14° CONGRESSO NAZIONALE SINut

SINut
Società Italiana di Nutraceutica

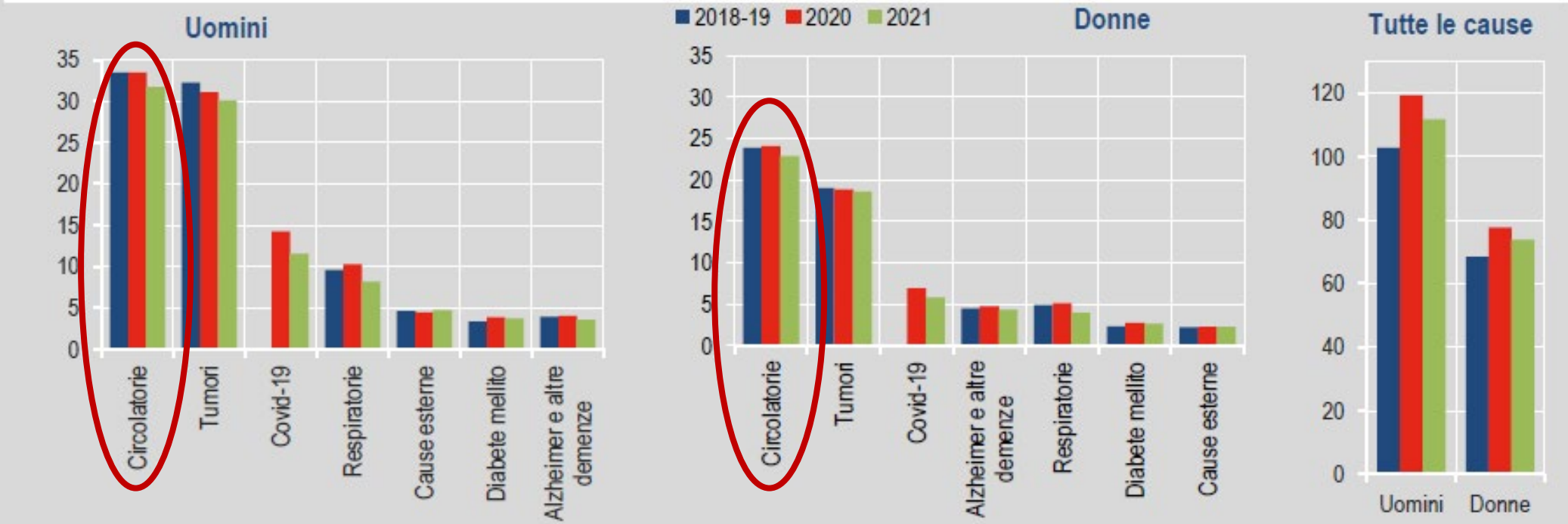
12-14 settembre 2024
Bologna

FITOCOMPLESSI DA ESTRATTI MEDITERRANEI: INTERAZIONI SINERGICHE PER LA CARDIOPROTEZIONE

Valentina Ferri

Istituto dei Tumori di Milano

FIGURA 2. MORTALITÀ PER LE PRINCIPALI CAUSE DI MORTE E SESSO. MEDIA 2018-2019. Anni 2020 e 2021.
Tassi standardizzati per età (per 10mila abitanti).

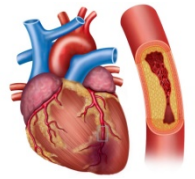


Fonte: Istat, Indagine sui decessi e le cause di morte.

Fonte: ISTAT

MALATTIA CORONARICA

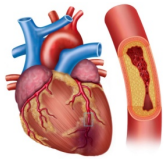
Fattori di rischio non modificabili



- Età: > 40 aa 49% ♂ - 32% ♀
- Sesso: M > F
- Etnia: neri, ispanici, latini, asiatici
- Familiarità

"Risk Factors for Coronary Artery Disease" J.C. Brown; T.E. Gerhardt; E. Kwon. Last Update: January 23, 2023.

Fattori di rischio modificabili



- Ipertensione arteriosa
- Fumo
- Sedentarietà
- Dieta inadeguata
- Obesità
- Dislipidemia
- Diabete mellito
- Non-alcoholic fatty liver disease (NAFLD)
- IBD – HIV – Distiroidismi

- Ruolo minore ma significativo
- Solo 2/3 pz adeguatamente trattato
- Se profilo fdr ottimali → ↓ R di morte per eventi cardiovascolari

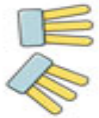
Berry JD et al., N Engl J Med. ***2012*** *Jan 26;366(4):321-9.*

"Risk Factors for Coronary Artery Disease" J.C. Brown; T.E. Gerhardt; E. Kwon. Last Update: January 23, ***2023****.*

Metabolic Syndrome
defined as 3 or more of the following

- Abdominal obesity

- Elevated plasma triglycerides



- Low plasma HDL cholesterol

- Elevated blood pressure

- Elevated fasting blood glucose

Diseases Associated with Metabolic Syndrome

- Type 2 Diabetes
- Hypertension
- Non-alcoholic Fatty Liver Disease (NAFLD)
- Cardiovascular Events

World Health Organization

a livello mondiale una prevalenza del 25%, in Europa una prevalenza del 24%

associandosi in realtà non sempre a condizioni di obesità.

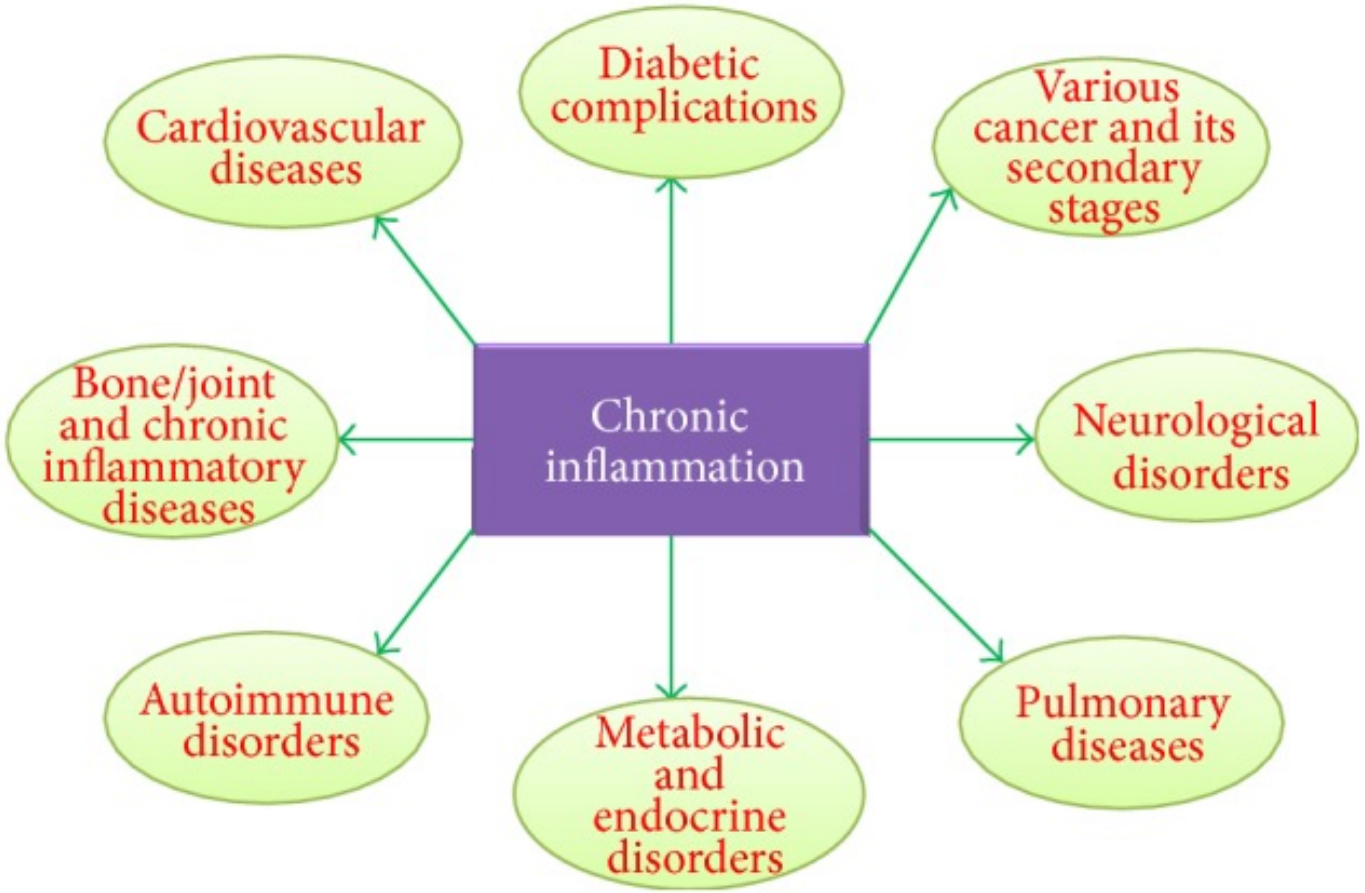
*Adapted from: Front. Pharmacol., 12 March **2021** Sec. Experimental Pharmacology and Drug Discovery Volume 11 - 2020*

