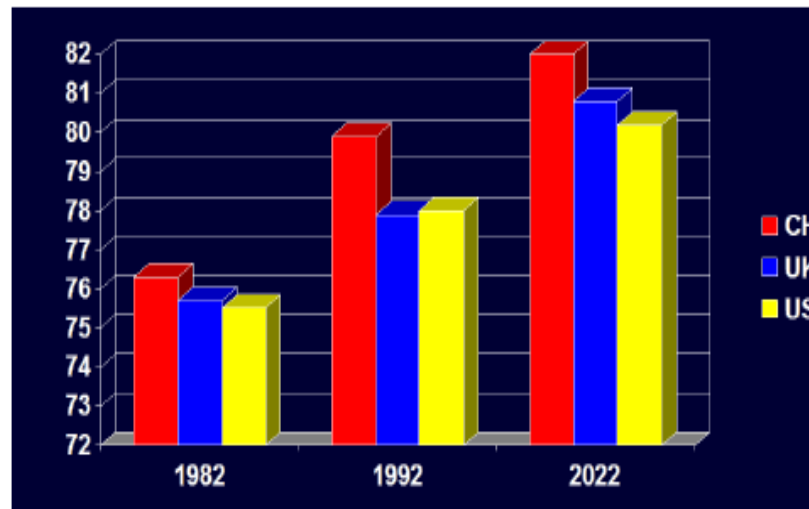


Entro il 2050 almeno 25 milioni di 80enni negli Stati Uniti

Rischio cardiovascolare

- Nel mondo occidentale le malattie cardiovascolari rappresentano la prima causa di morte: in Italia in particolare sono responsabili del 44% di tutte le morti.

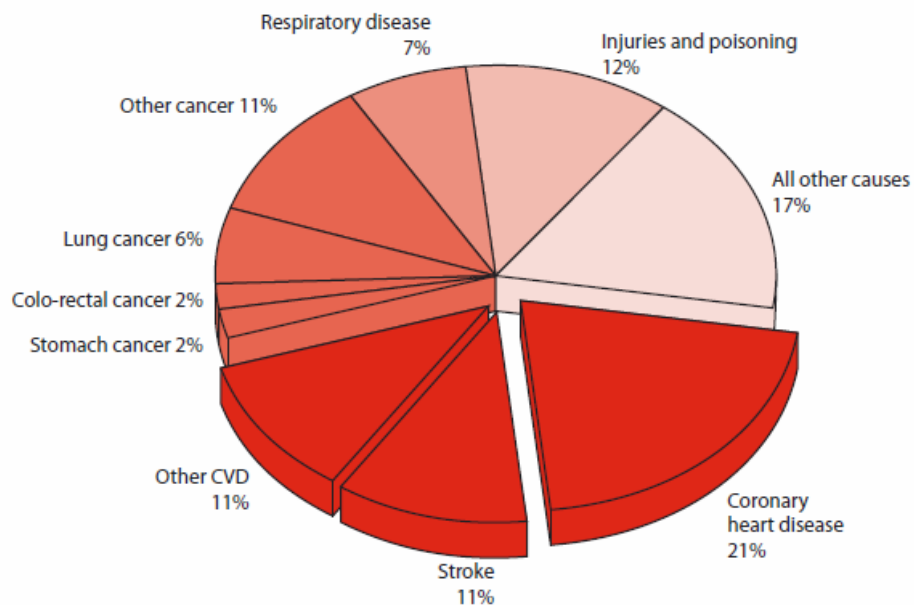
Nel 2020 circa 600 milioni di persone saranno ad alto rischio per eventi cardiovascolari maggiori



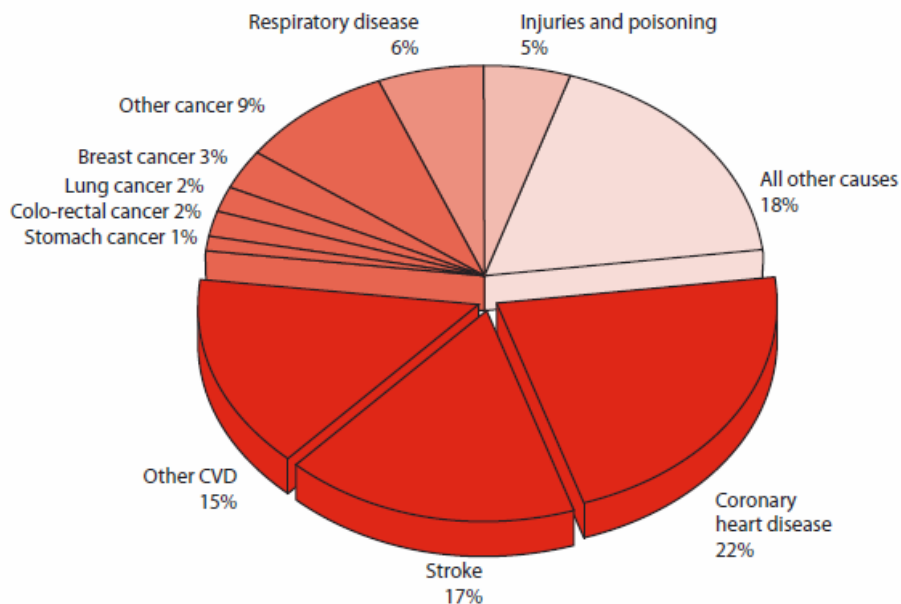
Deaths by cause in Europe

latest available year

MEN



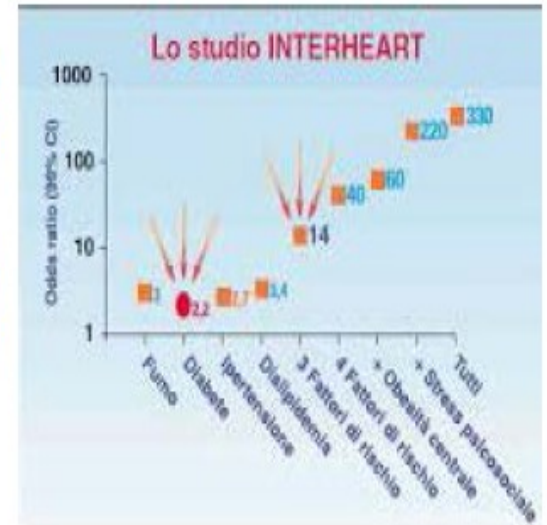
WOMEN



Studio INTERHEART

Nove fattori di rischio, facilmente misurabili, spiegano oltre il 90% degli infarti miocardici

6 fattori di rischio (fumo, dislipidemia, ipertensione arteriosa, diabete, obesità, fattori psico-sociali) e **3 fattori protettivi** (dieta ricca di frutta e verdura, attività fisica, “consumo di alcool”)



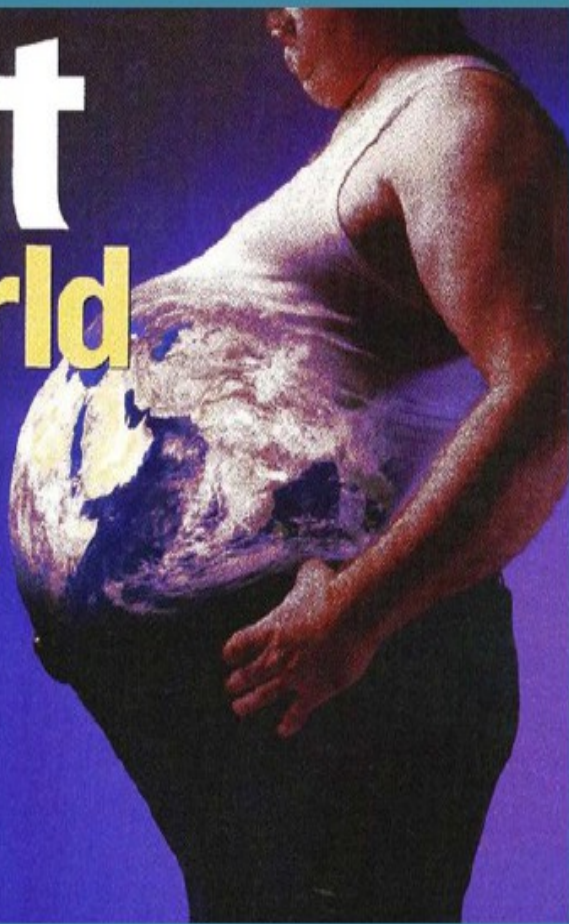
L'associazione di più fattori di rischio moltiplica enormemente la probabilità di infarto ...

... chi presenta tutti i nove fattori ha una probabilità di infarto che è più di 330 volte superiore a quella di chi non ne ha nessuno

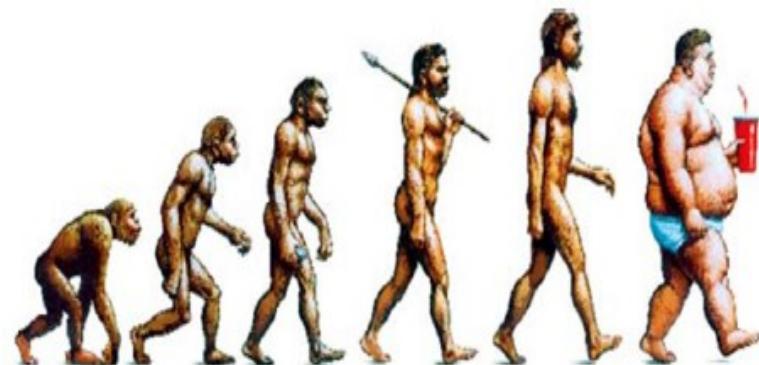
Fat World

We're Eating More Junk And Getting Less Exercise.

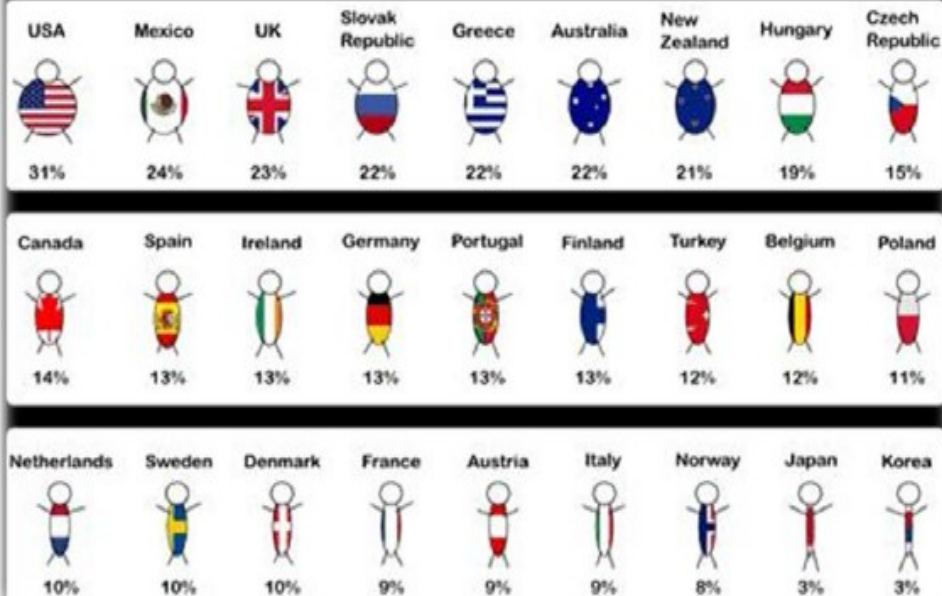
Obesity Is The Globe's Newest Epidemic.



