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cerfit*

Centro di riferimento per la Fitoterapia

Botanicals e sindrome metabolica

Fabio Firenzuoli

Resp. Del CERFIT - Centro di ricerca e innovazione in Fitoterapia

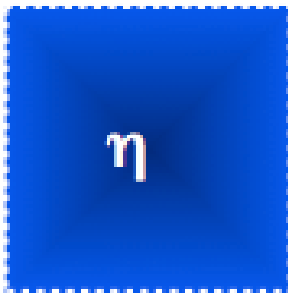
Struttura di riferimento per la Fitoterapia, Regione Toscana

Azienda Ospedaliero Universitaria Careggi, Firenze

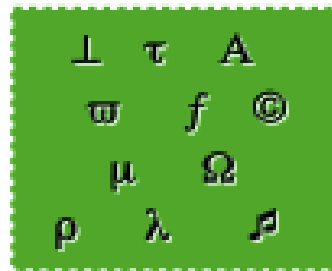
Professore a c. Fitoterapia Università di Firenze

www.cerfit.org

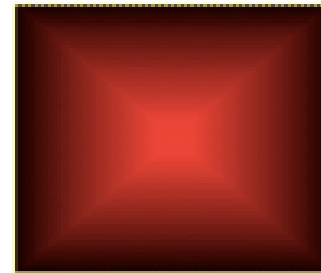
Peculiarità Botanicals



Farmaco
di sintesi



Fitoterapico

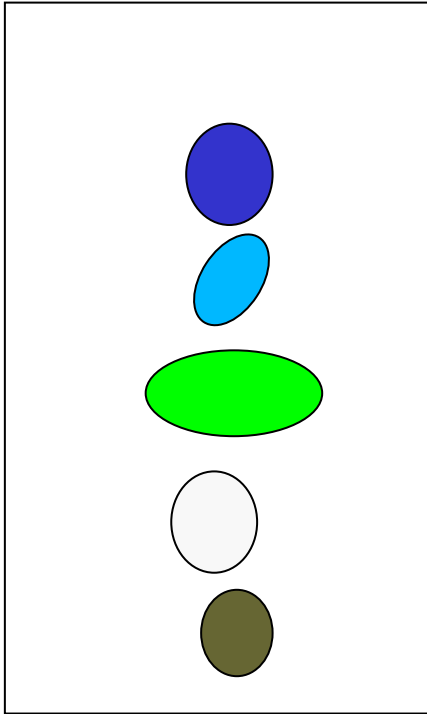


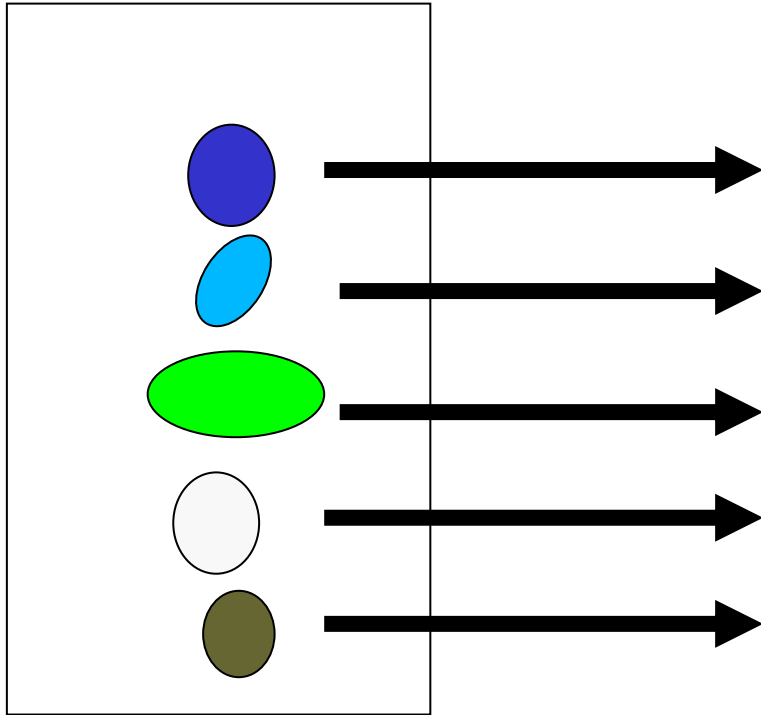
Omeopatico

Firenze F, Firenze



Fitocomplesso

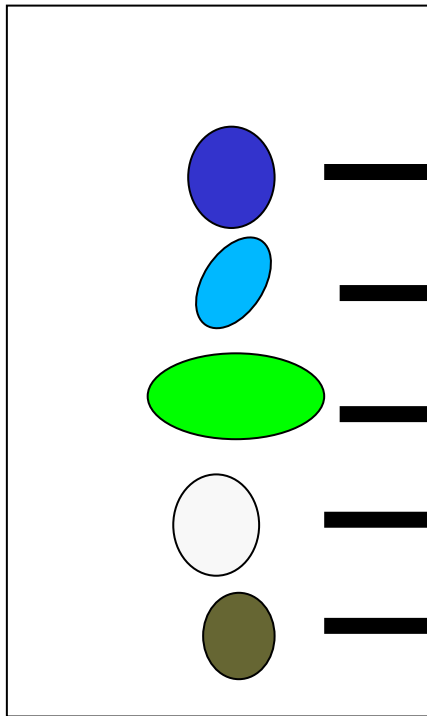




**Effetto
poli-Pill**



紅麴
紅曲



+

+

**Sommazione
di effetti
non desiderata**



a) Erbe medicinali di uso tradizionale



- ★ **Tarassaco**
- ★ Finocchio
- ★ Agrimonia
- ★ Aloe
- ★ **Carciofo**
- ★ Cardo mariano...