VALORE	NORMALE	ALTERATO
GLICEMIA	70-90 mg/dl	Alterata glicemia a digiuno 100-125 mg/dl Diabete > 126 mg/dl
EMOGLOBINA GLICATA	20 - 39 mmol	40 – 47 mmol pre diabete 48 mmol diabete
INSULINA	4 – 24 µU/ml	0,23 – 2,5 µU/ml
HOMA-IR	< 2,5	> 2,5

Review Article

Role of Antioxidants and Natural Products in Inflammation

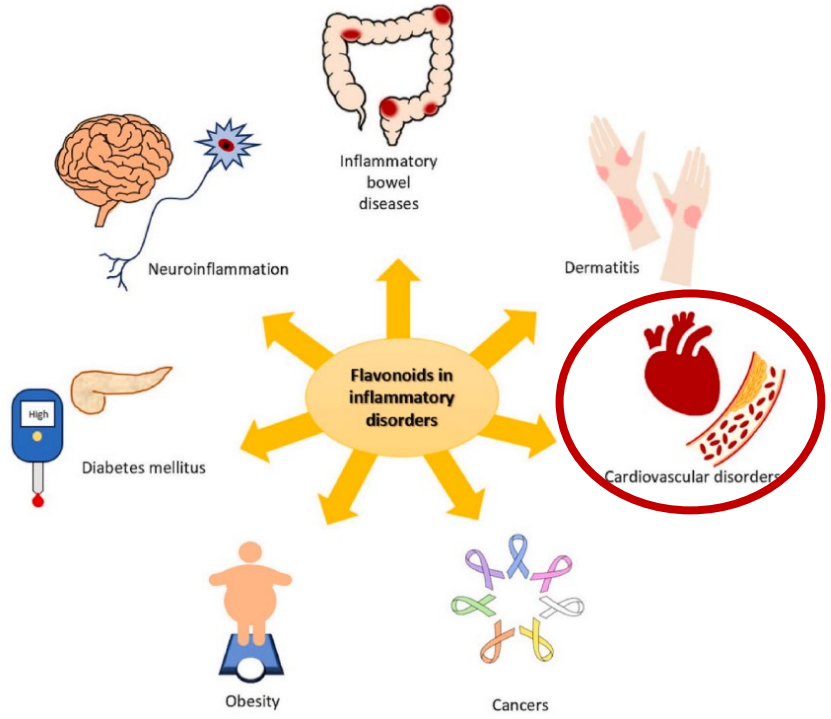
Palanisamy Arulselvan,[1] Masoumeh Tangestani Fard,[2] Woan Sean Tan,[1]
Sivapragasam Gothai,[1] Sharida Fakurazi,[1] Mohd Esa Norhaizan,[3] and S. Suresh Kumar[4]

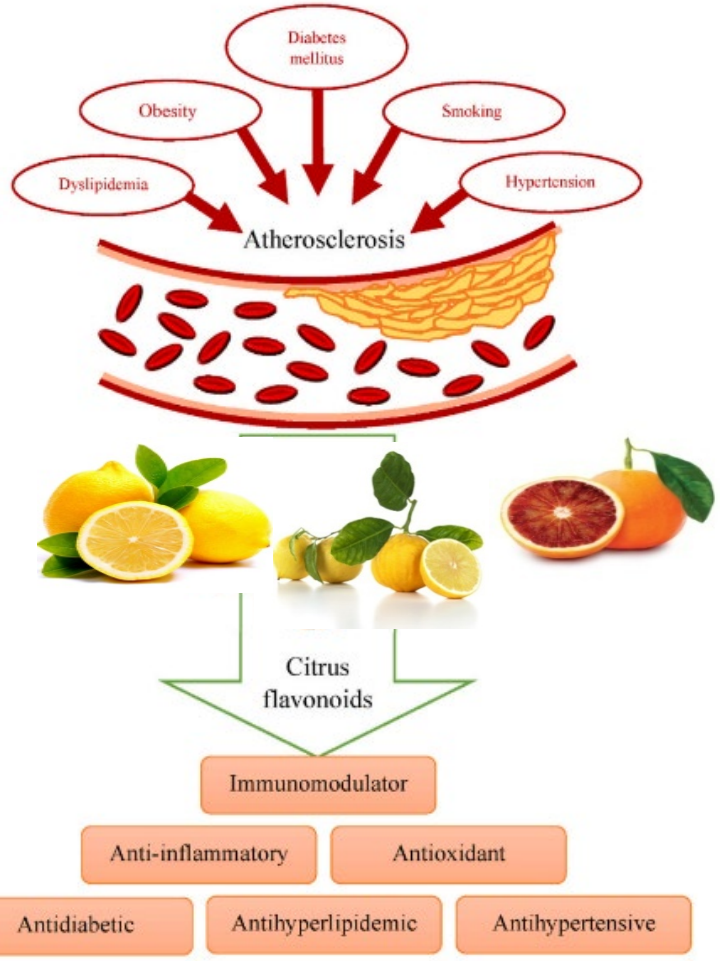


febbraio del 2004.

Review article

Citrus flavonoids and adhesion molecules: Potential role in the management of atherosclerosis





*Ebrahimi, F., et al; **2023**. Heliyon, 9(11), e21849*

AGRUMI

Citrus Bergamia (Bergamotto)

80 % prod. Mondiale in Calabria (zona Ionica)

- 1200 ettari coltivati a 3 cultivar
- 25000 tonnellate
- Industria cosmetica (essenza per profumi e cosmetici vari) >> scarti >> filiera nutraceutica.

Citrus Sinensis (Arancia)

- Sicilia, Calabria
- 1520000 tonnellate l'anno

Citrus Limon (Limone)

- Lago di garda, Sicilia, Calabria, Campania
- 380000 tonellate l'anno

Elevato contenuto in FLAVONOIDI

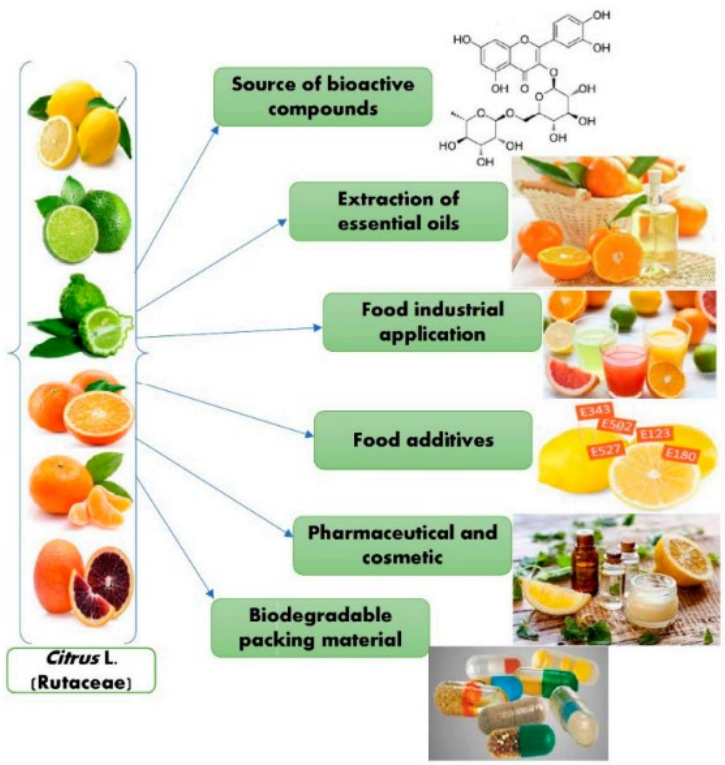
Eriocitrina – Esperidina – Naringina – Naringenina – Antociani (Cianidina)