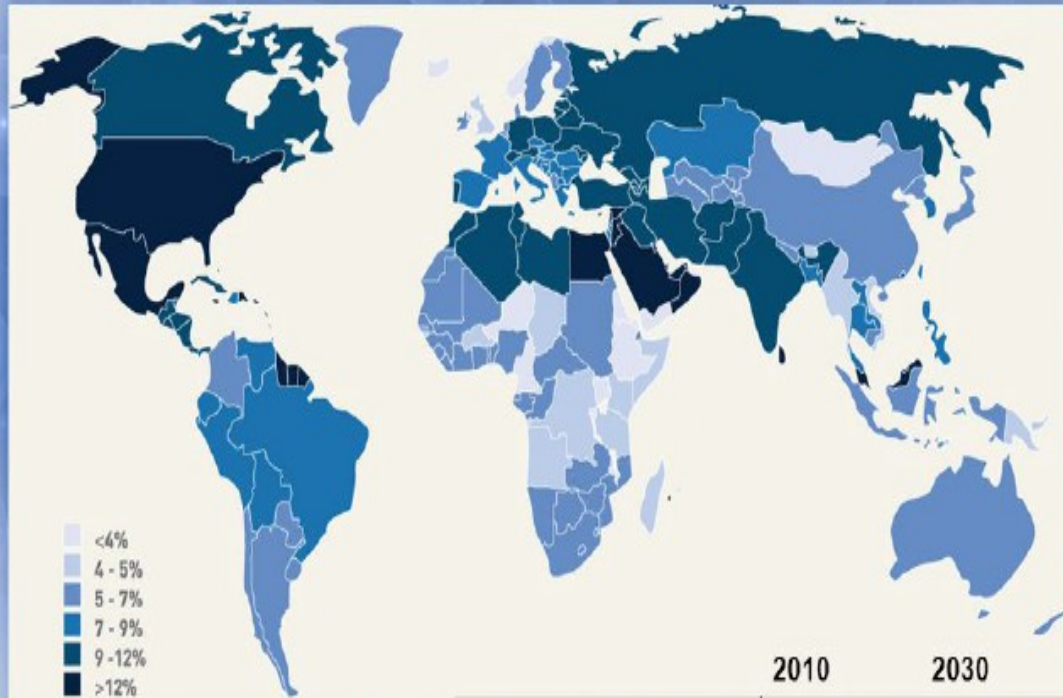
L'EVOLUZIONE DELL'UOMO



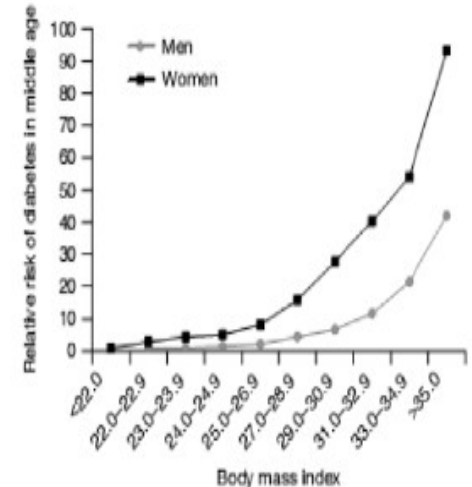
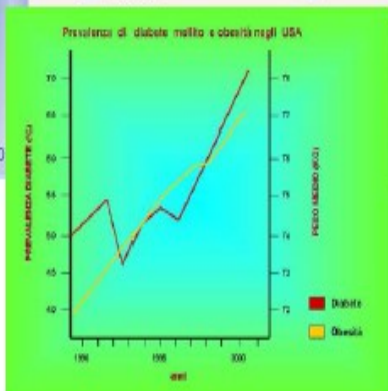
OBESITY: The percentage of the population older than 15 with a body-mass index greater than 30.



Prevalenza del diabete nel 2030



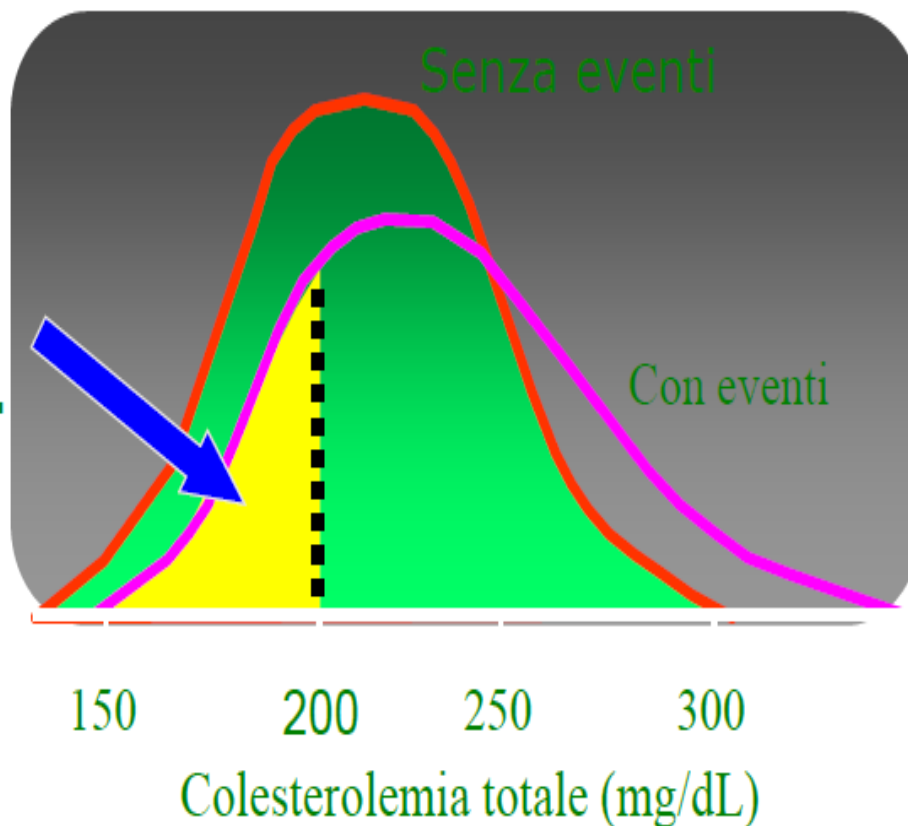
	2010	2030
Numero tot di persone con diabete (age 20-79)	285 milioni	438 milioni
Prevalenza di diabete (anni 20-79)	6.6 %	7.8 %



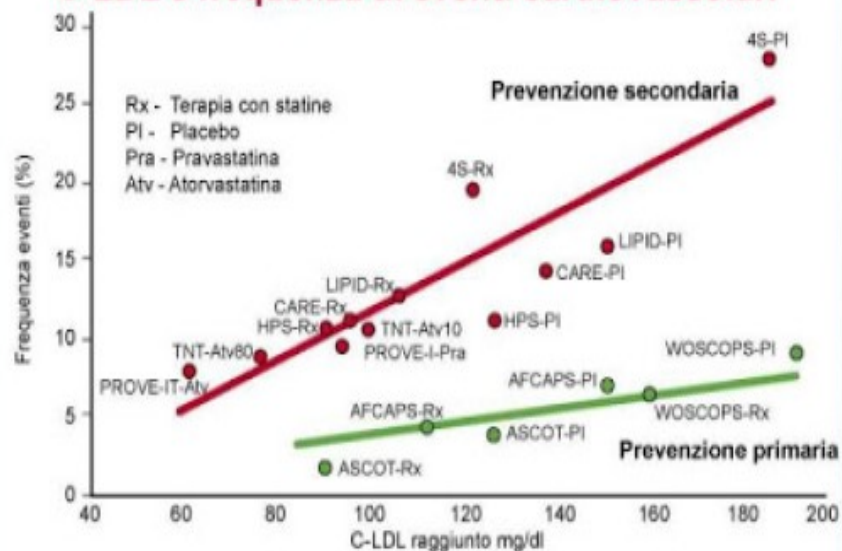
Distribuzione del colesterolo totale:
Pazienti con e senza eventi coronarici

Framingham Heart Study—26 anni di Follow-up

**Il 35% di
eventi
coronarici si
verifica in
pazienti con CT
< 200 mg/dL**

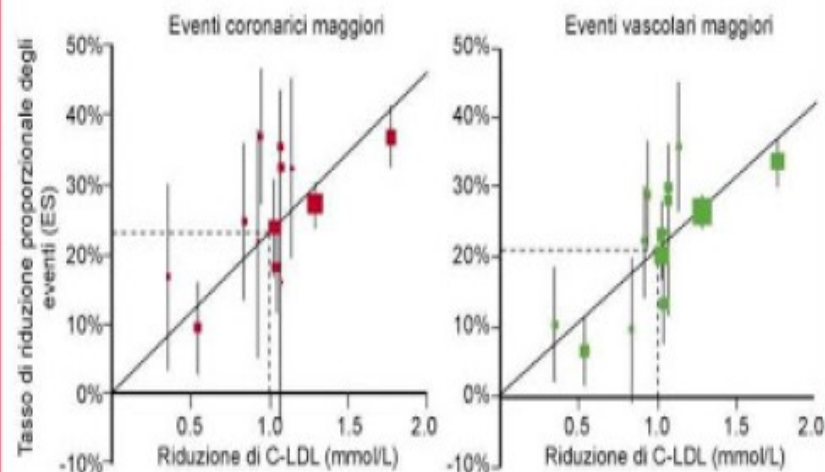


Più basso è meglio? Relazione tra livello di C-LDL e frequenza di eventi cardiovascolari



Rosenstock RS. *Exp Opin Emerg Drugs* 2004;9(2): 269-279; LaRosa JC et al. *N Engl J Med* 2005;352:1425-1435.

Riduzione degli eventi vascolari in relazione all'abbassamento assoluto di C-LDL



CTT Collaborators. *Lancet* 2005; 366: 1267-78

**E' POSSIBILE USARE I NUTRACEUTICI PER
RIDURRE IL RISCHIO CARDIOVASCOLARE**

.....E QUANDO?

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

brisk walking per week (or any equivalent activity) may increase HDL-C levels by 0.08–0.15 mmol/L (3.1–6 mg/dL).⁷⁷ Smoking cessation may also contribute to HDL-C elevation.^{5,81}

6.4 Dietary supplements and functional foods active on plasma lipid values

Innovative nutritional strategies to improve dyslipidaemias have been developed; they are based either on changing some 'risky' dietary components or on encouraging the consumption of specifically targeted 'healthy' functional foods and/or dietary supplements; these so-called 'nutraceuticals' can be used either as alternatives or in addition to lipid-lowering drugs.⁶⁹

Nutritional evaluation of functional foods includes not only the search for the clinical evidence of beneficial effects relevant to improved health or reduction of disease risk, but also the demonstration of good tolerability and the absence of major undesirable effects. The substantiation of health claims relevant for each food should be based on results from intervention studies in humans that are consistent with the proposed claims.⁶⁸

Overall, the available evidence on functional foods so far identified in this field is lacking the major gap is the absence of diet-based intervention trials of sufficient duration to be relevant for the natural history of dyslipidaemia and CVD.

Phytosterols

The natural sterols in plant foods are known as phytosterols. They are

tolerated, effective, and recommended for LDL-C lowering at a daily dose of 5–15 g/day soluble fibre.⁹¹

n-3 unsaturated fatty acids

Supplementation with 2–3 g/day of fish oil (rich in long chain n-3 fatty acids) can reduce TG levels by 25–30% in both normolipidaemic and hyperlipidaemic individuals. α-linolenic acid (a medium chain n-3 fatty acid present in chestnuts, some vegetables, and some seed oils) is less effective on TG levels. Long chain n-3 PUFAs also reduce the post-prandial lipaemic response. Long chain n-3 PUFAs, at doses of ~3 g/day given as supplements, may increase LDL-C by ~5% in severely hypertriglyceridaemic patients.⁹² However, a low dose supplementation of a margarine with n-3 PUFAs (400 mg/day) or α-linolenic acid (2 g/day) did not significantly reduce TG levels in an RCT involving 4837 post-MI patients; neither did this supplementation reduce the rate of major CV events.⁹³

Polycosanol and red yeast rice

Polycosanol is a natural mixture of long chain aliphatic alcohols extracted primarily from sugarcane wax.⁹⁴ Studies show that polycosanol from sugarcane, rice, or wheat germ has no significant effect on LDL-C, HDL-C, TG, apo B, Lp(a), homocysteine, hs-CRP, fibrinogen, or blood coagulation factors.⁹⁴

'Red yeast rice' (RYR) is a source of fermented pigment used in China as a food colourant and flavour enhancer for centuries. Possible bioactive effects of RYR are related to a statin-like mechanism. Inhibition of hydroxymethylglutaryl-CoA

5.1 Lifestyle changes

Appropriate lifestyle changes are the cornerstone for the prevention of hypertension. They are also important for its treatment, although they should never delay the initiation of drug therapy in patients at a high level of risk. Clinical studies show that the BP-lowering effects of targeted lifestyle modifications can be equivalent to drug monotherapy,³³⁷ although the major drawback is the low level of adherence over time—which requires special action to be overcome. Appropriate lifestyle changes may safely and effectively delay or prevent hypertension in non-hypertensive subjects, delay or prevent medical therapy in grade I hypertensive patients and contribute to BP reduction in hypertensive individuals already on medical therapy, allowing reduction of the number and doses of antihypertensive agents.³³⁸ Besides the BP-lowering effect, lifestyle changes contribute to the control of other CV risk factors and clinical conditions.¹⁴