Lipid-lowering activity of artichoke extracts: A systematic review and meta-analysis

Amirhossein Sahebkar^a, Matteo Pirro^b, Maciej Banach^{c,d}, Dimitri P. Mikhailidis^e, Stephen L. Atkin^f, and Arrigo F. G. Cicero^g

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ABSTRACT

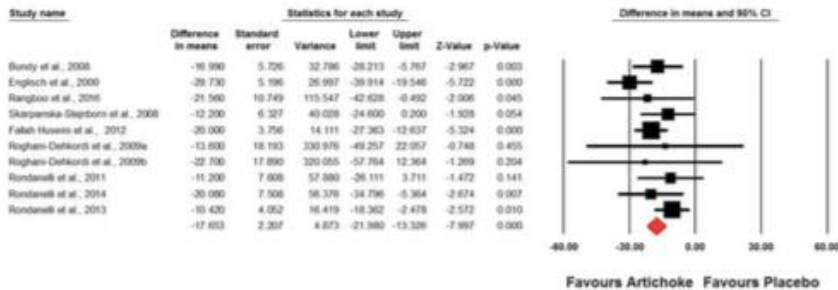
Artichoke is a component of the Mediterranean diet. Therefore, the aim of this meta-analysis was to determine if artichoke extract supplementation affected human lipid parameters. The search included PubMed-Medline, Scopus, Web of Science and Google Scholar databases up to March 28, 2017, to identify RCTs investigating the impact of artichoke extracts on plasma lipid levels. Quantitative data synthesis was performed using a random-effects model, with weighed mean difference (WMD) and 95% confidence interval (CI) as summary statistics. Meta-analysis of data from 9 trials including 702 subjects suggested a significant decrease in plasma concentrations of total cholesterol (WMD: -17.6 mg/dL, 95%CI: -22.0 , -13.3 , $p < 0.001$), Low Density Lipoprotein-Cholesterol (LDL-C; WMD: -14.9 mg/dL, 95%CI: -20.4 , -9.5 , $p = 0.011$) and triglycerides (WMD: -9.2 mg/dL, 95%CI: -16.2 , -2.1 , $p = 0.011$). No significant alteration in plasma High Density Lipoprotein-Cholesterol (HDL-C) concentrations was observed (WMD: 1.0 mg/dL, 95%CI: -1.1 , 3.1 , $p = 0.333$). A significant association between the LDL-lowering effect of artichoke and baseline LDL-C concentrations (slope: -0.170 ; 95%CI: -0.288 , 0.051 ; $p = 0.005$) was observed. Thus, supplementation with artichoke extract was associated with a significant reduction in both total and LDL-C, and triglycerides, suggesting that supplementation may be synergistic with lipid-lowering therapy in patients with hyperlipidemia.

KEYWORDS

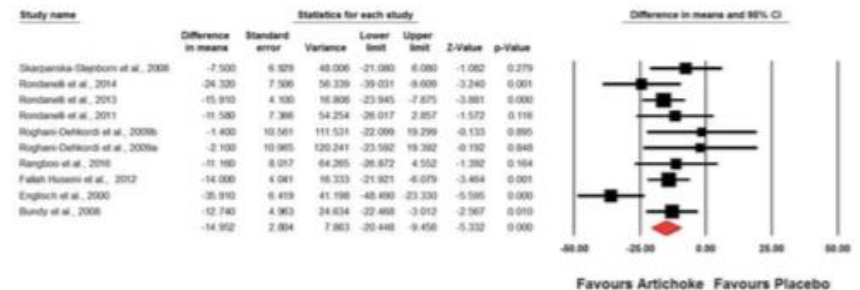
Artichoke leaf extract; hypercholesterolemia; meta-analysis; randomized clinical trial; triglycerides



TC



LDL-C



b) Fitoprotezione



- ★ **Silibina**
- ★ **Vitis vinifera**
- ★ **Ginkgo biloba**
- ★ **Rosa canina**
- ★ **Cacao**
- ★ **Esperidina** (*Citrus* spp)



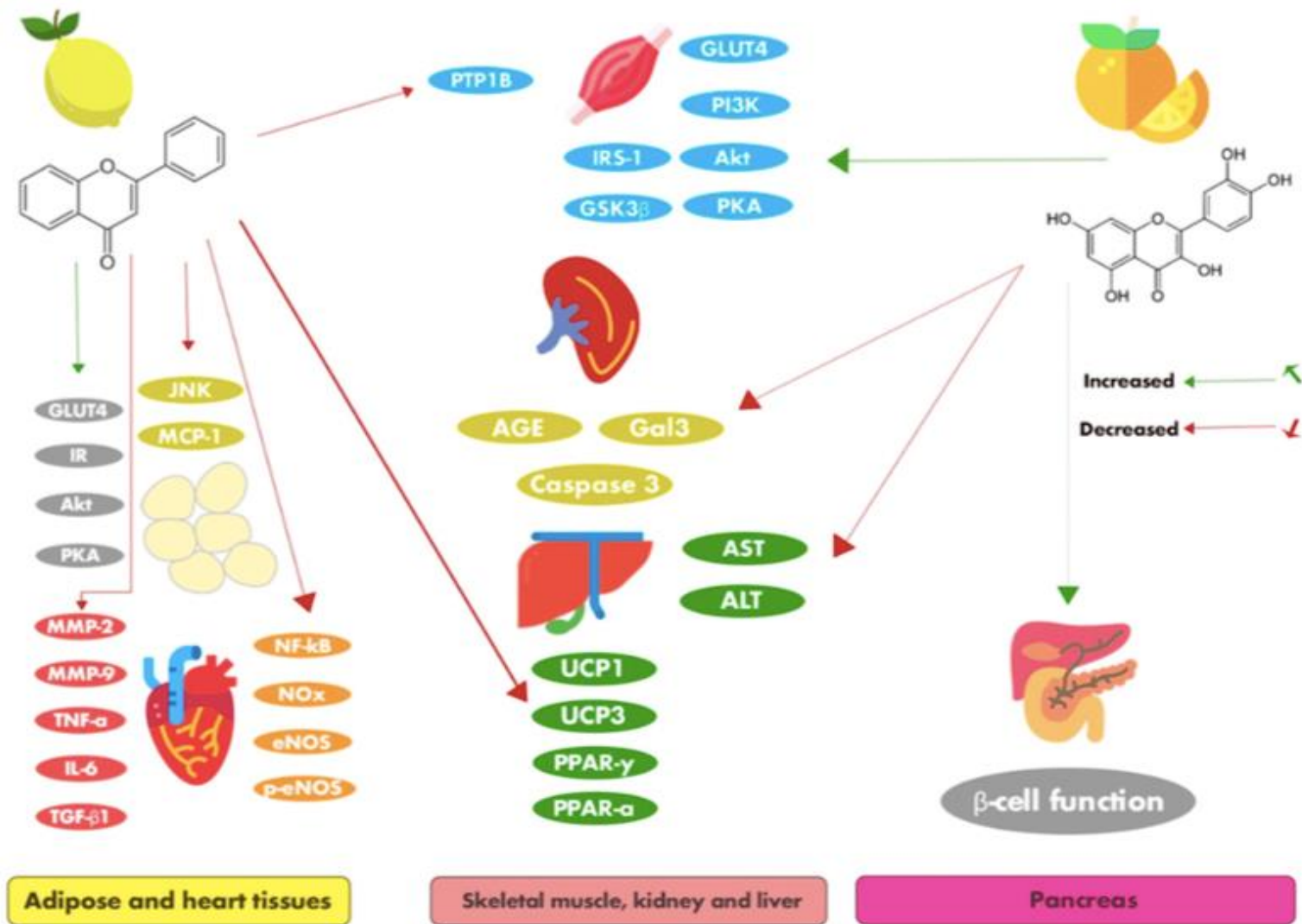
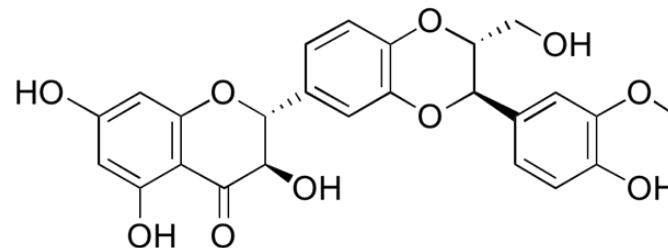