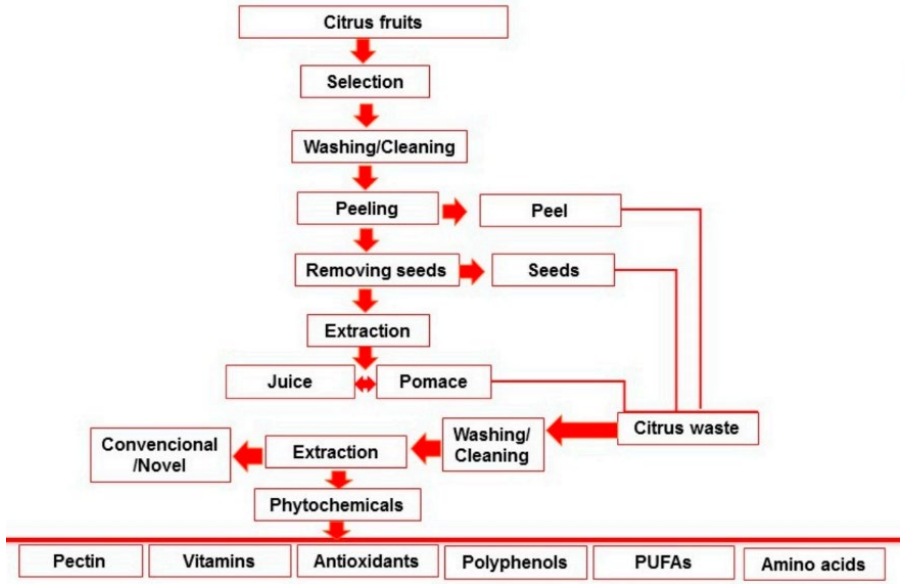
Alam, F., et al; ***2022****.. Phytotherapy Research, 36(4), 1417–1441.*

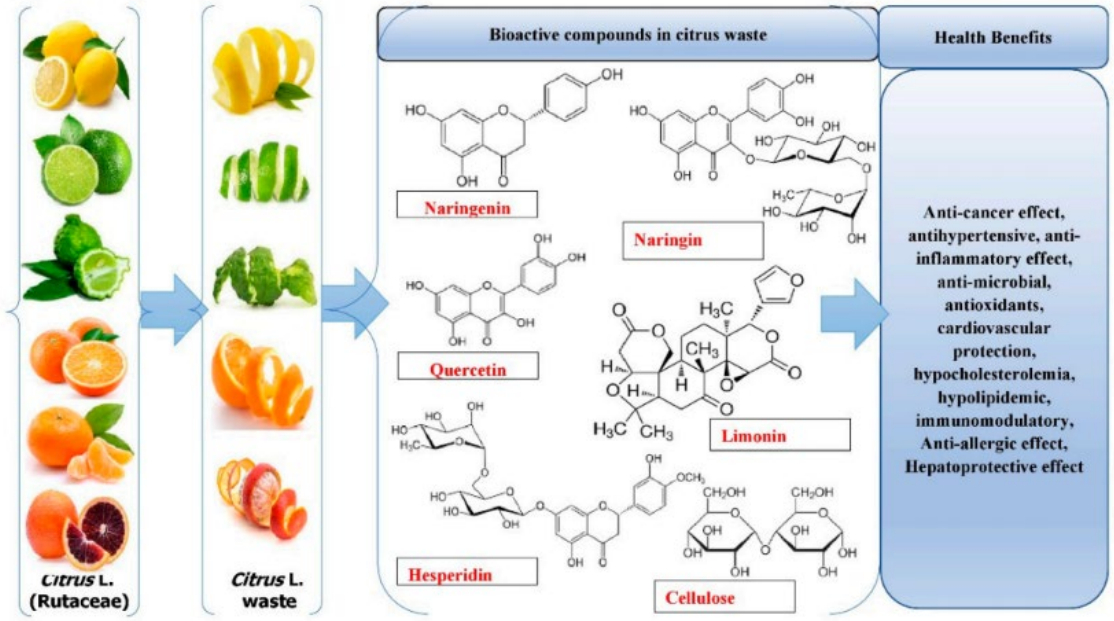
molecules

Review

Citrus Waste as Source of Bioactive Compounds: Extraction and Utilization in Health and Food Industry







*Maqbool, Z., et al; **2023**. Molecules (Basel, Switzerland), 28(4), 1636.*

Bergamotto

Inibizione della sintesi del colesterolo

Aumento del turnover del colesterolo e sintesi acidi biliari

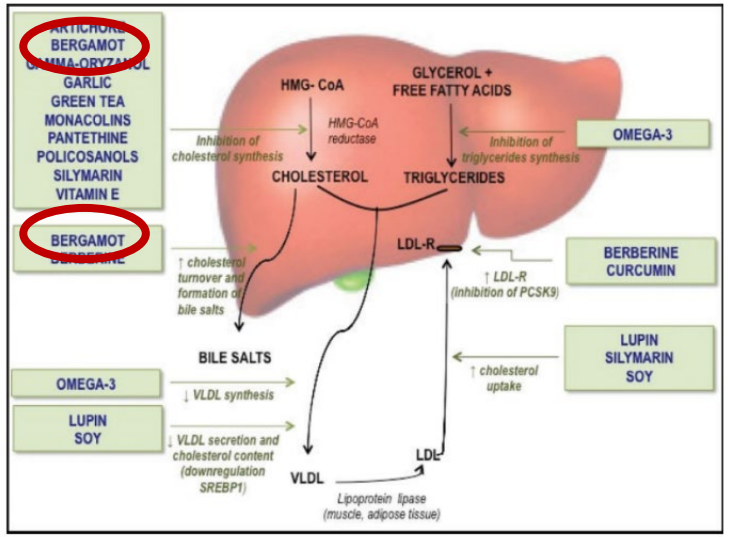
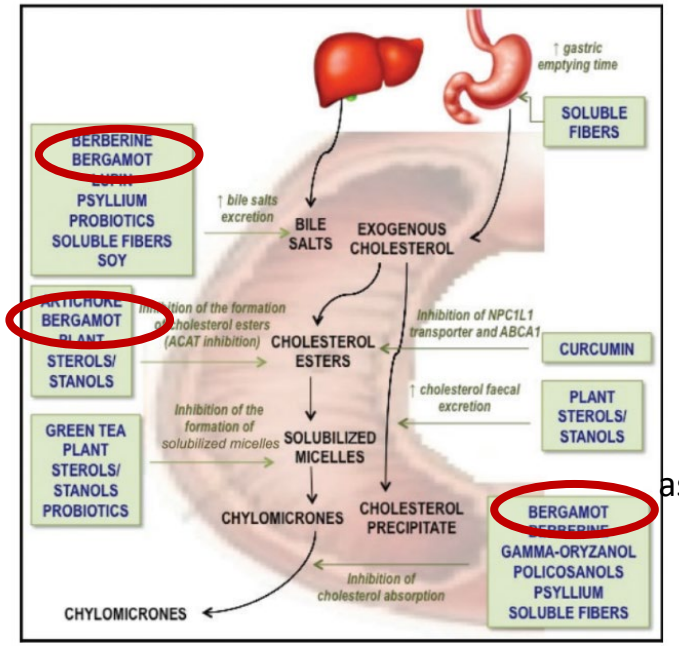


Figure 1 **Nutraceuticals acting as inhibitors of liver cholesterol synthesis.** *Abbreviations*: HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A; LDL-R, low-density lipoprotein receptor; PCSK9, proprotein convertase subtilisin/kexin type 9; SREBP1, sterol regulatory element-binding protein 1; VLDL, very-low-density lipoprotein.