The recommended lifestyle measures that have been shown to be capable of reducing BP are: (i) salt restriction, (ii) moderation of alcohol consumption, (iii) high consumption of vegetables and fruits and low-fat and other types of diet, (iv) weight reduction and maintenance and (v) regular physical exercise.³³⁹ In addition, insistence on cessation of smoking is mandatory in order to improve CV risk, and because cigarette smoking has an acute pressor effect that may raise daytime ambulatory BP.^{340–342}

5.1.1 Salt restriction

There is evidence for a causal relationship between salt intake and BP and excessive salt consumption may contribute to resistant

hypertension. Moderate alcohol consumption and regular physical activity result in an increase in quality-adjusted life-years.³⁵³

5.1.2 Moderation of alcohol consumption

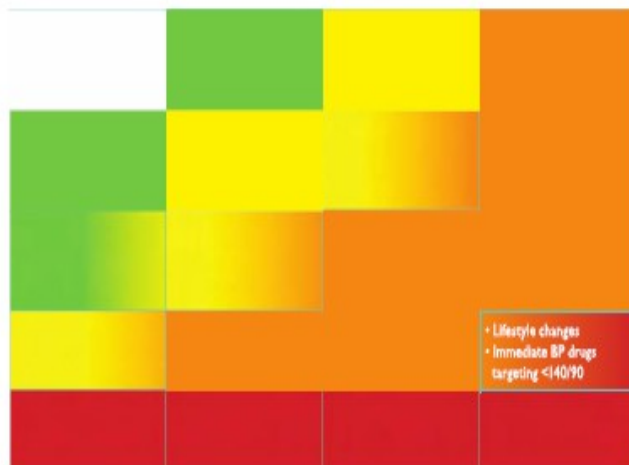
The relationship between alcohol consumption, BP levels and the prevalence of hypertension is linear. Regular alcohol use raises BP in treated hypertensive subjects.³⁵⁴ While moderate consumption may do no harm, the move from moderate to excessive drinking is associated both with raised BP and with an increased risk of stroke. The Prevention And Treatment of Hypertension Study (PATHS) investigated the effects of alcohol reduction on BP. The intervention group had a 1.2/0.7 mmHg greater reduction in BP than the control group at the end of the 6-month period.³⁵⁵ No studies have been designed to assess the impact of alcohol reduction on CV endpoints. Hypertensive men who drink alcohol should be advised to limit their consumption to no more than 20–30 g, and hypertensive women to no more than 10–20 g, of ethanol per day. Total alcohol consumption should not exceed 140 g per week for men and 80 g per week for women.

5.1.3 Other dietary changes

Hypertensive patients should be advised to eat vegetables, low-fat dairy products, dietary and soluble fibre, whole grains and protein from plant sources, reduced in saturated fat and cholesterol. Fresh fruits are also recommended—although with caution in overweight patients because their sometimes high carbohydrate content may promote weight gain.^{329,354} The Mediterranean type of diet, especially, has attracted interest in recent years. A number of studies and meta-analyses have reported on the CV protective effect of the Mediterranean diet.^{357,358} Patients with

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)



Intervention strategies as a function of total CV risk and LDL-C level

Total CV risk (SCORE) %	LDL-C levels				
	< 70 mg/dL < 1.8 mmol/L	70 to < 100 mg/dL 1.8 to < 2.6 mmol/L	100 to < 150 mg/dL 2.6 to < 3.9 mmol/L	150 to < 190 mg/dL 4.0 to < 4.9 mmol/L	> 190 mg/dL > 4.9 mmol/L
< 1	No lipid intervention	No lipid intervention	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled
Class/Level	I/C	I/C	I/C	I/C	IIa/A
≥ 1 to < 5	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled
Class/Level	I/C	I/C	IIa/A	IIa/A	IIa/A
> 5 to < 10, or high risk	Lifestyle intervention consider drug ^a	Lifestyle intervention consider drug ^a	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention
Class/Level	IIa/A	IIa/A	IIa/A	IIa/A	IIa/A
≥ 10 or very high risk	Lifestyle intervention consider drug ^a	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention	Lifestyle intervention and immediate drug intervention
Class/Level	IIa/A	IIa/A	IIa/A	IIa/A	IIa/A

European Heart Journal 2011;32 (14):1769–1818
Atherosclerosis 2011 Jul;217(1):3–46

www.escardio.org/guidelines



Recommendations on lifestyle changes

Are recommended	Class	LoE ^a	LoE ^b
Salt restriction to 5-6 g per day.	I	A	B
Moderation of alcohol consumption to no more than 20-30 g of ethanol per day in men and 10-20 g of ethanol per day in women.	I	A	B
Increased consumption of vegetables, fruits, and low-fat dairy products.	I	A	B
Reduction of weight to BMI of 25 kg/m ² and of waist circumference to <102 cm in men and <88 cm in women, unless contraindicated.	I	A	B
Regular exercise, i.e. at least 30 min of moderate dynamic exercise on 5 to 7 days per week.	I	A	B
Advice to quit smoking and to offer assistance to all smokers.	I	A	B

^a LoE: based on the effect on BP and/or CV risk profile

^b LoE: based on outcome studies

EUR Heart J, 2013; 34: 2168–2219
J Hypertens, 2013; 31: 1231–1257
Blood Pressure, 2013; 150–278

www.escardio.org/guidelines



European Society of Hypertension



EUROPEAN SOCIETY OF CARDIOLOGY

Impact of specific lifestyle changes on lipid levels (1)

	Magnitude of the effect	Level of evidence
Lifestyle interventions to reduce TC and LDL-C levels		
Reduce dietary saturated fat	+++	A
Reduce dietary trans fat	+++	A
Increase dietary fibre	++	A
Reduce dietary cholesterol	++	B
Utilize functional foods enriched with phytosterols	+++	A
Reduce excessive body weight	+	B
Utilize soy protein products	+	B
Increase habitual physical activity	+	A
Utilize red yeast rice supplements	+	B
Utilize policosanol supplements	-	B

European Heart Journal 2011;32 (14):1769–1818
Atherosclerosis 2011 Jul;217(1):3–46

www.escardio.org/guidelines



QUALI NUTRACEUTICI PER IL TRATTAMENTO DELL' IPERTENSIONE E DELLA DISLIPIDEMIA?

Orthosiphon



fitosteroli



Estratto di lievito rosso



Omega 3

Omega-3 fatty acids are found in oily fish like salmon and flaxseed and canola oils



Berberina



Policosanoli



Acido folico e Coenzima Q10

Berberina



La berberina è un preparato vegetale naturale estratto dalla corteccia di *Berberis aristata*, un arbusto spinoso originario dell'Himalaya e del Nepal appartenente alla famiglia delle Berberidaceae.

Le attività farmacologiche della Berberina possono interessare il trattamento delle malattie metaboliche associate a elevato rischio cardiovascolare, quali l'iperlipidemia mista, l'insulino-resistenza, la sindrome metabolica e il diabete di tipo 2.

Berberine: metabolic and cardiovascular effects in preclinical and clinical trials

This article was published in the following Dove Press journal:

Nutrition and Dietary Supplements

10 September 2009

Number of times this article has been viewed

Arrigo FG Cicero¹

Sibel Ertek²

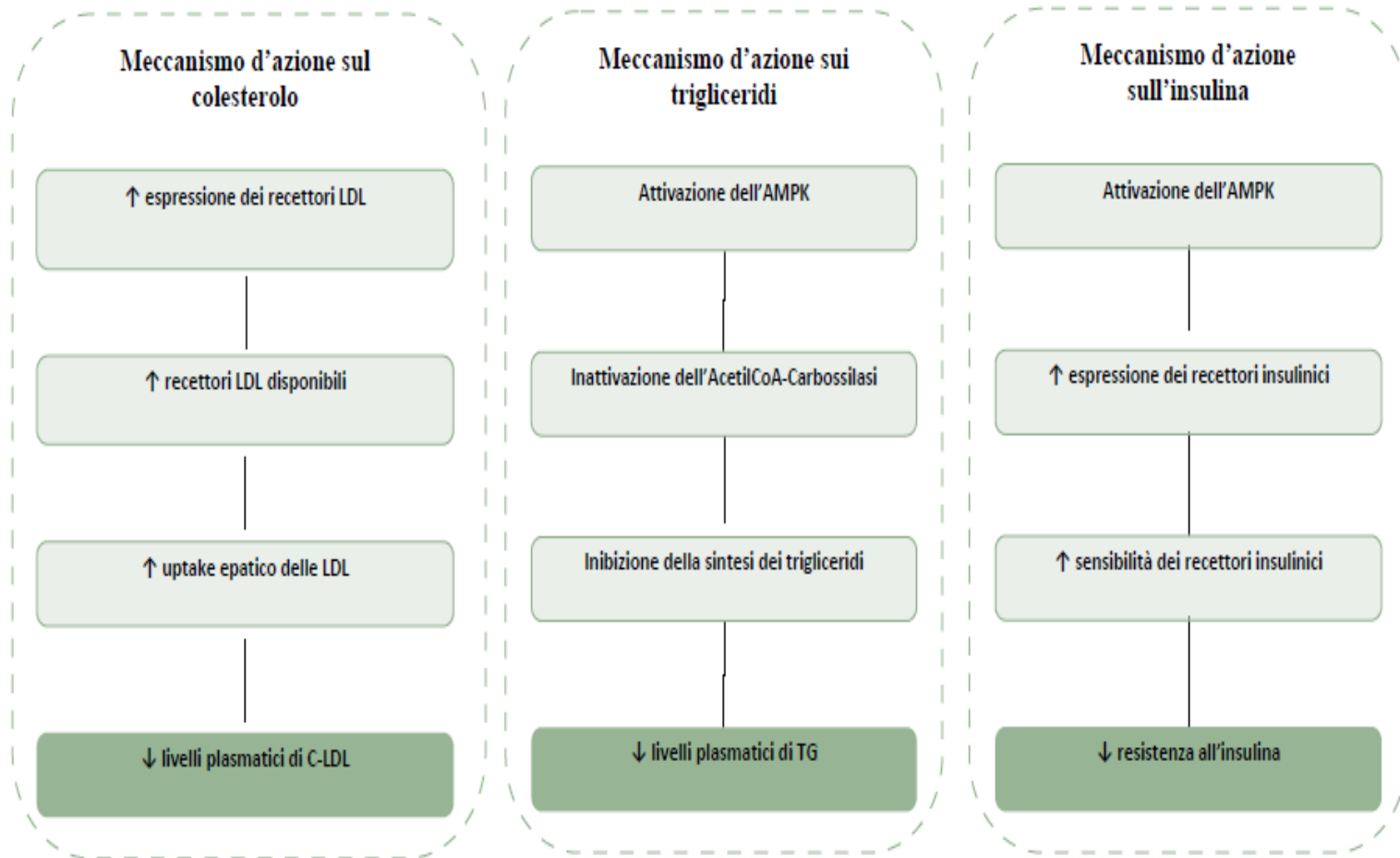
¹Internal Medicine, Aging and Kidney Diseases Department, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy;

²Ufuk University, Medical Faculty, Dr Ridvan Ege Hospital, Department of Endocrinology and Metabolic Diseases, Ankara, Turkey