Figure 4. Citrus flavonoids target several molecular markers that are involved in the regulation of blood glucose levels. Citrus flavonoids can increase adipose tissue glucose transporter 4 (GLUT4), insulin receptors (IR), protein kinase B (PKB) or Akt, and protein kinase A (PKA); decrease skeletal

Research Article

Evaluation of the Effect Derived from Silybin with Vitamin D and Vitamin E Administration on Clinical, Metabolic, Endothelial Dysfunction, Oxidative Stress Parameters, and Serological Worsening Markers in Nonalcoholic Fatty Liver Disease Patients



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 Marcello Dallio ¹,
 Mario Masarone ²,
 Antonietta Gerarda Gravina ³,
 Rosa Di Sarno ¹,
 Concetta Tuccillo ¹,
 Valentina Cossiga ³,
 Stefania Lama ¹,
 Paola Stiuso ¹,
 Filomena Morisco ³,
 Marcello Persico ²,
 and Carmelina Loguercio ¹

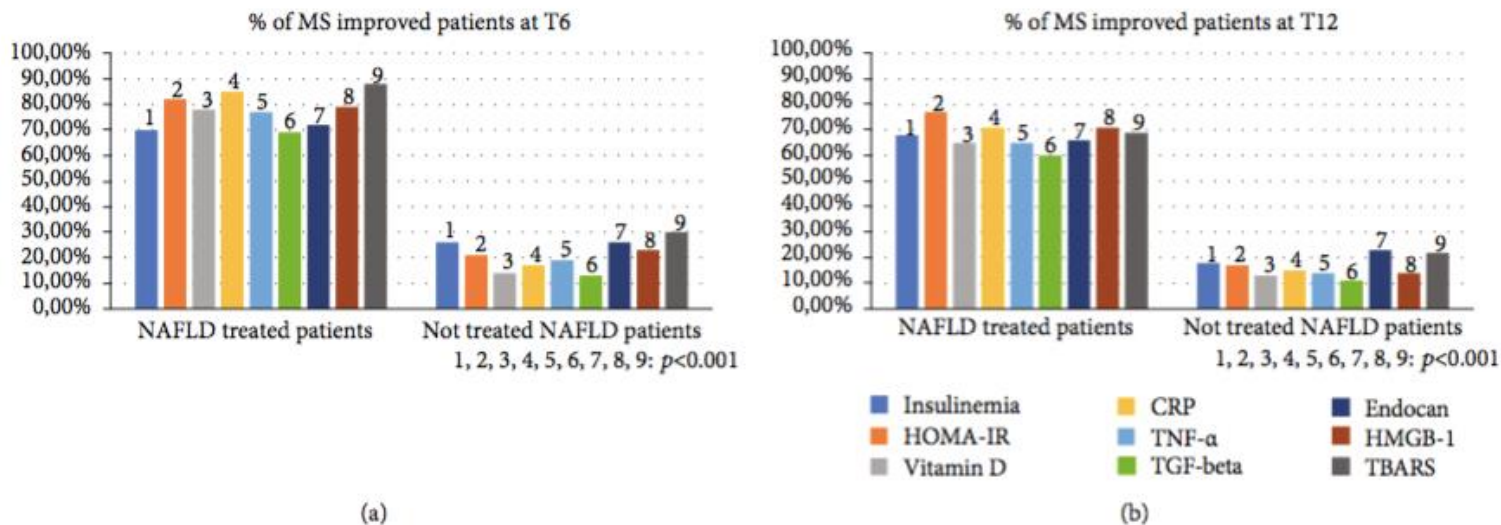


FIGURE 8: Comparison between the two NAFLD group patients with metabolic syndrome which presented an improvement of insulinemia, the homeostatic model assessment for insulin resistance, vitamin D, C reactive protein, tumor necrosis factor-alpha, transforming growth factor-beta, Endocan, high mobility group box-1, and thiobarbituric acid reactive substances. NAFLD: nonalcoholic fatty liver disease; MS: metabolic syndrome; HOMA-IR: homeostatic model assessment for insulin resistance; CRP: C reactive protein; TNF-α: tumor necrosis factor-alpha; TGF-beta: transforming growth factor-beta; HGMB-1: high mobility group box-1; TBARS: thiobarbituric acid reactive substances.