Aumento dell'escrezione dei Sali biliari

Inibizione dell'esterificazione del colesterolo endogeno dall'enzima ACAT (Acil-CoA colesterolo Acil-transferasi)



Inibizione assorbimento colesterolo

Figure 2 **Nutraceuticals acting as inhibitors of intestinal cholesterol absorption and enhancers of cholesterol excretion.** *Abbreviations*: ABCA1, ATP-binding cassette transporter; NPC1L1, Niemann-pick C1-like 1.

Aumenta la beta-ossidazione e riduce la sintesi dei trigliceridi

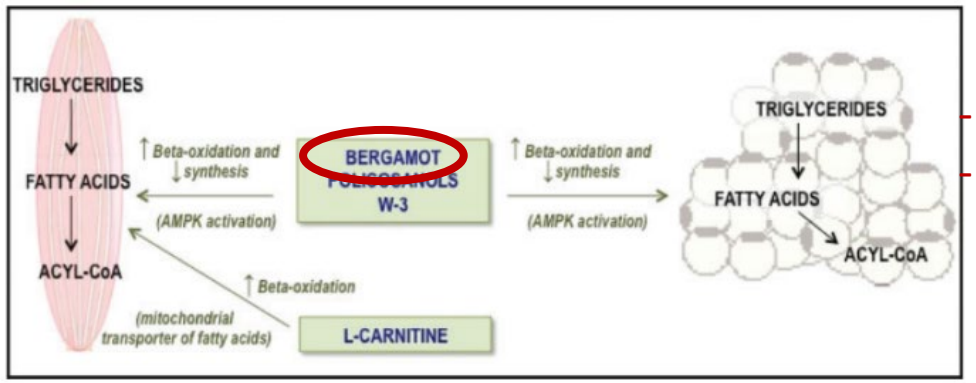


Figure 3 **Nutraceuticals acting on fatty acids.** *Abbreviations*: AMPK, AMP-activated protein kinase.

400-1200 mg/die

LDL / TG / insulina / leptina / PCR / TNF-α

infiammazione

un ormone prodotto dal tessuto adiposo, coinvolto nel metabolismo e nel dimagrimento

*Cicero et al, **2017**., Nutr. Rev. Vol 75,*
*Cicero , Fogacci et al **2021**, Curr. Ather. Rep.,*

RESEARCH ARTICLE

WILEY

Effect of *Citrus bergamia* extract on lipid profile: A combined in vitro and human study

Maria Pierdomenico[1] | Arrigo F. G. Cicero[2] | Maddalena Veronesi[2] | Federica Fogacci[2] | Costanza Riccioni[3] | Barbara Benassi[1]

- Brumex™ : estratto di bergamotto *(Citrus Bergamia Risso et Poiteau)*
- Studio clinico in doppio cieco, randomizzato, Brumex™ vs Placebo

  - 50 soggetti LDL 115/190 mg/dL
  - indicazioni dietetiche per dieta mediterranea
  - indicazione alla camminata rapida di 20/30 min per 3/5 vv a settimana
  - dopo 2 settimane per 12 settimane: A 400mg Brumex™ vs B placebo

*Pierdomenico, M., et al , **2023**; Phytotherapy research : PTR, 37(9), 4185–4195*

TABLE 1 Effect of placebo or Brumex™ intake on anthropometric, haemodynamic and laboratory parameters.

	Pre-run-in	Placebo T0	Bergamot T0	Placebo T1	Bergamot T1
Age (years)	52.6 ± 5.0	54.5 ± 4.2	54.1 ± 4.4	-	-
BW (kg)	63.4 ± 4.2	64.3 ± 5.4	63.8 ± 5.4	63.8 ± 5.4	62.7 ± 4.3
WC (cm)	88.3 ± 6.1	90.4 ± 4.4	89.6 ± 4.3	89.1 ± 4.7	87.9 ± 6.5
BMI (kg/m^2)	22.8 ± 2.2	23.7 ± 1.7	23.6 ± 1.5	23.6 ± 1.5	22.6 ± 2.3
SBP (mmHg)	134.5 ± 5.6	136.3 ± 4.8	134.9 ± 4.3	134.9 ± 4.3	135.7 ± 4.3
DBP (mmHg)	87.3 ± 2.2	88.6 ± 3.2	86.9 ± 2.4	86.9 ± 2.4	86.9 ± 3.5
TC (mg/dL)	248.3 ± 13.0	239.8 ± 11.7	237.6 ± 9.5	241.1 ± 13.5	219.1 ± 13.8*
HDL-C (mg/dL)	44.1 ± 2.7	46.5 ± 3.5	46.1 ± 2.7	44.3 ± 2.7	48.3 ± 2.8*
LDL-C (mg/dL)	161.4 ± 8.5	150.7 ± 9.9	149.1 ± 8.6	157.3 ± 8.9	137.7 ± 9.4*,§
Non-HDL-C (mg/dL)	204.7 ± 11.4	197.4 ± 10.2	195.5 ± 9.9	197.1 ± 11.8	171.5 ± 14.7*,§
TG (mg/dL)	216.8 ± 19.1	205.4 ± 13.7	198.5 ± 17.9	198.5 ± 17.9	171.8 ± 11.9*,§
ApoB (mg/dL)	146.3 ± 9.4	140.1 ± 8.5	138.4 ± 8.1	141.5 ± 7.4	126.5 ± 8.6*,§
ApoAI (mg/dL)	118.7 ± 12.4	101.9 ± 11.7	117.4 ± 13.5	118.2 ± 13.7	129.5 ± 11.7*,§
FPG (mg/dL)	88.9 ± 3.3	89.5 ± 3.5	88.2 ± 3.5	88.3 ± 3.2	85.3 ± 2.1*
GOT (mg/dL)	23.7 ± 3.8	24.5 ± 3.2	25.3 ± 3.4	25.3 ± 3.4	21.1 ± 2.3*
GPT (mg/dL)	22.0 ± 3.3	21.9 ± 2.4	22.1 ± 2.9	22.1 ± 2.9	19.3 ± 1.8*
gGT (mg/dL)	32.4 ± 2.1	34.6 ± 2.3	34.4 ± 2.4	32.7 ± 2.2	23.9 ± 3.1*
CPK (U/mL)	104.7 ± 19.2	101.3 ± 21.3	121.9 ± 15.1	111.9 ± 25.1	106.1 ± 18.9

*Pierdomenico, M., et al , **2023**; Phytotherapy research : PTR, 37(9), 4185–4195*

Phytotherapy Research

Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects

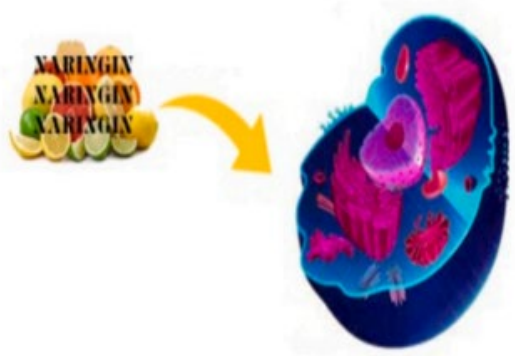
- Studio monocentrico randomizzato in doppio cieco
- 90 soggetti sovrappeso, TC 200-280 mg/dL, LDL 130-190 mg/dL.
- 24 settimane di trattamento
- Dieta mediterranea: 50%CHO – 20 %P – 30 %L, 6% sat, col < 300 mg – fibra 35 g
- Fitocomposto con bergamotto + fitosteroli + estratto di carciofo + vit C
- A: 2 cp di fitocomp (high-dose arm)
  B: 1 cp di fitocomp+ 1 cp di placebo (low-dose arm)
  C: 2 cp di placebo