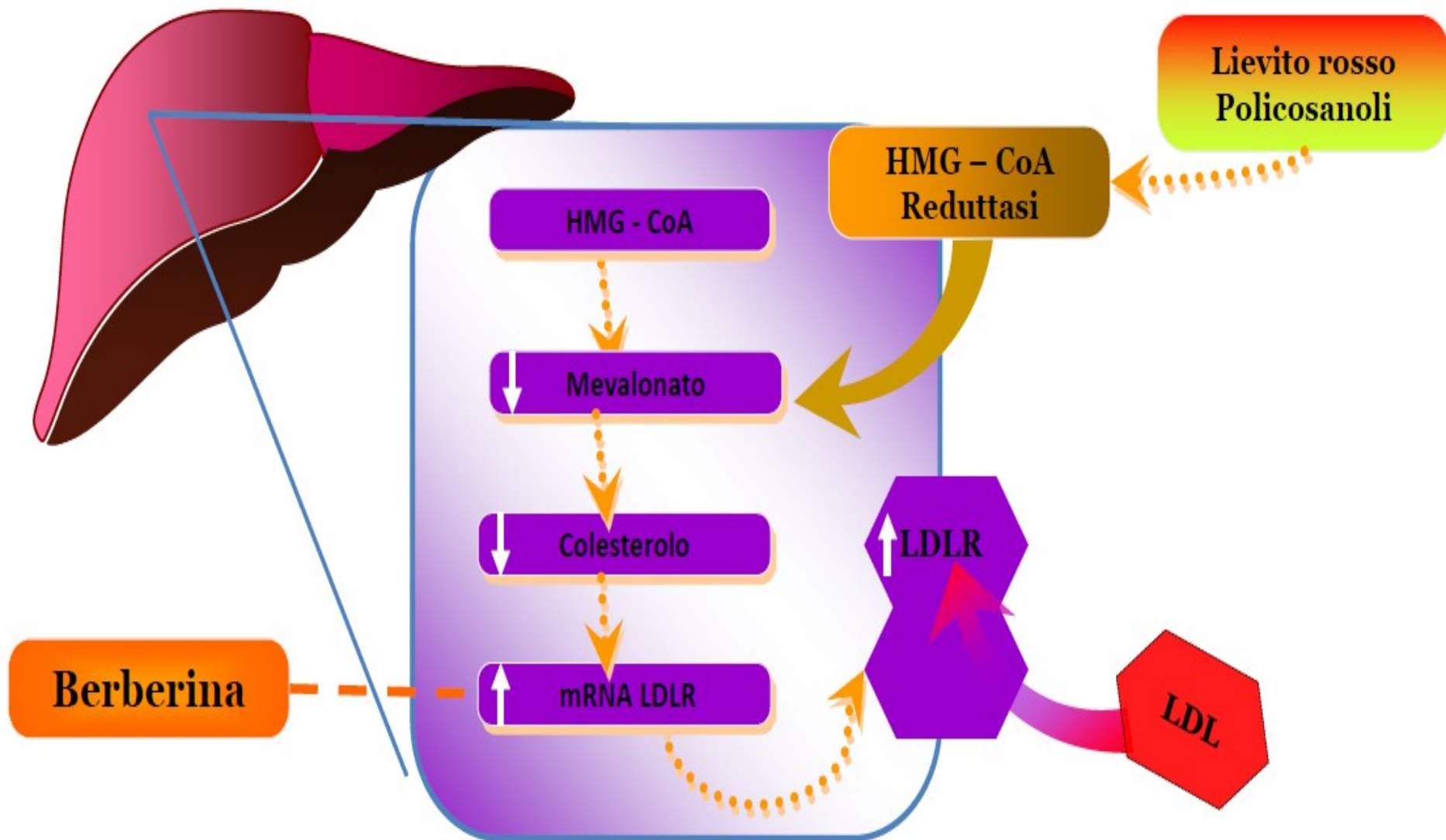
Abstract: Berberine is a plant alkaloid with numerous biological activities. A large body of preclinical *in vitro* and *in vivo* studies support different pharmacological actions of berberine that could be potentially useful in the management of metabolic diseases associated with high cardiovascular disease risk, such as mixed hyperlipidemia, insulin resistance, metabolic syndrome, and type 2 diabetes. Moreover, it seems that berberine also exerts anti-inflammatory and antiproliferative effects that could play a role in the development of atherosclerosis and its clinical consequences. Recently, the metabolic effects of berberine have been demonstrated in humans, opening new perspectives for the use of this molecule in patient therapy. Larger and longer clinical studies need to be carried out to implement the definition of the therapeutic role of berberine in humans.

Keywords: berberine, cardiovascular disease, diabetes, cholesterol

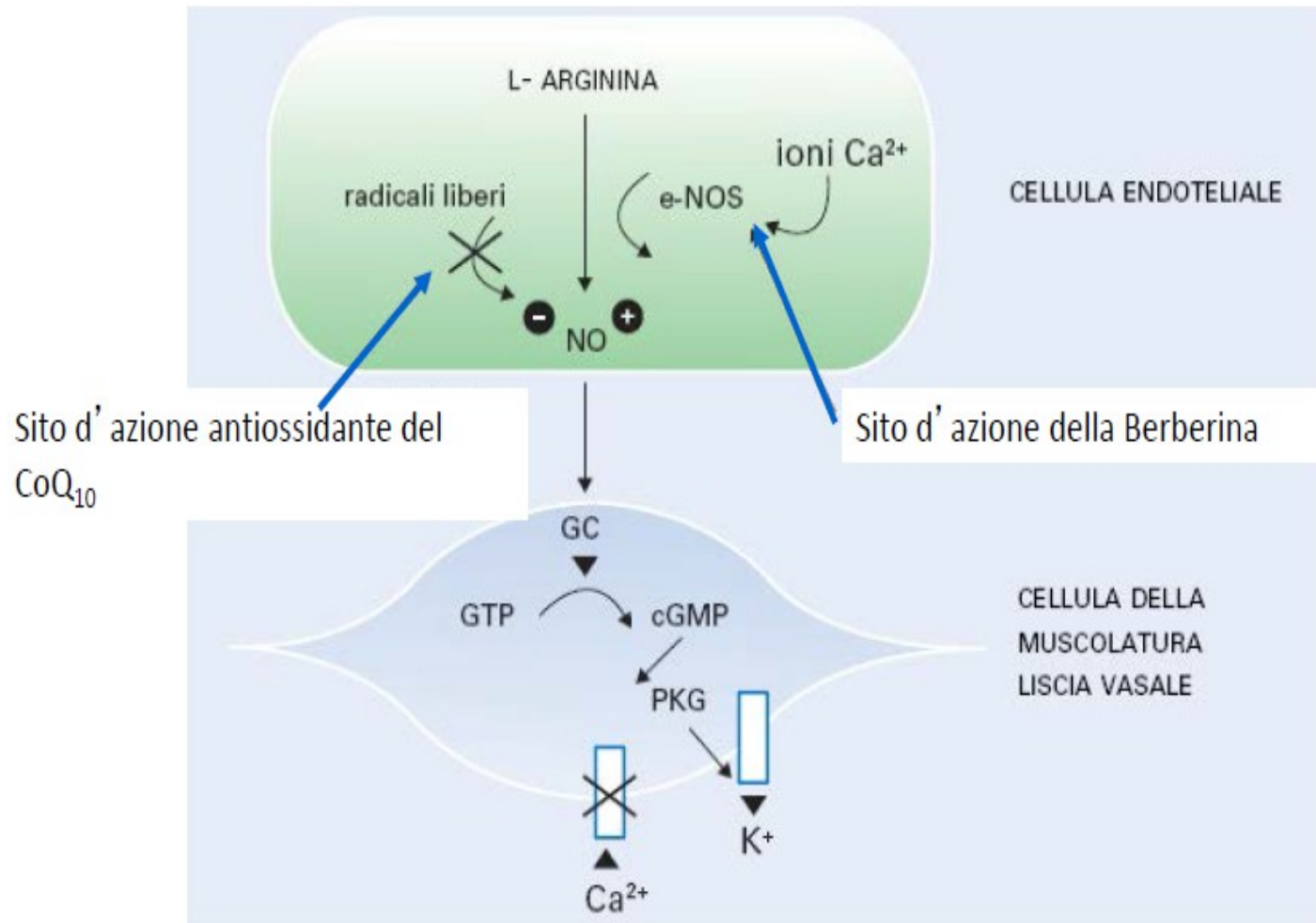
Berberina: effetto sul colesterolo, trigliceridi e insulina



Meccanismo d'azione sul colesterolo di Berberina + Lievito rosso + Policosanolo



Berberina e Coenzima Q10: effetto antipertensivo



Treatment of Type 2 Diabetes and Dyslipidemia with the Natural Plant Alkaloid Berberine

Yifei Zhang,* Xiaoying Li,* Dajin Zou, Wei Liu, Jialin Yang, Na Zhu, Li Huo, Miao Wang, Jie Hong, Peihong Wu, Guoguang Ren, and Guang Ning

Shanghai Clinical Center for Endocrine and Metabolic Diseases and Division of Endocrine and Metabolic Diseases (Y.Z., X.L., N.Z., L.H., J.H., G.N.), E-Institutes, Shanghai Universities, Rui-Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, People's Republic of China; Department of Endocrinology (D.Z., M.W.), Chang-Hai Hospital, the Second Military Medical University, Shanghai 200433, People's Republic of China; Department of Endocrinology (W.L., P.W.), Ren-Ji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, People's Republic of China; and Department of Endocrinology (J.Y., G.R.), Min-Hang Hospital, Shanghai 201100, People's Republic of China

Context: Berberine, a natural plant alkaloid, is usually used as an antibiotic drug. The potential glucose-lowering effect of berberine was noted when it was used for diarrhea in diabetic patients. *In vitro* and *in vivo* studies have then showed its effects on hyperglycemia and dyslipidemia.

Objective: The objective of the study was to evaluate the efficacy and safety of berberine in the treatment of type 2 diabetic patients with dyslipidemia.

Design: One hundred sixteen patients with type 2 diabetes and dyslipidemia were randomly allocated to receive berberine (1.0 g daily) and the placebo for 3 months. The primary outcomes were changes in plasma glucose and serum lipid concentrations. Glucose disposal rate (GDR) was measured using a hyperinsulinemic euglycemic clamp to assess insulin sensitivity.

Results: In the berberine group, fasting and postload plasma glucose decreased from 7.0 ± 0.8 to 5.6 ± 0.9 and from 12.0 ± 2.7 to 8.9 ± 2.8 mmol/liter, HbA1c from $7.5 \pm 1.0\%$ to $6.6 \pm 0.7\%$, triglyceride from 2.51 ± 2.04 to 1.61 ± 1.10 mmol/liter, total cholesterol from 5.31 ± 0.98 to 4.35 ± 0.96 mmol/liter, and low-density lipoprotein-cholesterol from 3.23 ± 0.81 to 2.55 ± 0.77 mmol/liter, with all parameters differing from placebo significantly ($P < 0.0001$, $P < 0.0001$, $P < 0.0001$, $P = 0.001$, $P < 0.0001$, and $P < 0.0001$, respectively). The glucose disposal rate was increased after berberine treatment ($P = 0.037$), although no significant change was found between berberine and placebo groups ($P = 0.063$). Mild to moderate constipation was observed in five participants in the berberine group.

Conclusions: Berberine is effective and safe in the treatment of type 2 diabetes and dyslipidemia. (*J Clin Endocrinol Metab* 93: 2559–2565, 2008)

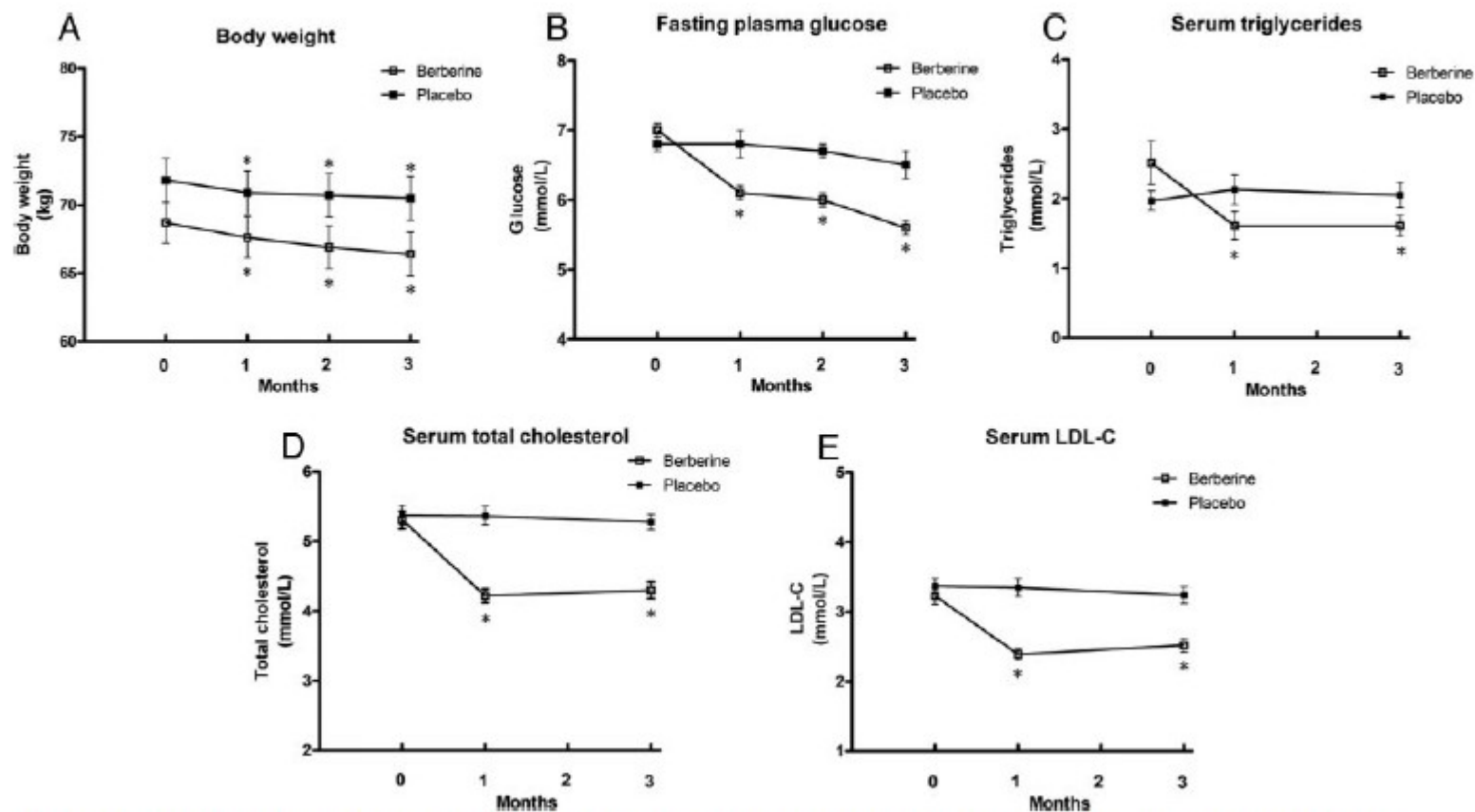


FIG. 3. Body weight (A), fasting plasma glucose concentrations (B), serum triglyceride concentrations (C), serum cholesterol concentrations (D), and serum LDL-C concentrations (E) during treatment of berberine (□) and placebo (■). Data displayed as means $\pm$ SE. *, $P < 0.0001$ after 1, 2, or 3 months treatment vs. before treatment within each group.