c) Fitoterapia

★ Fibre

★ Aglio

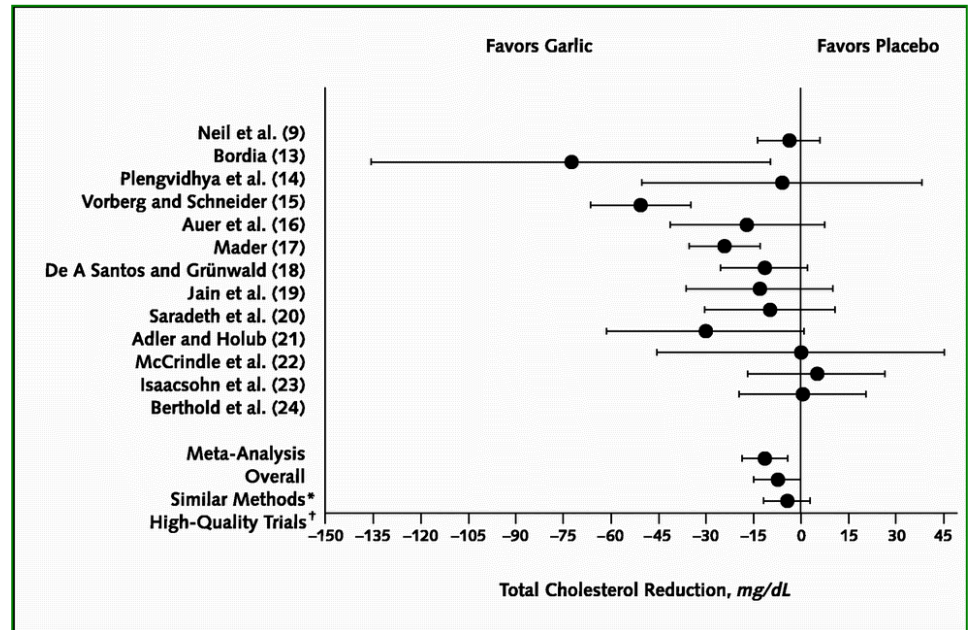
★ Bergamotto

★ Cannella

★ Fieno greco

★ Gymnema

★ Riso rosso



Review

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A systematic review of *Gymnema sylvestre* in obesity and diabetes management

Ramesh Pothuraju,* Raj Kumar Sharma, Jayasimha Chagalamarri, Surender Jangra and Praveen Kumar Kavadi

Abstract

The prevalence of obesity is associated with many health-related problems. Currently, more than 300 million people are considered to be obese. According to the World Health Organization (WHO), by 2030, 87 and 439 million people will be affected in India and the world, respectively. Today, herbal medicines are gaining interest in the treatment of obesity and diabetes, because of their minimal side effects. Gymnemic acid – an active component isolated from *Gymnema sylvestre* – has anti-obesity and antidiabetic properties, decreases body weight and also inhibits glucose absorption. Several components extracted from *Gymnema* prevent the accumulation of triglycerides in muscle and liver, and also decrease fatty acid accumulation in the circulation. In this paper, an attempt has been made to review the effects of various extracts from *Gymnema sylvestre* in the regulation of carbohydrate and lipid metabolism in both animal and clinical studies.

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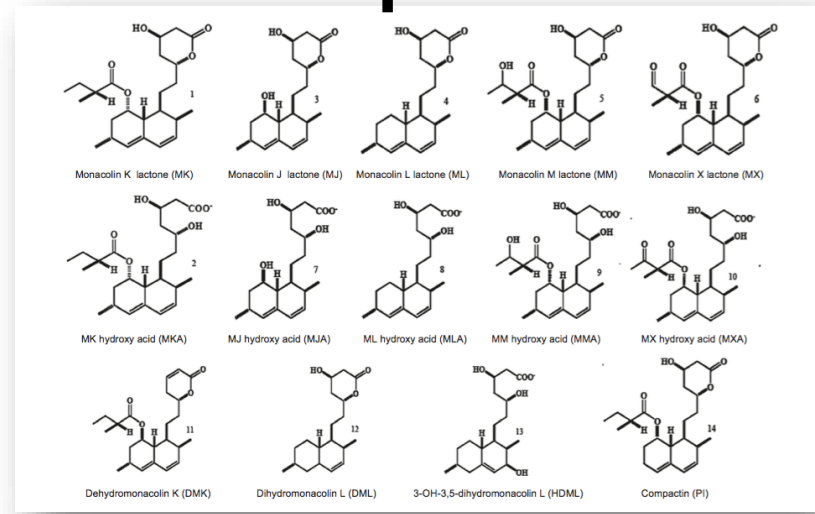
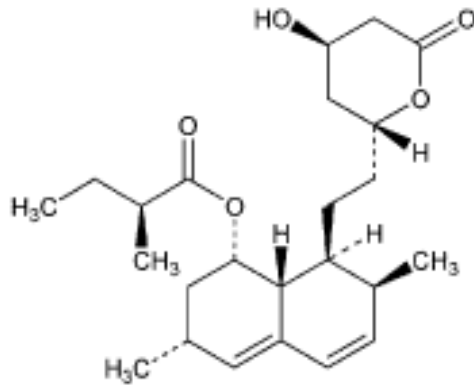
Keywords: *Gymnema sylvestre*; obesity; diabetes; metabolism

紅麴
紅曲

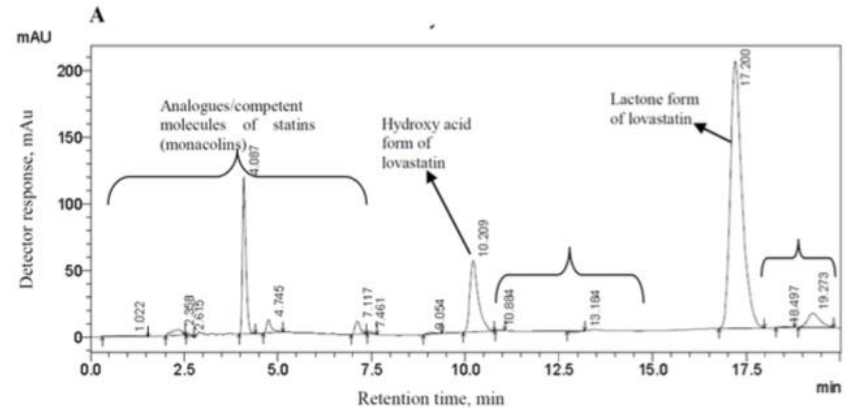


Hong Qu
Riso rosso fermentato

Complesso



Monacolina K
=
Lovastatina

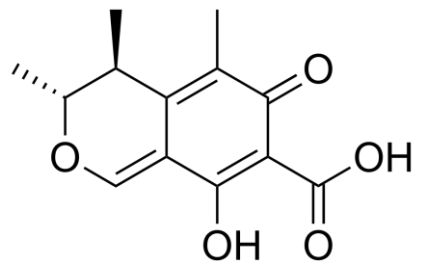


Complesso, variabile e... Citrinina

Table 2: Levels of monacolins in 12 commercial products available in the US market (Gordon et al., 2010)