*Cicero, A. F. G.; **2019**; Phytotherapy research : PTR, 33(8), 2094–2101*

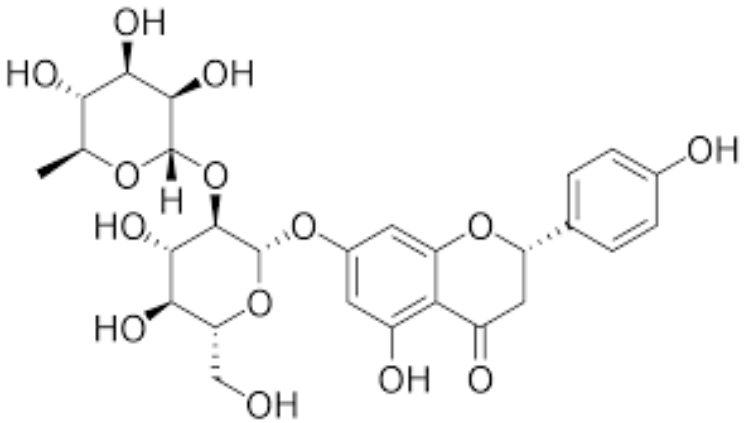
Variable	Baseline	8-week follow-up	24-week follow-up	Baseline	8-week follow-up	24-week follow-up	Baseline	8-week follow-up	24-week follow-up
Age (years)	44 ± 2	—	—	43 ± 4	—	—	45 ± 4	—	—
BMI (kg/m^2)	27.0 ± 1.8	26.8 ± 1.6	26.7 ± 1.7	26.8 ± 1.7	26.6 ± 1.5	26.4 ± 1.4	26.5 ± 1.9	26.3 ± 1.2	26.0 ± 1.1
SBP (mmHg)	131 ± 7	130 ± 9	130 ± 7	128 ± 8	126 ± 7	126 ± 6	126 ± 9	124 ± 8	124 ± 7
DBP (mmHg)	84 ± 5	83 ± 7	83 ± 6	85 ± 6	85 ± 5	84 ± 5	84 ± 7	83 ± 5	83 ± 6
TC (mg/dl)	253 ± 15	249 ± 11	248 ± 12	248 ± 12	238 ± 11	230 ± 9*	255 ± 13	218 ± 10*°	212 ± 9*°
LDL-C (mg/dl)	176 ± 10	175 ± 10	174 ± 11	171 ± 9	159 ± 7*°	156 ± 6*°	167 ± 12	148 ± 8*°	141 ± 7*°
HDL-C (mg/dl)	44 ± 4	45 ± 3	45 ± 3	45 ± 2	46 ± 3	47 ± 3	44 ± 3	46 ± 3	47 ± 4*
Non-HDL-C (mg/dl)	209 ± 12	204 ± 11	203 ± 11	203 ± 11	183 ± 11	183 ± 10	211 ± 13	172 ± 11*	165 ± 10*°
TG (mg/dl)	165 ± 11	147 ± 12*	149 ± 10*	159 ± 12	140 ± 13*	137 ± 12*°	151 ± 13	126 ± 14*°	121 ± 12*°
FPG (mg/dl)	90 ± 9	88 ± 7	88 ± 9	87 ± 6	85 ± 5	84 ± 6	91 ± 8	87 ± 6	86 ± 5*
FPI (µU/ml)	18.1 ± 4.2	17.7 ± 3.8	17.5 ± 3.9	18.5 ± 4.6	18.3 ± 4.4	17.3 ± 4.6	18.4 ± 4.5	17.8 ± 4.0	16.4 ± 3.4*
HOMA-IR	4.1 ± 0.9	3.9 ± 1.0	3.9 ± 0.9	3.9 ± 0.9	3.8 ± 0.8	3.5 ± 0.7*°	4.1 ± 0.8	3.9 ± 0.9	3.5 ± 0.9*°
GOT (U/L)	21 ± 6	22 ± 6	21 ± 5	18 ± 6	17 ± 4	17 ± 5	21 ± 7	19 ± 5	20 ± 5
GPT (U/L)	23 ± 7	23 ± 6	22 ± 7	21 ± 5	20 ± 5	20 ± 6	22 ± 6	21 ± 5	22 ± 6
γ-GT (U/L)	28 ± 9	26 ± 8	25 ± 9	25 ± 7	22 ± 6	24 ± 6	26 ± 9	21 ± 7*	23 ± 6
LAP	64 ± 14	63 ± 11	63 ± 12	63 ± 12	62 ± 10	63 ± 12	64 ± 12	63 ± 11	62 ± 10
HSI	38 ± 5	38 ± 4	37 ± 4	37 ± 5	36 ± 4	37 ± 4	38 ± 5	37 ± 6	37 ± 5
FLI	57 ± 11	57 ± 10	56 ± 11	55 ± 9	53 ± 8	54 ± 9	57 ± 9	54 ± 7	53 ± 8
SUA (mg/dl)	5.4 ± 0.9	5.2 ± 0.9	5.4 ± 1	5.3 ± 0.9	5.3 ± 0.9	5.1 ± 0.7	5.1 ± 1.1	5.2 ± 1.0	5.0 ± 0.9
CPK (U/L)	121 ± 23	131 ± 39	147 ± 38	134 ± 42	114 ± 37	127 ± 28	129 ± 37	131 ± 39	133 ± 21
Adiponectin (pg/ml)	8.3 ± 1.9	8.2 ± 1.5	8.3 ± 1.7	8.0 ± 2.1	8.1 ± 1.8	8.1 ± 1.7	8.4 ± 1.8	8.4 ± 1.3	8.6 ± 1.1*°
Leptin (pg/ml)	0.9 ± 0.7	1.0 ± 0.9	1 ± 0.9	1.1 ± 0.9	1.2 ± 0.8	1.1 ± 0.7	1.0 ± 0.9	1.0 ± 0.8	0.9 ± 0.7*°
Leptin/adiponectin ratio	0.11 ± 0.03	0.12 ± 0.05	0.12 ± 0.04	0.13 ± 0.05	0.15 ± 0.06	0.13 ± 0.05	0.12 ± 0.05	0.12 ± 0.08	0.10 ± 0.07*°
hs-CRP (mg/L)	2.96 ± 0.23	2.94 ± 0.19	2.98 ± 0.25	2.90 ± 0.25	2.76 ± 0.21	2.71 ± 0.23	3.01 ± 0.22	2.71 ± 0.19*	2.49 ± 0.18*°
TNF-α (pg/ml)	1.9 ± 0.2	1.8 ± 0.1	1.8 ± 0.2	1.8 ± 0.2	1.7 ± 0.1	1.6 ± 0.2	1.9 ± 0.1	1.6 ± 0.2*	1.5 ± 0.3*°

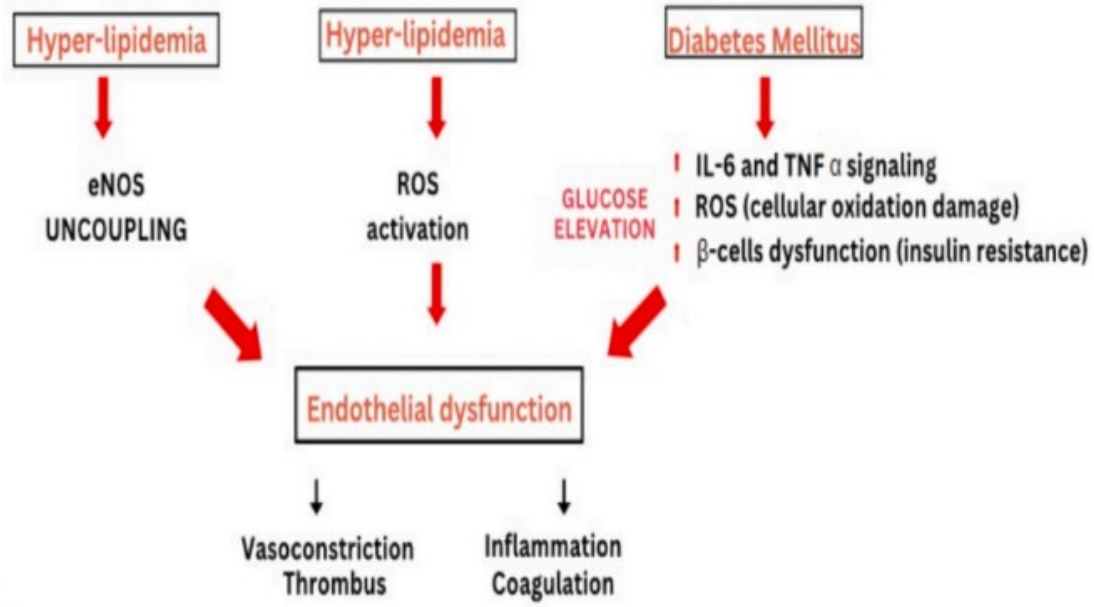
Review

Naringin: Cardioprotective properties and safety profile in diabetes treatment



- ↓ PCR, IL6, TNFα, MDA
- ↑ SOD, glutatione





*Yaseen HS et al., Fitoterapia 176, **2024**, 106011*

Naringin reduces body weight, plasma lipids and increases adiponectin levels in patients with dyslipidemia