Policosanolo



estratto dalla matrice cerosa della canna da zucchero. L'alcol più abbondante è l'1-octacosanolo.

Il policosanolo riduce la biosintesi del colesterolo, mediante inibizione della sintesi dell'enzima 3-idrossi-3-metilglutaril CoA (HMG-CoA) reduttasi.

**Si riduce la sintesi del mevalonato,
da cui origina il colesterolo endogeno.**

Estratto di Lievito Rosso



Le monacoline competono strutturalmente a livello dell'HMG-CoA Reduttasi con l'HMG-CoA, precursore del mevalonato, inibendo la sintesi epatica del colesterolo.



**Si riduce la sintesi del mevalonato,
da cui origina il colesterolo endogeno.**

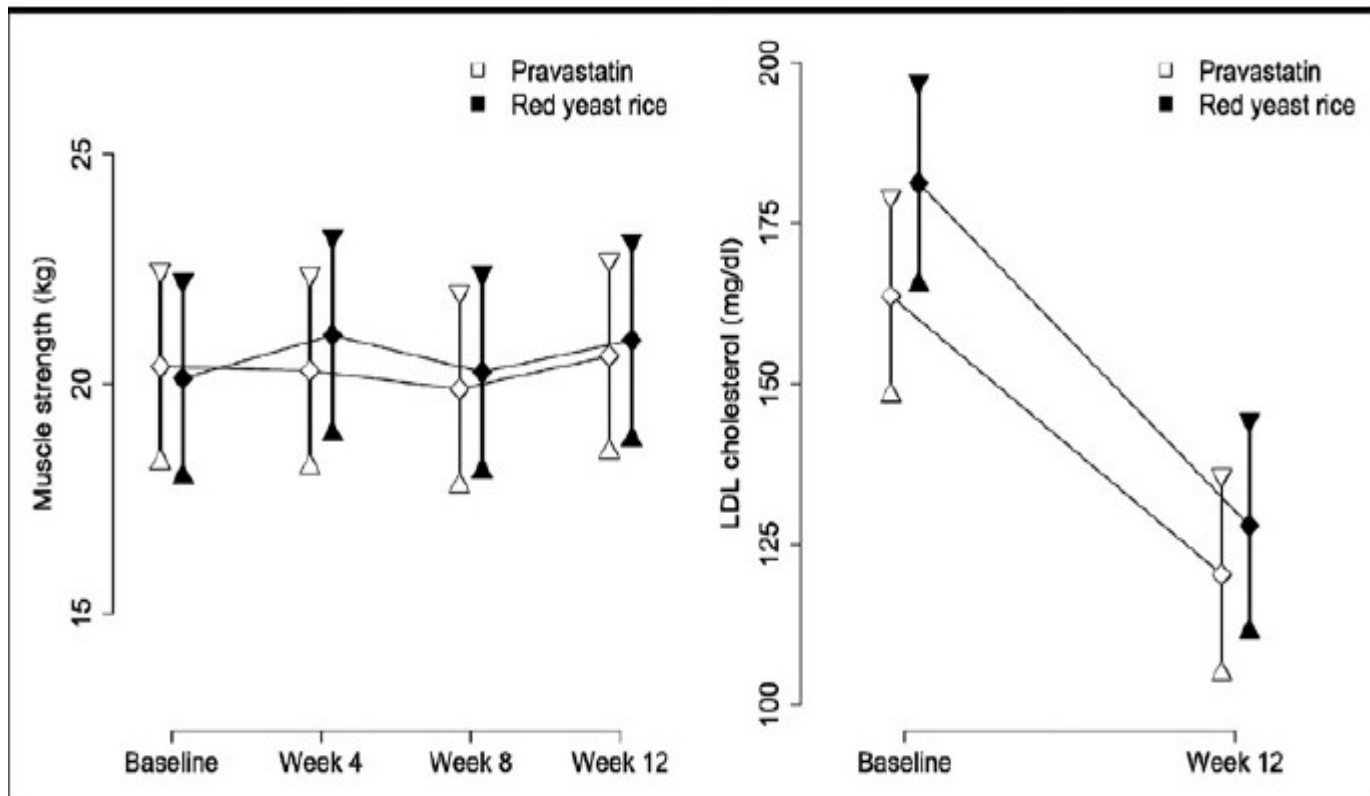
Tolerability of Red Yeast Rice (2,400 mg Twice Daily) Versus Pravastatin (20 mg Twice Daily) in Patients With Previous Statin Intolerance

Steven C. Halbert, MD^{a,e}, Benjamin French, PhD^{a,b}, Ram Y. Gordon, MD^f, John T. Farrar, MD^a, Kathryn Schmitz, PhD^a, Patti B. Morris, RD^f, Paul D. Thompson, MD^g, Daniel J. Rader, MD^{c,d}, and David J. Becker, MD^{f,*}

Currently, no consensus has been reached regarding the management of hyperlipidemia in patients who develop statin-associated myalgia (SAM). Many statin-intolerant patients use alternative lipid-lowering therapies, including red yeast rice. The present trial evaluated the tolerability of red yeast rice versus pravastatin in patients unable to tolerate other statins because of myalgia. The study was conducted in a community-based setting in Philadelphia, Pennsylvania. A total of 43 adults with dyslipidemia and a history of statin discontinuation because of myalgia were randomly assigned to red yeast rice 2,400 mg twice daily or pravastatin 20 mg twice daily for 12 weeks. All subjects were concomitantly enrolled in a 12-week therapeutic lifestyle change program. The primary outcomes included the incidence of treatment discontinuation because of myalgia and a daily pain severity score. The secondary outcomes were muscle strength and plasma lipids. The incidence of withdrawal from medication owing to myalgia was 5% (1 of 21) in the red yeast rice group and 9% (2 of 22) in the pravastatin group ($p = 0.99$). The mean pain severity did not differ significantly between the 2 groups. No difference was found in muscle strength between the 2 groups at week 4 ($p = 0.61$), week 8 ($p = 0.81$), or week 12 ($p = 0.82$). The low-density lipoprotein cholesterol level decreased 30% in the red yeast rice group and 27% in the pravastatin group. In conclusion, red yeast rice was tolerated as well as pravastatin and achieved a comparable reduction of low-density lipoprotein cholesterol in a population previously intolerant to statins. © 2010 Elsevier Inc. All rights reserved. (Am J Cardiol 2010;105:198–204)

Tolerability of Red Yeast Rice (2,400 mg Twice Daily) Versus Pravastatin (20 mg Twice Daily) in Patients With Previous Statin Intolerance

Steven C. Halbert, MD^{a,e}, Benjamin French, PhD^{a,b}, Ram Y. Gordon, MD^f, John T. Farrar, MD^a, Kathryn Schmitz, PhD^a, Patti B. Morris, RD^f, Paul D. Thompson, MD^g, Daniel J. Rader, MD^{c,d}, and David J. Becker, MD^{f,*}



Marked Variability of Monacolin Levels in Commercial Red Yeast Rice Products

MONACOLINA, MON K, MON KA, CITRININA / CP 600 mg

Red Yeast Rice Product in 600-mg Capsules	Monacolin Level, mg/cap			Citrinin, ppm	Citrinin, µg/cap
	Total Monacolins	Monacolin K (Lovastatin)	Monacolin KA		
A	5.30	2.53	1.96	ND	0.0
B	2.16	1.02	0.61	ND	0.0
C	4.18	1.74	1.63	ND	0.0
D	1.65	1.12	0.22	24	14.3
E	6.03	3.63	1.22	ND	0.0
F	0.31	0.10	0.00	189	114.2
G	6.18	2.50	2.30	ND	0.0
H	11.15	10.09	0.52	ND	0.0
I	1.60	0.99	0.23	75.5	57.5
J	3.97	2.66	0.46	ND	0.0
K	1.36	0.97	0.19	119	70.4
L	6.13	3.12	2.07	ND	0.0
Mean (SD)	4.17 (3.00)	2.54 (2.60)	0.95 (0.84)	34.0 (62.1)	21.4 (38.2)
Median	4.08	2.12	0.57	0.00	0.00

Buyer Beware!

Grande variabilità nel contenuto di monacolina, 1/3 contenevano citrinina una micotossina nefro-tossica nell'animale

MONACOLINA, MON K, MON KA, CITRININA / DOSE GIORNALIERA

Red Yeast Rice Product in 600-mg Capsules	Monacolin, mg/d			Citrinin, µg/d
	Total Monacolins	Monacolin K (Lovastatin)	Monacolin K and Monacolin KA	
A	21.20	10.12	17.96	0.0
B	8.64	4.08	6.52	0.0
C	4.18-8.36	1.74-3.48	3.37-6.74	0.0
D	3.30	2.25	2.69	28.5
E	24.12	14.54	19.43	0.0
F	0.62	0.20	0.20	228.3
G	24.71	9.99	19.18	0.0
H	11.15	10.09	10.62	0.0
I	3.21	1.98	2.43	115.1
J	7.94	5.33	6.25	0.0
K	2.71	1.94	2.32	140.9
L, range	12.26-24.52	6.24-12.48	10.38-20.76	0.0
Mean (SD)	11.0 (8.80)	6.04 (4.57)	9.02 (7.22)	42.7 (76.3)
Median	8.29	4.71	6.38	0.00

Necessità di standardizzazione dei prodotti del riso rosso e di etichettatura

P Prevenzione Primaria

Red yeast rice improves lipid pattern, high-sensitivity C-reactive protein, and vascular remodeling parameters in moderately hypercholesterolemic Italian subjects

- a crossover, double-blind, placebo-controlled randomized clinical trial
- short-term treatment with 10 mg monacolins to evaluate lipid pattern, high-sensitivity C-reactive protein (hs-CRP), and vascular remodeling biomarkers in a small cohort of Mediterranean subjects (**25 healthy moderate hypercholesterolemic subjects**)

A 10-mg monacolin nutraceutical appears to safely reduce cholesterolemia: total cholesterol (-12.45%), low-density lipoprotein cholesterol (-21.99%), non-high-density lipoprotein cholesterol (-14.67%), hs-CRP (-23.77%), and markers of vascular remodeling: matrix metalloproteinase 2 (-28.05%), matrix metalloproteinase 9 (-27.19%) in Italian subjects.

Nutraceutical approach to moderate cardiometabolic risk: Results of a randomized, double-blind and crossover study with Armolipid Plus

BACKGROUND: Primary cardiovascular prevention may be achieved by lifestyle/nutrition improvements and specific drugs, although a relevant role is now emerging for specific functional foods and nutraceuticals.

OBJECTIVES: The aim of this study was to evaluate the usefulness of a nutraceutical multitarget approach in subjects with moderate cardiovascular risk and to compare it with pravastatin treatment.