Product	Daily intake Capsule	Total monacolins mg/600 mg-capsule	MK	MKA	MKA/ MK	µg/600 mg-capsule										Citrinin
						MJ	MJA	MX	MXA	ML	MLA	MM	MMA	DMK		
A	4	5.3	2.53	1.96	0.77	4	27	76	59	122	19	29	NT	473	0	
B	4	2.16	1.02	0.61	0.59	19	12	0	8	55	80	7	NT	212	0	
C	1-2	4.18	1.74	1.63	0.93	32	49	108	24	67	33	18	73	281	0	
D	2	1.65	1.12	0.22	0.19	0	13	55	0	49	11	0	0	140	14.3	
E	4	6.03	3.63	1.22	0.33	31	169	125	18	88	85	64	31	380	0	
F	2	0.31	0.1	0	0	0	0	0	0	0	0	0	160	5	114.2 *	
G	4	6.18	2.5	2.3	0.92	43	54	104	20	36	49	19	51	929	0	
H	1	11.15	10.09	0.52	0.05	0	58	73	0	43	38	45	71	141	0	
I	2	1.60	0.99	0.23	0.23	0	0	0	0	42	0	210	0	93	57.5	
J	2	3.97	2.66	0.46	0.17	0	25	98	0	126	53	88	41	305	0	
K	2	1.36	0.97	0.19	0.19	0	14	0	0	39	0	0	0	110	70.4	
L	2-4	6.13	3.12	2.07	0.66	42	64	112	16	56	83	59	19	315	0	
m ± SD		4.17 ± 3.00	2.54 ± 2.60	0.95 ± 0.84		14 ± 18	40 ± 46	63 ± 49	12 ± 17	60 ± 36	38 ± 33	40 ± 59	45 ± 49	286 ± 239	21.4 ± 38.2	
Median		4.08	2.12	0.57		20	26	75	4	52	36	24	36	246	0	

MK: monacolin K; MKA: monacolin K hydroxyacid; MJ: monacolin J; MJA: monacolin J hydroxyacid; MX: monacolin X; MXA: monacolin X hydroxyacid; ML: monacolin L; MLA: monacolin L hydroxyacid; MM: monacolin M; MMA: monacolin M hydroxyacid; DMK: dehydroxymonacolin K.



micotossina epato e nefrotossica
prodotta anche dai generi Aspergillus e Penicillium

*190 mg/Kg

Aprile 2020: **limite 100 mcg/kg** (prima 2 mg/Kg)

Letter to the Editors

Myopathies associated with red yeast rice and liquorice: spontaneous reports from the Italian Surveillance System of Natural Health Products

Francesco Lapi,^{1,2,3} Eugenia Gallo,^{1,2} Sara Bernasconi,² Michele Vietri,^{1,2}
Francesca Menniti-Ippolito,⁴ Roberto Raschetti,⁴ Luigi Gori,⁵ Fabio Firenzuoli,⁵
Alessandro Mugelli^{1,2} & Alfredo Vannacci^{1,2}

¹Tuscan Regional Centre of Pharmacovigilance, ²Department of Preclinical and Clinical Pharmacology, University of Florence, ³Regional Agency for Healthcare Services of Tuscany, Epidemiology Unit, Florence, ⁴National Centre of Epidemiology, Surveillance and Health Promotion, National Institute of Health, Rome and ⁵Centre of Natural Medicine, S. Giuseppe Hospital, Empoli, Italy

Miopatie da riso rosso fermentato

Sex, age (years)	Product; dosage; indication	Concomitant medications and notes	Reported ADRs; time to onset	Action taken; outcome
F, 53	xxxxxx contains red yeast rice (<i>Monascus purpureus</i>); 1 tablet a day; hypercholesterolaemia	None	Increase of CPK ζ (288 IU l ⁻¹), ALT and AST and GGT 2 months	Drug withdrawn; complete recovery
M, 49	xxxxxx nos [®] , contains red yeast rice (<i>Monascus purpureus</i>); 5 mg, 1 tablet a day; hypercholesterolaemia	None	Increase of CPK ζ (386 IU l ⁻¹), total cholesterol, ALT and AST; 2 months	Drug withdrawn; complete recovery
F, 43	xxxxxx rice (<i>Monascus purpureus</i>) 400 mg, 1 tablet 3 times a day; hypercholesterolaemia	None	Increase of CPK ζ (401 IU l ⁻¹), muscle pain; 6 months	Drug withdrawn; complete recovery
F, 60	xxxxxxx us [®] , contains red yeast rice (<i>Monascus purpureus</i> 200 mg + berberine extract <i>Berberis aristata</i> 500 mg); 1 tablet a day; hypercholesterolaemia	None; statin-intolerant	Increase of CPK ζ (356 IU l ⁻¹), AST# 37 IU l ⁻¹ , ALT# 28 IU l ⁻¹ ; 6 months	Drug withdrawn; reaction unresolved
M, 30*	Liquorice, (<i>Glycyrrhiza glabra</i>); 30g day ⁻¹ orally; nutrient	None	Increase of CPK, rhabdomyolysis; 1 month	Drug withdrawn; complete recovery
M, 73*	xxxxxxxxxxxxx a [®] , contains liquorice (<i>Glycyrrhiza glabra</i>); 2 tablets a day; laxative	Simvastatin, atenolol, cardioaspirin, lansoprazole, ursodesossilic acid, lisinopril, nitrodur (from 8 years)	Rhabdomyolysis, increase of CPK ζ (8000 IU l ⁻¹), blood nitrogen t 6.0 mg dl ⁻¹ ; 20 days	Drug withdrawn; reaction unresolved
M, 81*	Liquorice (<i>Glycyrrhiza glabra</i>) concentrate juice; 2-3 g day ⁻¹ , chronic hypotension	β -blockers, anxiolytics	Hypertension, hypokalaemia, hypematraemia, increase of CPK, 3 months	Drug withdrawn, anthialdosterone therapy, supplementation; complete recovery

F.Firenzuoli, Firenze

Scientific opinion on the safety of monacolins in red yeast rice

Agenzie regolatorie

Appendix B – Case collected by FDA and European phytovigilance Units with assessment of level of causality^(a)

Organ/system involved	ANSES (2009–May 2013)			Italian surveillance system (Apr 2002–Sep 2015)			FDA (CAERS)		
	Number cases for symptom ^(b)	% Total cases	Causality	Number cases for symptom ^(b)	% total cases	Causality	Number cases for symptom ^(b)	% Total cases	Causality
Musculoskeletal and connective tissue	8	32.0	VL = 1 L = 7	19	36.5	L = 11 P = 8	47	28.7	SP = 31 CM = 16
Rhabdomyolysis	1	4.0	L = 1	1	1.9	C = 1	2	1.2	SP = 2
Nervous system (including psychiatric disorders)	0	0		0	0		21	12.8	SP = 9 CM = 12
Gastrointestinal system	3	12.0	L = 2 UN = 1	12	23.1	L = 6 P = 5 UN = 1	31	18.9	SP = 21 CM = 10
Skin and subcutaneous tissue	2	8.0	VL = 1 P = 1	9	17.3	L = 3 P = 4 UN = 2	20	12.2	SP = 10 CM = 10
Hepatobiliary system	8	32.0	L = 3 P = 4 UN = 1	10	19.2	L = 7 P = 1 UN = 2	25	15.2	SP = 8 CM = 17
Other	7	28.0	P = 3 UN = 3 EX = 1	4	7.7	L = 4	56	34.1	SP = 41 CM = 15
TOTAL CASES	25	–		52			164		

NR: Not Reported; C: Certain; VL: Very Likely; L: Likely; P: Possible; UN: unassessable, unlikely; EX: Excluded; SP: Suspected; CM: concomitant.