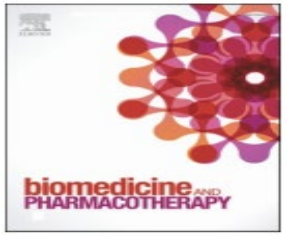
Jessica Lucia Barajas-Vega, Abdel Kerim Raffoul-Orozco ✉, Diego Hernandez-Molina, Ana Elisa Ávila-González, Teresa Arcelia García-Cobian, Edy David Rubio-Arellano, and Ernesto Javier Ramirez-Lizardo

Published Online: 9 Jun 2020 • **Doi:** https://doi.org/10.1024/0300-9831/a000658

Naringin is a citrus-flavonoid which has been shown to have positive metabolic and anti-inflammatory effects. For this reason, we believe it would be interesting to study the effects of Naringin administration on body weight, BMI, lipid profile and adiponectin levels in patients with dyslipidemia, especially considering that dyslipidemias along with obesity and subsequent cardiometabolic complications are some of the most important public health issues plaguing our society today. A double-blind, randomized clinical trial was conducted in a group of 28 adult patients previously diagnosed with dyslipidemia who attended the Institute of Experimental and Clinical Therapeutics. Patients were divided into two groups; the first group (n = 14) received 450 mg of naringin every 24 hours, in the mornings, while the second group (n = 14) was given a homologated placebo over the course of a 90-day period. Significant differences were observed in naringin group compared to the placebo group in terms of decreased BMI (30.6 ± 3.19 vs 33.3 ± 3.23 kg/m^2; p = 0.03), total cholesterol (182 ± 20.2 vs 245 ± 24.1 mg/dl; p < 0.01), LDL cholesterol (100 ± 17.5 vs 125 ± 38.3 mg/dl; p = 0.03) and an increase in adiponectin levels (0.82 ± 0.25 vs 0.59 ± 0.19 µg/ml; p = 0.01). Our results support the use of Naringin as a potential therapeutic agent which could play an important role in the management of metabolic disorders.

Barajas-Vega JL, et al.. Int J Vitam Nutr Res. ***2022****;92(3-4):292-298*

Eriocitrina

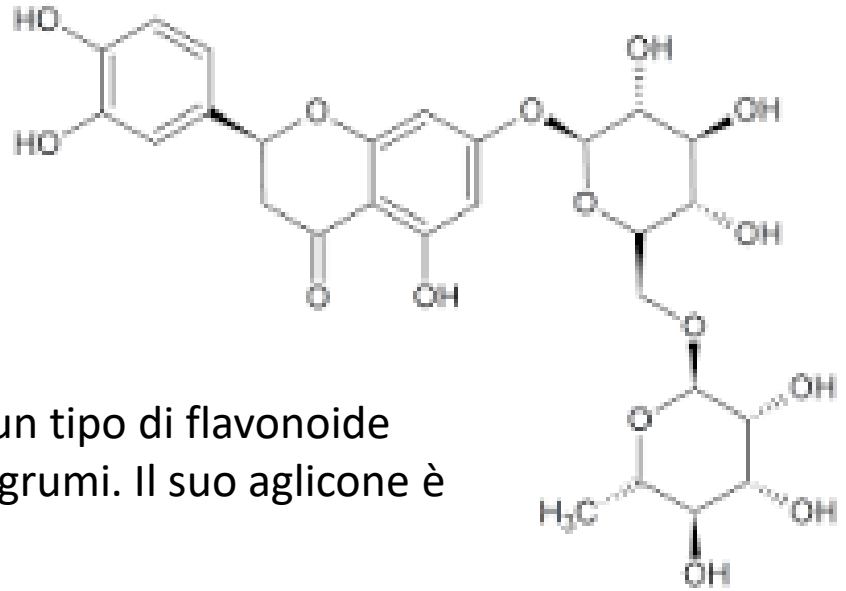


Review

Eriocitrin: A review of pharmacological effects

Liangliang Yao [a], Wei Liu [b,*], Mariam Bashir [d], Muhammad Farrukh Nisar [c,d,**], Chunpeng (Craig) Wan [c]

- Ruolo antinfiammatirio
- ROS
- NF-kB / TNFα / IL1β / IL6



L'**eriocitrina** è un flavanone glicosilato, un tipo di flavonoide presente all'interno dei frutti di alcuni agrumi. Il suo aglicone è l'eriodictiolo

*Yao et al., Biomed. Pharmacot., **2022**; 154:113563*

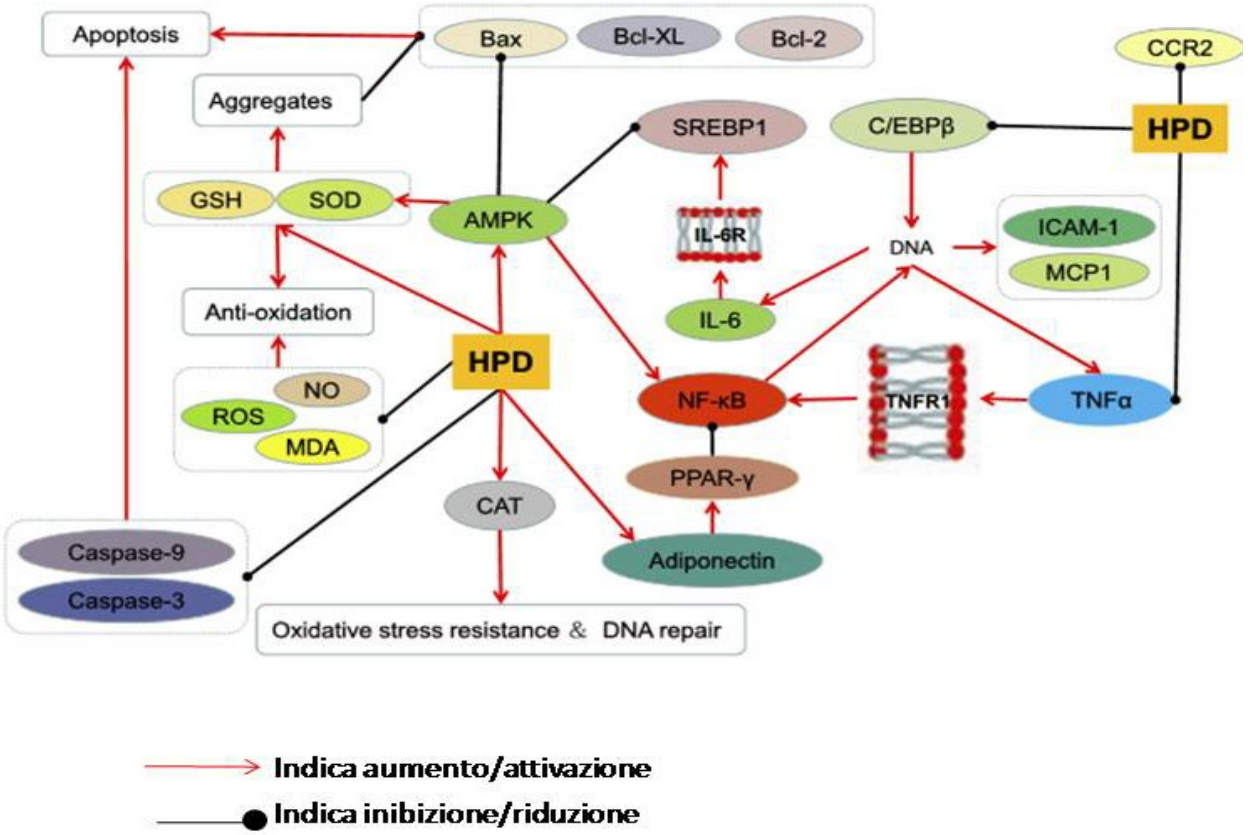
Esperidina

Open Access Full Text Article

REVIEW

Hesperidin: A Therapeutic Agent For Obesity

Stress ossidativo



Riduzione delle specie reattive dell'ossigeno (ROS) e della malonilaldede (MDA);