SUBJECTS: Thirty patients with moderate dyslipidemia and metabolic syndrome (according to the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults) were included in an 8-week randomized, double-blind crossover study and took either placebo or a nutraceutical combination that contained red yeast rice extract, berberine, policosanol, astaxanthin, coenzyme Q10, and folic acid (Armolipid Plus). Subsequently, they were subjected to another 8-week treatment with pravastatin 10 mg/d. This dosage was selected on the basis of its expected -20% efficacy in reducing low-density lipoprotein-cholesterol.

RESULTS: Treatment with Armolipid Plus led to a significant reduction of total cholesterol (-12.8%) and low-density lipoprotein-cholesterol (-21.1%), similar to pravastatin (-16% and -22.6%, respectively), and an increase of high-density lipoprotein-cholesterol (4.8%). Armolipid Plus improved the leptin-to-adiponectin ratio, whereas adiponectin levels were unchanged.

CONCLUSIONS: These results indicate that this nutraceutical approach shows a lipid-lowering activity comparable to pravastatin treatment. Hence, it may be a safe and useful option, especially in conditions of moderate cardiovascular risk, in which a pharmacologic intervention may not be appropriate.

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Prevenzione secondaria

Effect of Xuezhikang, an extract from red yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction.

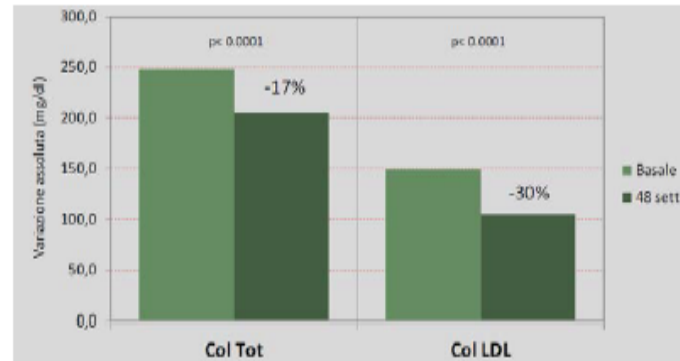
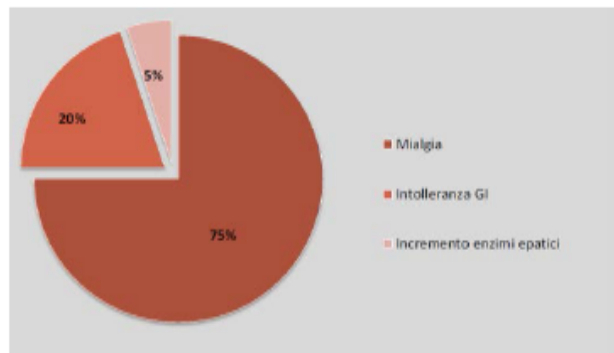
- 5000 patients with previous myocardial infarction
- Xuezhikang vs placebo
- The primary end point was a major coronary event that included nonfatal myocardial infarction and death from coronary heart disease

Frequencies of the primary end point were 10.4% in the placebo group and 5.7% in the XZK-treated group, with absolute and relative decreases of 4.7% and 45%, respectively. Treatment with XZK also significantly decreased CV and total mortality by 30% and 33%, the need for coronary revascularization by 1/3, and lowered total and low-density lipoprotein cholesterol and triglycerides, but raised high-density lipoprotein cholesterol levels.

P Intolleranti alle statine

Abstract 8523: Randomized Trial of Nutraceuticals in Statin-Intolerant Patients Treated with Percutaneous Coronary Intervention

- Randomized, prospective, parallel group, single-blind trial to investigate the efficacy, safety, and tolerability of a nutraceutical-based protocol in statin-intolerant patients treated with PCI
- 80 patients with stable (70%) or unstable angina (30%)
- Patients were randomized to receive for 1 year either nutraceutical combined pill (1 capsule/day containing red yeast rice 200 mg, policosanol 10 mg, and berberine 500 mg) or daily placebo



After 12 months only 2 side effects (myalgia, GE disturbance).

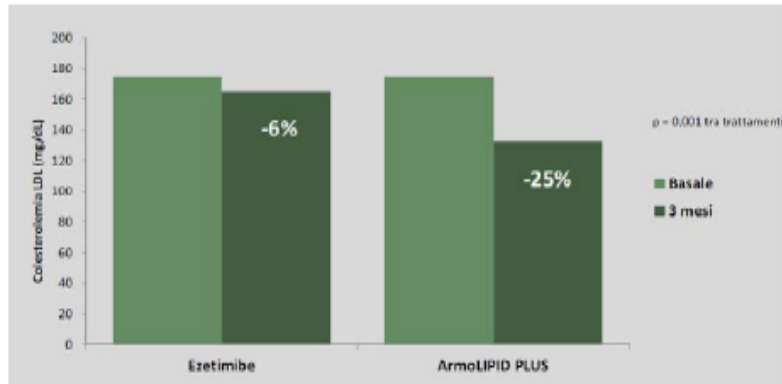
Total cholesterol level (205±31 vs 241±41 mg/dl) and low-density lipoprotein cholesterol (105±31 vs 131±41 mg/dl) were significantly ($P=0.001$) lower in the nutraceutical-group than in the placebo-group.

P_{Intolleranti} alle statine

Randomized Trial of Ezetimibe versus Nutraceuticals in Statin-intolerant Patients Treated With Percutaneous Coronary Intervention

Session Therapeutic Interventions in Chronic Ischemic Heart Disease

- 100 stable angina pts treated by PCI with statin intolerance
- Pts were randomized to receive for 3 months either ezetimibe (10 mg/day) or a commercially available nutraceutical combined pill (1 capsule/day containing red yeast rice 200 mg, policosanol 10 mg, and berberine 500 mg).



- Gruppo trattato con EZE: nessun paziente ha raggiunto il target terapeutico
- Gruppo trattato con ARM: 16 pazienti (32%) hanno raggiunto il target terapeutico
- Gruppo EZE: 2 pazienti hanno interrotto lo studio per intolleranza gastrointestinale
- Gruppo ARM: 3 pazienti hanno interrotto lo studio per mialgia

A combination of nutraceuticals with lipid-lowering biological activity can significantly decrease cholesterol levels (175 ± 13 to 133 ± 10 mg/dl (-24%) vs. 175 ± 10 to 165 ± 8 mg/dl (-5,8 %) ($P=0.001$) without causing clinical or metabolic side effects and that it is more effective than ezetimibe 10 mg/day in statin-intolerant patients treated with PCI

Hypercholesterolemia poligenica primitiva

RESEARCH

Open Access

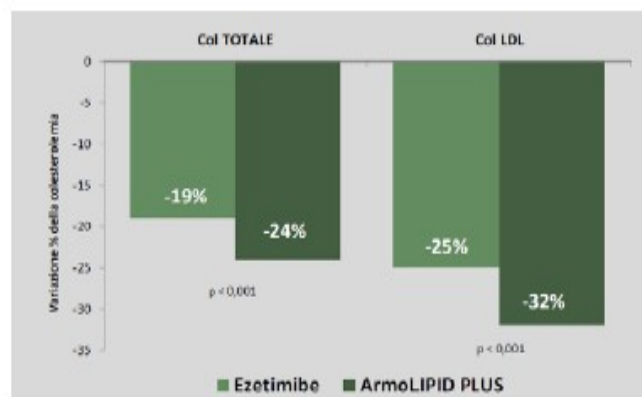
Nutraceutical pill containing berberine versus ezetimibe on plasma lipid pattern in hypercholesterolemic subjects and its additive effect in patients with familial hypercholesterolemia on stable cholesterol-lowering treatment

Livia Pisciotta, Antonella Bellocchio and Stefano Bertolini*

Plasma lipids (mmo/L)	BBR/P/RR			EZE			†p
	Baseline	On treatment	Percent change	Baseline	On treatment	Percent change	
TC	7.63 ± 0.50	5.77 ± 0.49*	-24.2 ± 5.2	7.72 ± 0.49	6.25 ± 0.51*	-19.0 ± 4.6	< 0.001
LDL-C	5.36 ± 0.48	3.66 ± 0.48*	-31.7 ± 7.0	5.36 ± 0.52	4.00 ± 0.52*	-25.4 ± 6.4	< 0.001
HDL-C	1.55 ± 0.35	1.54 ± 0.37	-0.64 ± 7.2	1.57 ± 0.34	1.58 ± 0.35	+1.24 ± 6.9	NS
non-HDL-C	6.07 ± 0.54	4.22 ± 0.53*	-30.3 ± 6.5	6.15 ± 0.55	4.66 ± 0.58*	-24.2 ± 5.9	< 0.001
TG	1.46 (1.22-1.90)	1.12 (0.95-1.41)*	-19.5 ± 16.1	1.67 (1.24-2.12)	1.43 (1.08-1.80)*	-14.9 ± 11.5	NS

Data are means ± SD or medians (interquartile ranges). *P < 0.001 vs baseline values (Student's *t* test for paired data or Wilcoxon test); †P: significance of the differences between percent changes induced by BBR/P/RR and by EZE treatments (Student's *t* test and Mann-Whitney test, respectively). NS: not significant.

N=228 (152 BRB/P/RR vs
76 EZE) per 6 mesi



Orthosiphon stamineus

Pianta medicinale proveniente dal sudest asiatico, detta tè di giava, dalle cui foglie si estraggono:

1. diterpeni,
2. triterpeni,
3. saponine,
4. flavonoidi,
5. derivati dell' acido cinnamico e cromeni.

La sinensetina (flavone) è il componente ad attività diuretica.



I flavonoidi dell' estratto di *O. stamineus* sono ligandi attivi del recettore adenosina A_1 a dosi micro molari.



Gli antagonisti dei recettori dell' adenosina A_1 inducono diuresi ed escrezione di sodio:

-direttamente

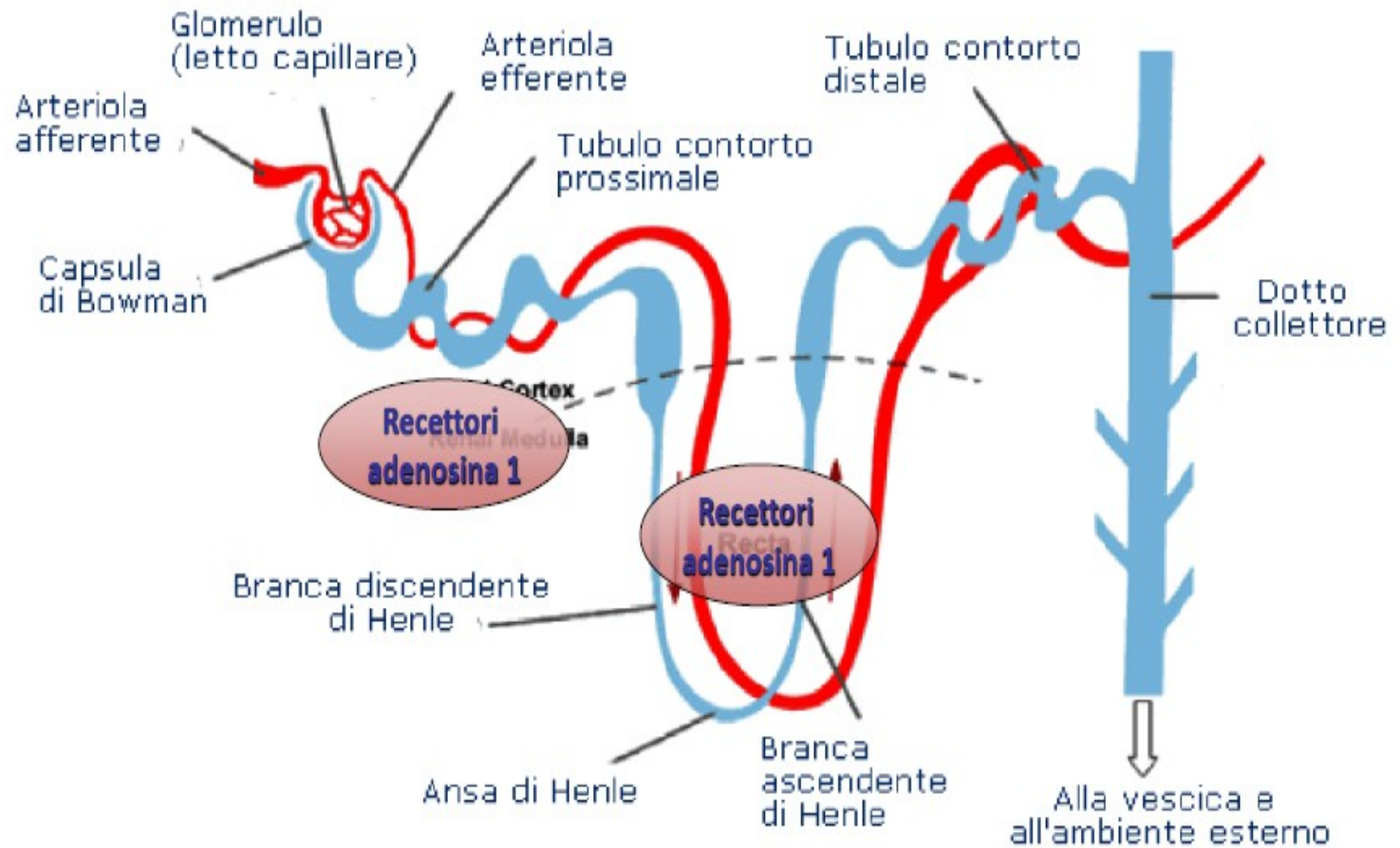
mediante inibizione del riassorbimento del sodio nei tubuli prossimali

-indirettamente

promuovendo la dilatazione delle arteriole afferenti.