(a): www.vigiaccess.org, <https://www.fda.gov>; ANSES; 2014; Mazzanti et al., 2017.

(b): Symptoms for each subject can be more than one.

Scientific opinion on the safety of monacolins in red yeast rice

Clinical trials

Table 8: Adverse effects reported in 36 papers (20 clinical trials) (modified from Gerards et al., 2015)

Organ/system	RYR-treated group	Control group
Gastrointestinal disorders (diarrhoea, GI discomfort, other symptoms)	51	20
Musculoskeletal (arthralgia, weakness)	15	9
Laboratory value alterations (LDL, leucocytosis, leukopenia, hyperglycaemia)	3	2
Infectious problems (influenza, urinary tract, pneumonia)	10	5
Immunologic problems (rash, alopecia, allergic reactions)	7	4
General problems (dizziness, malaise, fatigue)	6	6
CNS disorders (headache)	5	5
Cardiovascular disorders (QT prolongation, uncontrolled hypertension, oedema, erectile dysfunction)	2	6
Miscellaneous problems (breast cancer, unspecified)	23	29

RYR: red yeast rice; LDL: low-density lipoprotein; CNS: central nervous system.

Table 9: Case reports of myopathy and rhabdomyolysis associated with intake of food supplements containing monacolin K from RYR preparations, published in the scientific literature

Patient data	Daily intake of monacolin K	Period of intake	Adverse effects	Reference
Female, 52 years old	2.6 mg	90 days	Increase level of serum CK; Myalgia	Philibert et al. (2016)
Female, 53 years old	3 mg	60 days	Increased level of serum CK	Lapi et al. (2008)
Sex unknown, 48 years old	3 mg	60 days	Rhabdomyolysis (hospitalisation)	Mazzanti et al. (2017)
Female, 45 years old	3 mg	24 days	Nocturnal leg muscle cramps	Mazzanti et al. (2017)
Female, 45 years old	3 mg	54 days	Myalgia in the leg	Mazzanti et al. (2017)
Female, 53 years old	3 mg	97 days	Generalised muscle aches	Mazzanti et al. (2017)
Female, 57 years old	3 mg	60 days	Increased level of serum CK (10 times).	Mazzanti et al. (2017)
Female, 65 years old	3 mg	31 days	Cramps and myalgia of lower extremities	Mazzanti et al. (2017)
Female, 67 years old	3 mg	31 days	Increased level of serum CK, myopathy, asthenia. Previous myopathy by statins	Mazzanti et al. (2017)
Female, 68 years old	3 mg	62 days	Localised muscle pain; increased level of serum CK	Mazzanti et al. (2017)
Female, 69 years old	3 mg	25 days	Myalgia of lower extremities	Mazzanti et al. (2017)
Female, 70 years old	3 mg	90 days	Myalgia, increased level of serum CK, Previous statin intolerance	Mazzanti et al. (2017)
Female, age unknown	3 mg	> 365 days	Increased level of serum CK, previously observed with statins	Mazzanti et al. (2017)
Male, 60 years old	3 mg	165 days	Increased level of serum CK	Mazzanti et al. (2017)
Female,	4–8 mg	4 months	Myalgia	Venhuis et al. (2016)
Male, 49 years old	5 mg	60 days	Increased level of serum CK	Lapi et al. (2008)
Female, 64 years old	10.2 mg	30 days	Increase level of serum CK	Philibert et al. (2016)
Female, 51 years old	19.8 mg	30 days	Myalgia	Philibert et al. (2016)
Male, 37 years old	19.2 mg	48 days	Rhabdomyolysis, increased level of serum CK	Philibert et al. (2016)
Female, 51 years old	19.8 mg	30 days	Myalgia	Philibert et al. (2016)