aumento della superossidodismutasi (SOD) e del glutatione ridotto (GSH);

minore concentrazione degli indicatori dell'infiammazione

*Xiong H et al., Drug design, develop. Ther **2019**: 13, 3855–3866*

Metabolismo lipidico

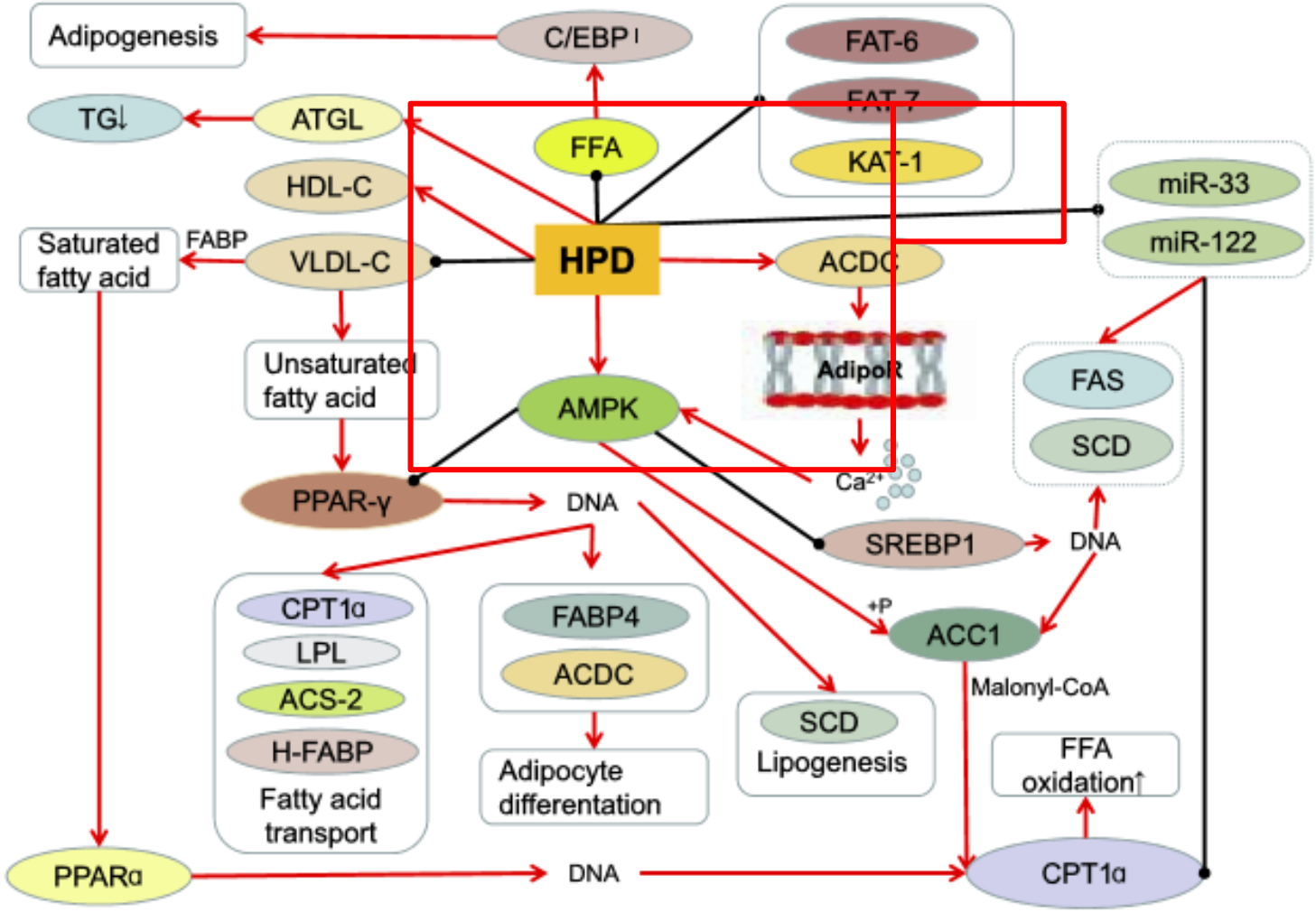


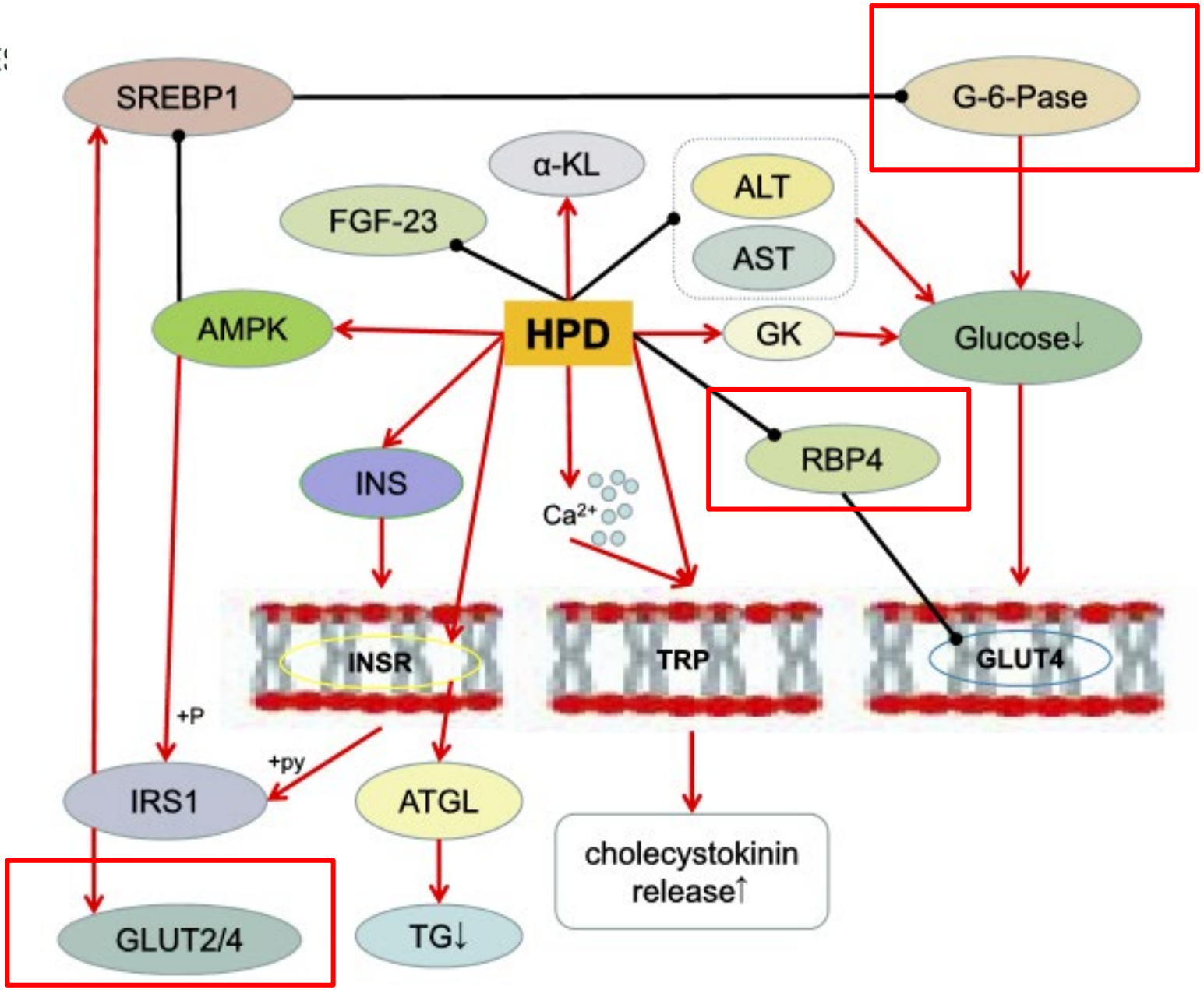
Figure 2 The effect of hesperidin on lipid metabolism.
Note: —● indicate inhibition/reduction while → indicate increase/promotion.