Orthosiphon stamineus

Sinensetina: attività antipertensiva

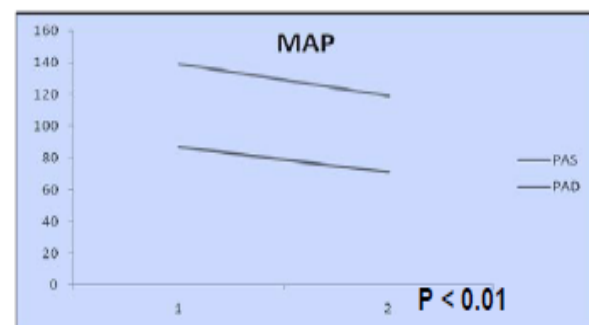
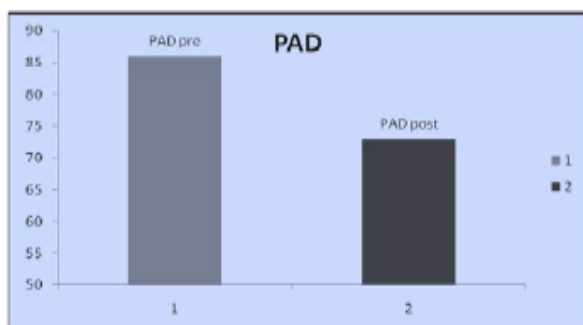
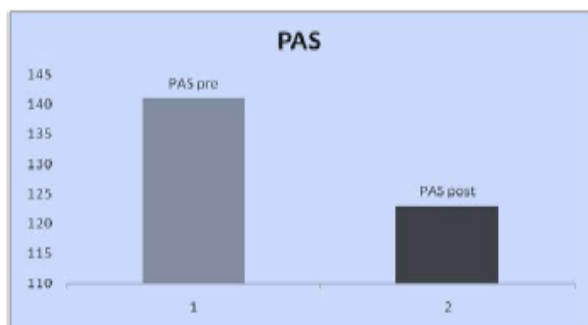


Antagonismo dei recettori dell'adenosina A1 per il riassorbimento di sodio a livello renale nelle arteriole afferenti, nel glomerulo, nei tubuli prossimali e nei dotti collettori: **AZIONE VASODILATRICE E MIOLITICA**

PRESSIONE NORMALE ALTA

- indagare la presenza di danno d'organo subclinico e di altri fattori di rischio nei soggetti con pressione normale alta
- valutare l'efficacia di supplementazione con ortosiphon stamineus, policosanolo, lievito rosso, berberina, acido folico e coenzima Q10, associata a modificazioni dello stile di vita, su valori pressori e profilo lipidico
- valutarne la tollerabilità

45 soggetti con pressione normale alta trattati con Orthosiphon Stamineus, Policosanolo, Lievito rosso, Berberina, Acido Folico E Coenzima Q10." per 6 settimane



BASALE

POST TERAPIA

COL TOT	201±1.8 mg/dl	186±2.1 mg/dl
COL LDL	133±3.7 mg/dl	113±1.5 mg/dl
TG	162±1.6 mg/dl	141±2.4 mg/dl
COL HDL	36±3.1 mg/dl	45±1.4 mg/dl
URICEMIA	8.6±2.1 mg/dl	5.3±3.1 mg/dl
FCVR	7±2.1%	2±1.8%
GLICEMIA	108±3.2 mg/dl	99±1.11 mg/dl

- Riduce significativamente i valori pressori
- Migliora efficacemente il profilo lipidico aterogeno
- Riduce il rischio cardiovascolare globale
- Agisce in modo sicuro, senza effetti collaterali

Le antocianine in natura

Le antocianine sono una sottoclasse dei flavonoidi

Esse costituiscono i pigmenti **rossi**, **porpora**, **viola** e **blu** di foglie, fiori e frutti



Il mais blu ricco di antocianine

Il mais blu è stato ottenuto attraverso incroci di varietà tradizionali gialle con antiche varietà di mais colorato, coltivate nel Centro e Sud America.



Incrocio e
selezione



Il mais blu protegge dall'infarto?



Anthocyanin-free

Dieta senza antocianine

20% di farina di mais giallo nella dieta
standard per ratti



**Effetto sull'infarto
del miocardio**



Anthocyanin-rich

Dieta ricca di antocianine

20% di farina di mais blu nella dieta
standard per ratti



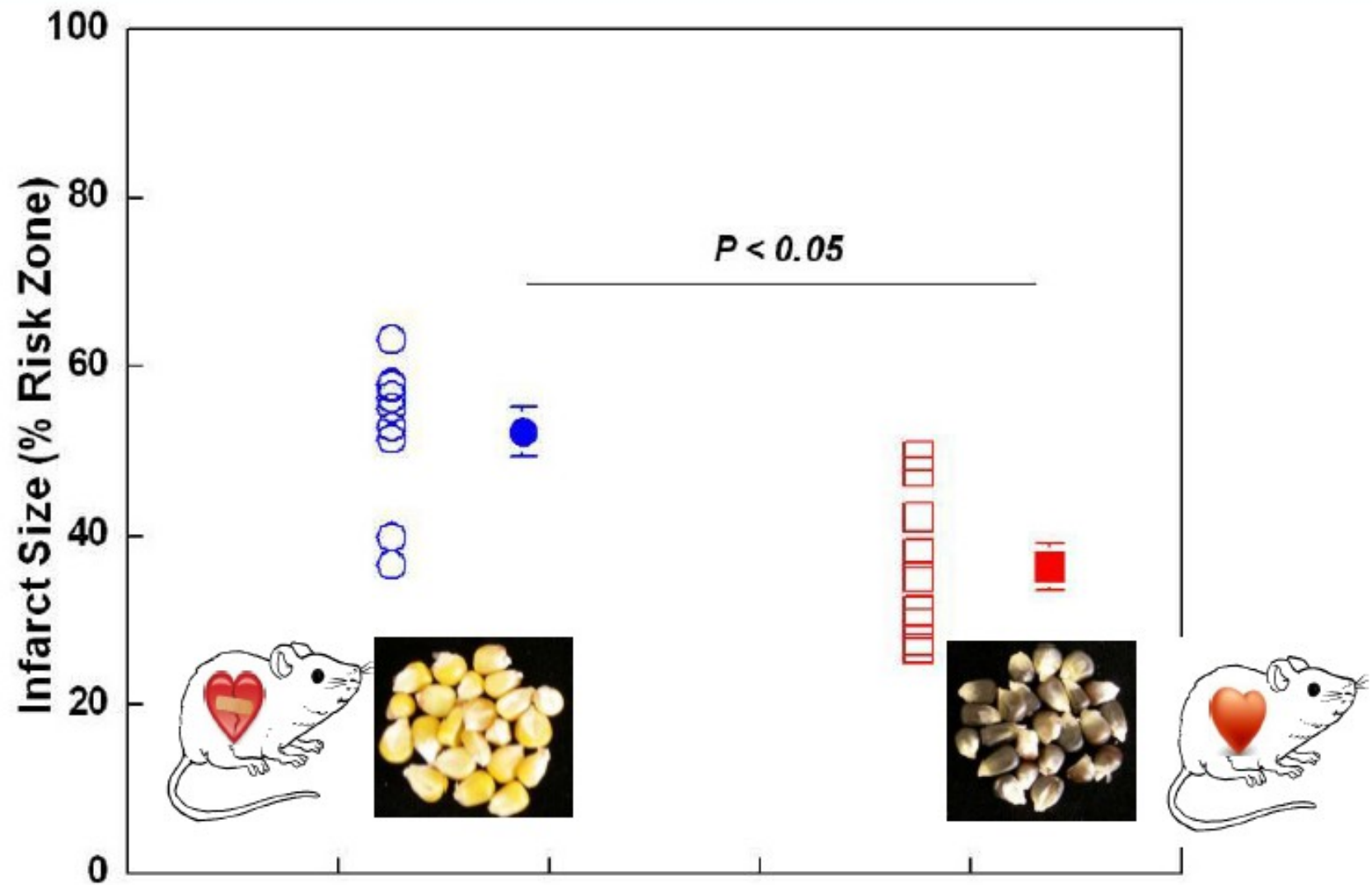
**Effetto sull'infarto
del miocardio**

8-settimane di trattamento

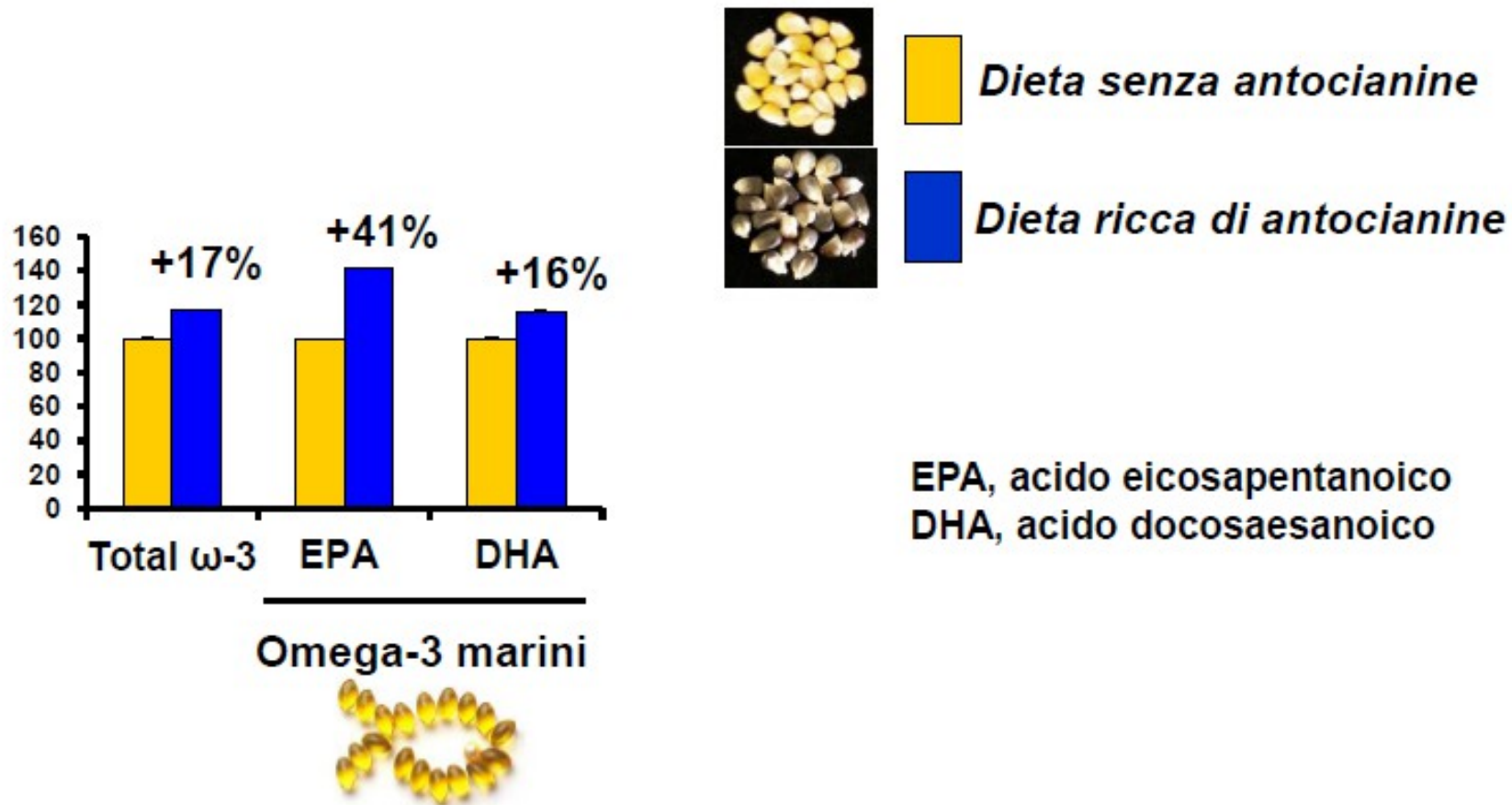
Marie-Claire Toufektsian, Michel de Lorgeril, Chiara Tonelli, Roberto Pilu, Katia Petroni