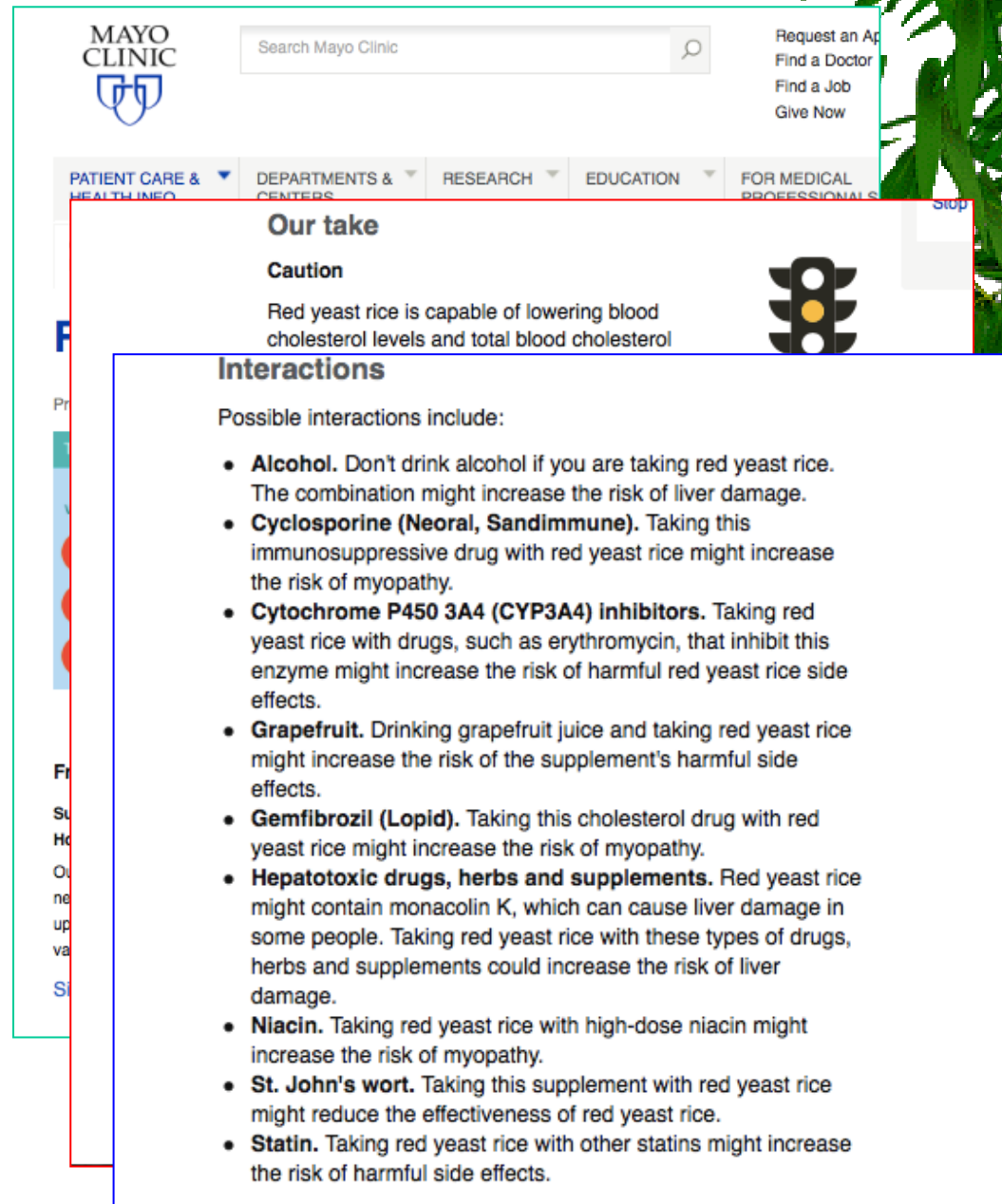


Table 10: Case reports of liver function alteration associated with intake of food supplements containing monacolin K from RYR preparations, published in the scientific literature

Patient data	Daily intake of monacolin K ^(a)	Period of intake	Adverse effects	Reference
Female, 63 years old	15–30 mg	6 months	Severe lobular necroinflammatory changes at liver biopsy; previous mild hepatotoxicity during therapy with lovastatin	Grieco et al. (2009)
Female, 53 years old	3 mg	60 days	Increased level of ALT and AST, GGT	Lapi et al. (2008)
Male, 49 years old	5 mg	60 days	Increased level of ALT and AST	Lapi et al. (2008)
Female, 42 years old	3 mg	30 days	Acute hepatitis with hospitalisation	Mazzanti et al. (2017)
Female, 46 years old	3 mg	50 days	Acute hepatitis with hospitalisation	Mazzanti et al. (2017)
Female, 58 years old	3 mg	60 days	Increased level of AST (2x normal level)	Mazzanti et al. (2017)
Female, 68 years old	3 mg	15 days	Increased level of pancreas and hepatic enzymes	Mazzanti et al. (2017)
Female, 68 years old	3 mg	1 year	Increased level of transaminases; previous statin intolerance	Mazzanti et al. (2017)
Male, 35 years old	3 mg	60 days	Toxic acute hepatitis with hospitalisation	Mazzanti et al. (2017)
Male, 36 years old	3 mg	76 days	Acute hepatitis with hospitalisation	Mazzanti et al. (2017)

Conclusioni EFSA

- ✳ Monacolina K e lovastatina identici principi attivi del medicinale autorizzato
- ✳ (EFSA NDA Panel, 2013), 10 mg/die dosaggio che si sovrappone alla dose terapeutica più bassa di 10 mg / die
- ✳ Reazioni avverse anche gravi anche a soli 3 mg / die



The screenshot shows the Mayo Clinic website interface. At the top left is the Mayo Clinic logo. To its right is a search bar labeled "Search Mayo Clinic". Further right are links: "Request an Appointment", "Find a Doctor", "Find a Job", and "Give Now". Below the search bar is a navigation menu with categories: "PATIENT CARE & HEALTH INFO", "DEPARTMENTS & CENTERS", "RESEARCH", "EDUCATION", and "FOR MEDICAL PROFESSIONALS". The main content area is titled "Our take" and features a "Caution" section with a traffic light icon (yellow light lit) and the text: "Red yeast rice is capable of lowering blood cholesterol levels and total blood cholesterol". Below this is an "Interactions" section with the heading "Possible interactions include:" followed by a bulleted list of seven items: Alcohol, Cyclosporine (Neoral, Sandimmune), Cytochrome P450 3A4 (CYP3A4) inhibitors, Grapefruit, Gemfibrozil (Lopid), Hepatotoxic drugs, herbs and supplements, Niacin, St. John's wort, and Statin.

Our take

Caution

Red yeast rice is capable of lowering blood cholesterol levels and total blood cholesterol

Interactions

Possible interactions include:

- **Alcohol.** Don't drink alcohol if you are taking red yeast rice. The combination might increase the risk of liver damage.
- **Cyclosporine (Neoral, Sandimmune).** Taking this immunosuppressive drug with red yeast rice might increase the risk of myopathy.
- **Cytochrome P450 3A4 (CYP3A4) inhibitors.** Taking red yeast rice with drugs, such as erythromycin, that inhibit this enzyme might increase the risk of harmful red yeast rice side effects.
- **Grapefruit.** Drinking grapefruit juice and taking red yeast rice might increase the risk of the supplement's harmful side effects.
- **Gemfibrozil (Lopid).** Taking this cholesterol drug with red yeast rice might increase the risk of myopathy.
- **Hepatotoxic drugs, herbs and supplements.** Red yeast rice might contain monacolin K, which can cause liver damage in some people. Taking red yeast rice with these types of drugs, herbs and supplements could increase the risk of liver damage.
- **Niacin.** Taking red yeast rice with high-dose niacin might increase the risk of myopathy.
- **St. John's wort.** Taking this supplement with red yeast rice might reduce the effectiveness of red yeast rice.
- **Statin.** Taking red yeast rice with other statins might increase the risk of harmful side effects.