Toufektsian et al., (2008) J Nutr 138: 747-752

Le antocianine del mais riducono del 30% il danno da infarto del miocardio



Il mais blu aumenta i livelli di Omega-3 marini nel sangue come una dieta ricca di pesce



Nella *Dieta Western*,
povera di fibre e ricca di grassi,
l'assunzione giornaliera di antocianine è circa 12 mg/giorno

In proporzione,
i ratti alimentati con mais blu hanno ricevuto
circa 13 volte più antocianine
rispetto alla tipica dieta Western

... e hanno dimostrato di avere
un cuore del 30% più resistente contro l'infarto
grazie a livelli di Omega-3 più elevati nel sangue

Per l'uomo,
la dose di antocianine corrisponde a circa 156 mg/giorno
pari a 50 g di mirtilli

Le antocianine negli alimenti

27 mg/L



1650 mg/Kg



730 mg/Kg

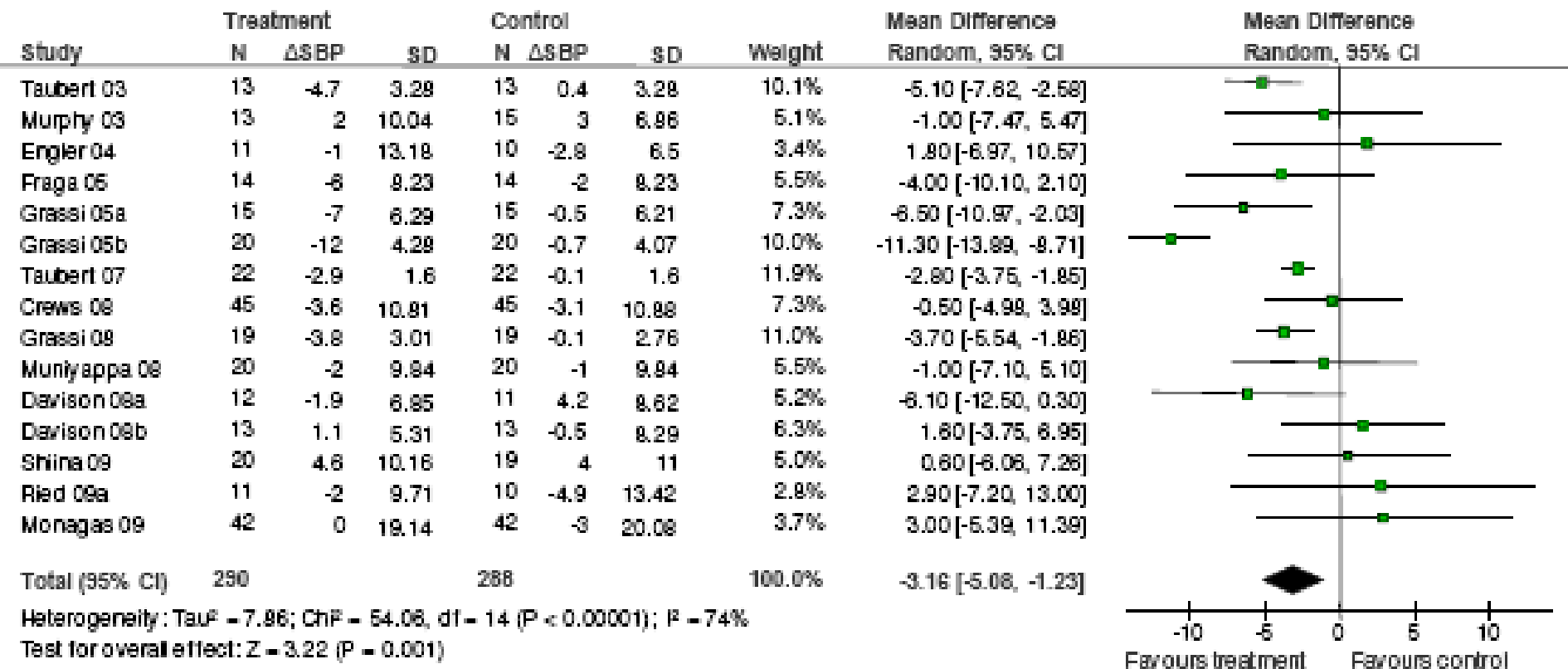


80 mg/L

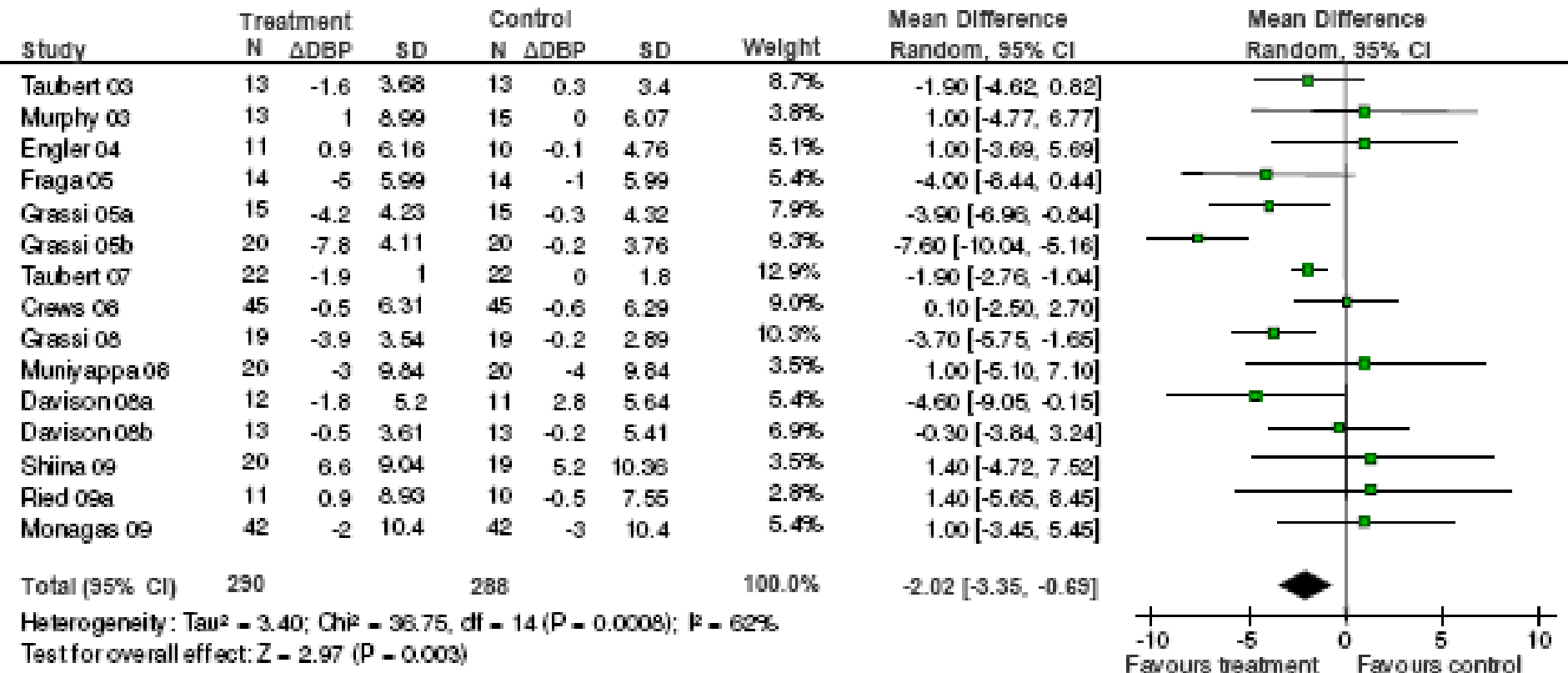


600-3500 mg/Kg

Cioccolato e pressione sistolica



Cioccolato e pressione diastolica





**THE COCHRANE
COLLABORATION®**

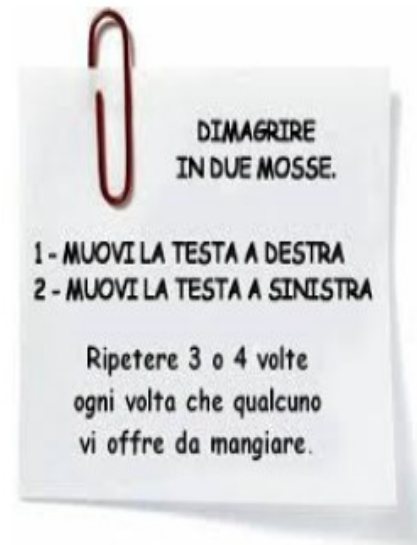
The effect depends on age !

	< 50yrs	> 50yrs
Mean difference SBP (95% CI)	-4.57 (7.41, -1.73) mm Hg, p=0.002, n=10	-0.96 (-3.44, 1.52) mm Hg, p=0.45, n=10
Mean difference DBP (95% CI)	-3.85 (-5.45, -2.26) mm Hg, p<0.001, n=9	-0.89 (-1.80, 0.01) mm Hg, p=0.05, n=10

Cochrane Database of Systematic
Reviews 2012, Issue 8. Art. No.: CD008893.



- Identificare i fattori di rischio cardiovascolari/stratificare il rischio
- Lo stile di vita, l'esercizio fisico e l'alimentazione sono punti cardine nella prevenzione cardiovascolare
- I nutraceutici in associazione a modificazioni dello stile di vita:
 - Riducono significativamente i valori pressori
 - Migliorano efficacemente il profilo lipidico aterogeno
 - Riducono il rischio cardiovascolare globale
 - Agiscono in modo sicuro, senza effetti collaterali

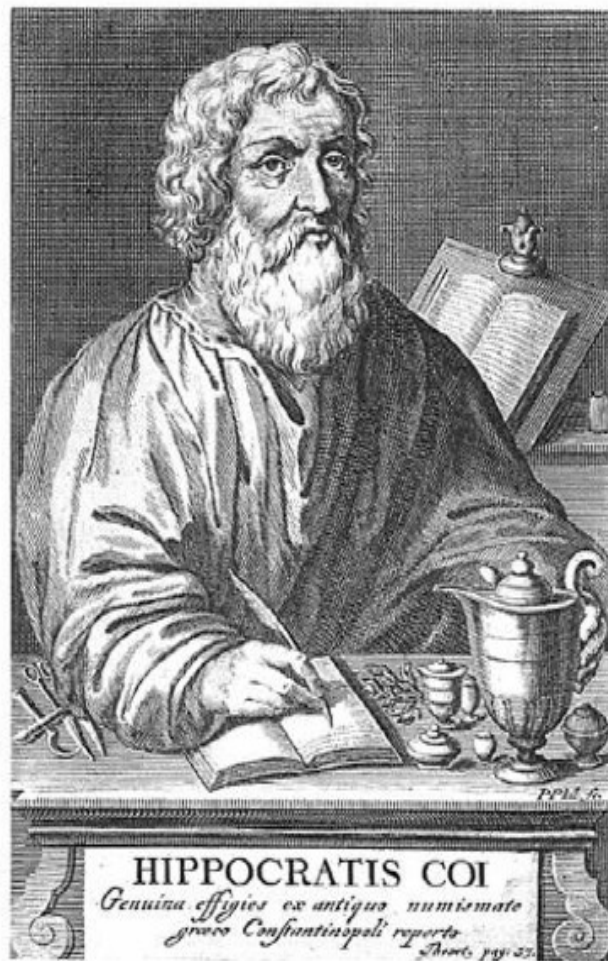


**DIMAGRIRE
IN DUE MOSSE.**

- 1 - MUOVI LA TESTA A DESTRA**
- 2 - MUOVI LA TESTA A SINISTRA**

Ripetere 3 o 4 volte
ogni volta che qualcuno
vi offre da mangiare.

Storia della nutraceutica



“...le differenze nelle malattie dipendono dall' alimentazione”

“... lasciate che il cibo sia la vostra medicina e che la medicina sia il vostro cibo”

Ippocrate (460-377 a.C.)