Contents lists available at ScienceDirect

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



Review

Safety of red yeast rice supplementation: A systematic review and meta-analysis of randomized controlled trials



Federica Fogacci^{a,1}, Maciej Banach^{b,c,d,*,1}, Dimitri P. Mikhailidis^e, Eric Bruckert^f, Peter P. Toth^{g,h}, Gerald F. Wattsⁱ, Željko Reiner^j, John Mancini^k, Manfredi Rizzo^l, Olena Mitchenko^m, Daniel Pellaⁿ, Zlatko Fras^o, Amirhossein Sahebkar^{p,q}, Michal Vrablik^r, Arrigo F.G. Cicero^{a,*}, on behalf of the Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group, the International Lipid Expert Panel (ILEP)

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- ★ **In realtà in 38/53 studi il prodotto a base di riso rosso fermentato conteneva anche altre sostanze attive** *coenzima Q10, fitosteroli, estratto di carciofo, acido folico, berberina, idrossitirosolo, policosanoli, astaxantina, silimarina, nattokinasi, estratto di tè verde, quercetina, resveratrolo, estratto di guggul, estratto di semi d'uva, estratto di pepe nero, estratto di aglio, estratto di corteccia di pino, niacina, vitamina E, procianidine o melone amaro.*
- ★ **I gruppi di controllo** hanno generalmente ricevuto un **placebo**. In alcuni studi, nei gruppi di controllo sono state somministrate sostanze medicinali attive come *atorvastatina 10 mg, pravastatin 40 mg, fluvastatina 20 mg, simvastatina 20 mg, una "statina a basso dosaggio" (non ulteriormente specificato), berberina 500 mg*
- ★ **24/53 studi clinici della metanalisi non chiariscono** se e come siano stati registrati dati sulla sicurezza e tollerabilità del trattamento 2 studi in cinese non sono stati esaminati

In definitiva, le conclusioni tratte dagli Autori della meta-analisi in questione, vale a dire che *l'integrazione di "RYR è sicura e non è associata ad una maggiore incidenza di effetti avversi muscolari che questo composto nutraceutico può essere usato per promuovere la salute nella popolazione generale con un lieve aumento del rischio di malattie cardiovascolari e nei pazienti intolleranti alle statine"* (Fogacci et al., 2019),

non può essere adeguatamente motivata.

Ultimately, the conclusions as drawn by the authors of the meta-analysis in question, namely that " RYR [Red Yeast Rice] supplementation is safe and is not associated with increased incidence of muscular adverse effects this nutraceutical compound can be used in order to promote health in general population with mildly increased cardiovascular disease risk and in statin-intolerant patients" (Fogacci et al., 2019), cannot be adequately substantiated. As a result of the stated limitations, the meta-analysis in question is not sufficiently reliable and therefore offers no appropriate basis on which to rebut the significant health concerns about red yeast rice food supplement products containing monacolin K.

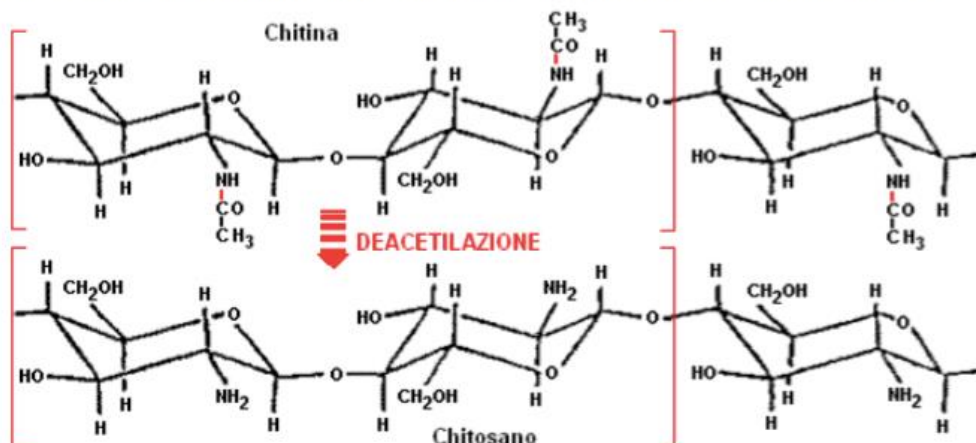
d) Chitosano

Il **chitosano** è un polisaccaride cationico lineare composto da D-glucosamina e N-acetil-D-glucosamina collegate in modo casuale (1-4) prodotte commercialmente dalla deacetilazione della chitina. Il peso molecolare del chitosano nelle preparazioni commerciali varia da 3.800 a 20.000 Da. Il chitosano è insolubile in acqua. Il grado di deacetilazione varia dal 60 al 100% nelle preparazioni commerciali.

La **chitina** un polisaccaride tra i più diffusi in natura: consiste in un glicano composto da unità β 1-4 a unità di N-acetilglucosamina, componente dell'esoscheletro di crostacei e insetti nonché della parete cellulare dei funghi. Più spesso è ottenuta dai gusci di granchi e gamberi.

I **COS Chito-Oligosaccaridi (COS)** sono derivati del chitosano (polimeri policationici composti principalmente da unità di glucosammina) che possono essere prodotti sia tramite idrolisi enzimatica che chimica dal chitosano.

Recentemente, queste sostanze sono state oggetto di un aumento di attenzione da parte dei ricercatori nonché dei clinici nonché delle aziende produttrici di farmaci, integratori e cosmetici.



Chitosano EFSA

Gli esperti dell' EFSA hanno valutato la revisione sistematica della **Cochrane collaboration (Jull et al., 2008)** relativa agli effetti del chitosano sui lipidi del sangue e ha incluso l'unico studio di intervento umano presentato per la fondatezza scientifica dell'indicazione.

Il gruppo di esperti scientifici ha osservato che il consumo di chitosano ha mostrato un piccolo ma statisticamente significativo effetto sulla riduzione sia delle concentrazioni totali (combinando cinque studi) che del colesterolo LDL (combinando due studi), nessun effetto è stato osservato sulle concentrazioni di colesterolo HDL.

Concludono che è stato stabilito un rapporto di causa ed effetto tra il consumo di chitosano e il mantenimento delle normali concentrazioni di colesterolo LDL nel sangue.

La seguente formulazione riflette le prove scientifiche: "Il chitosano può contribuire a mantenere normali livelli di colesterolo nel sangue".

Chitosano legato a fosfoserina riduce assorbimento dei grassi alimentari (Fratter, 2014)

Un'altra **metanalisi di studi clinici controllati** (Baker W. et al., 2009) relativa alla valutazione d'efficacia del chitosano come agente ipocolesterolemizzante è stata condotta mediante una ricerca sistematica di letteratura su Medline, Embase, Cochrane Central e il database completo di Natural Medicines è stata condotta fino a maggio 2008. Selezionati studi clinici randomizzati, controllati di chitosano vs placebo in pazienti ipercolesterolemici e segnalati dati di efficacia su lipoproteine totali, a bassa densità (LDL), colesterolo o trigliceridi ad alta densità di lipoproteine