Agisce su diversi pathway cellulari

- Acidi grassi
- Trigliceridi
- Lipogenesi
- Lipoproteine

*Xiong H et al., Drug design, develop. Ther **2019**: 13, 3855–3866*

Metabolismo glucidico



Agisce su diversi pathway cellulari

- Miglior utilizzo del glucosio
- + energia
- -glicemia
- - adipogenesi

- Aumento espressione dei recettori per l'insulina

- Aumento lipasi
- - trigliceridi sierici

*Xiong H et al., Drug design, develop. Ther **2019**: 13, 3855–3866*

Nutraceutical Effects of Mediterranean Citrus *Extracts* in Dysglycemia: A Pilot Study

Di Folco Ugo[1*], Noemi Vallecorsa[1], Giampiero Forte[2], Flavia Tubili[3], Claudio Tubili[1]

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LEMOTRIN

20% polifenoli tra cui eriocitrina ed esperidina da Citrus limon
+ 28% esperidina da Citrus sinensis
+ antocianine da arancia rossa

Abstract

Background: Dysglycemia is a subclinical condition of altered glucose levels (intermediate hyperglycaemia), considered as a high-risk factor for diabetes and cardiovascular diseases. Lifestyle change, including diet and exercise, along with the management of blood glucose levels is the primary prevention of diabetes. **Aim:** In this clinical study, we investigated the potential role of a nutraceutical compound, based on Mediterranean citrus extracts, in regulating blood glucose in dysglycemic adults. **Material and Methods:** 40 adults with dysglycemia (100-125 mg/dl) were instructed to take a food supplement based on 460 mg Lemotrin® complex plus 100 µg chromium picolinate, 1 tablet twice a day during main meals for 12 weeks, in addition to general indications of a Mediterranean diet, maintaining overall constant dietary habits. Reduction of blood glucose levels was set as primary endpoint, while reduction of HOMA index, insulinemia, body weight, abdominal circumference and improvement of the lipid profile as secondary endpoints. **Results:** After 12 weeks significant reductions of fasting blood glucose (-7.7%), fasting insulin (-31.6%), HOMA-index (-35.73%), glycated haemoglobin (A1c) (-4.78%) levels were observed, with a non-significant body weight reduction. **Conclusion**: Our findings suggest that the supplementation of Mediterranean citrus complex improves the glycemic profile in subjects with dysglycemia.

*Di Folco U. et al **2022**., Ann Med Health Sci Res 2022;12*

FBG

INS

HOMAindex

HbA1c

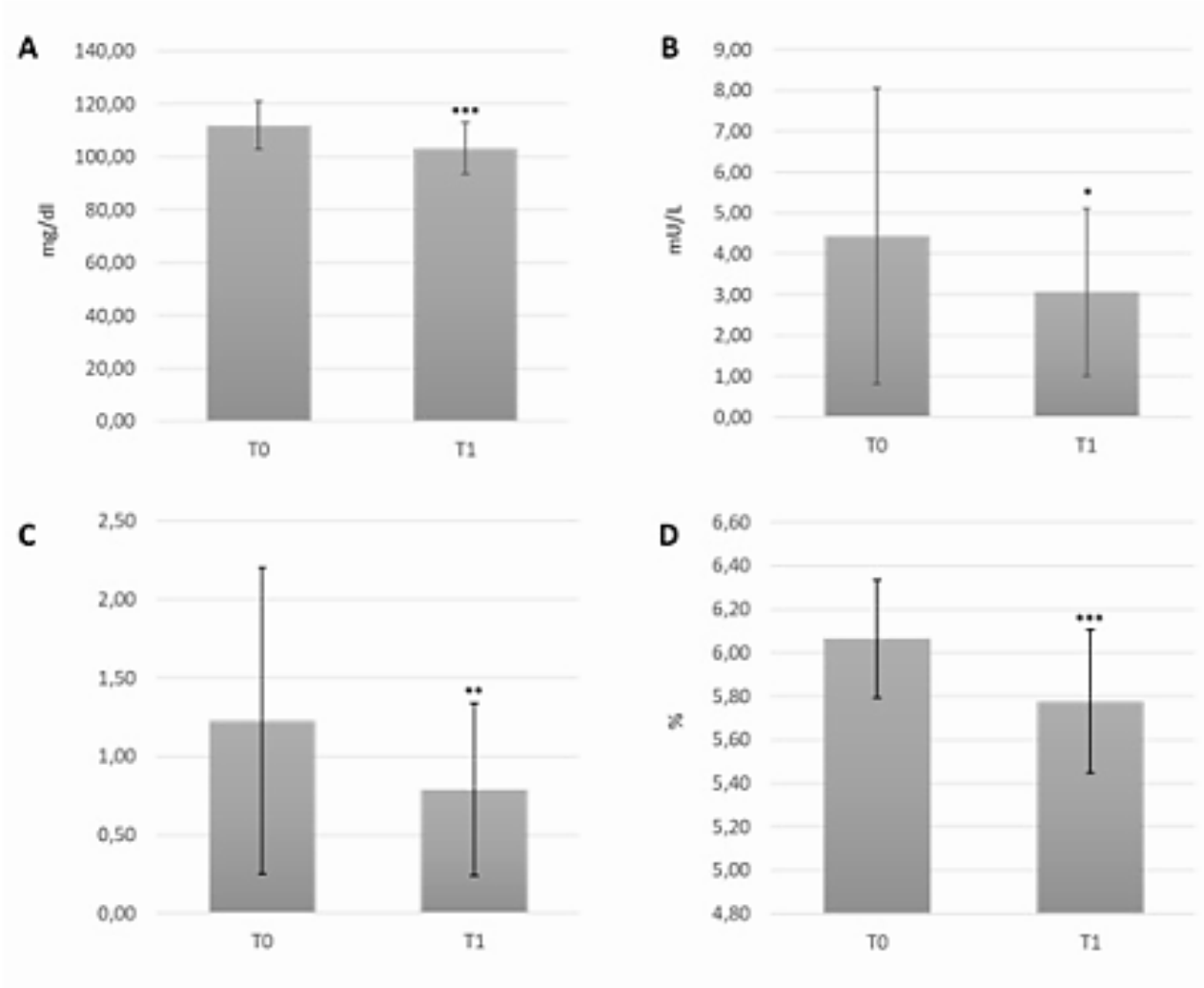

Figure 1: (A) Fasting blood glucose; (B) Fasting insulin; (C) HOMA-index; (D) HbA1c; measures on 39 subjects at the baseline and after 3 months of supplementation with the food supplement based on Mediterranean citrus extracts. One-way repeated measures ANOVA test. *p<0.05, **p ≤ 0.01, ***p ≤ 0.0001 T1 *vs* baseline.

*Di Folco U. et al **2022**., Ann Med Health Sci Res 2022;12*

FICO D'INDIA

Opuntia ficus-indica ((L.) Mill.,

- Pianta dicotelidone angiosperme; famiglia delle Cactaceae
- Diffusa nel Mediterraneo → Italia: Sicilia, Calabria, Puglia, Campania
- Specie CAM (Crassulacean Acid Metabolism)
- Polpa: parte edibile (60/70% frutto)
- 100/400 semi

consente alla pianta di assimilare ingenti quantitativi d'acqua anche di notte. Le vere foglie sono piccolissime e quasi inesistenti

- Tutto utilizzabile → scozzolatura - rimozione del primo flusso di fiori e nuovi **cladodi**
- **<u>Claim ministeriale (1 DM 10 agosto 2018): CLADODIUM → equilibrio del peso corporeo, modulazione/limitazione assorbimento di nutrienti.</u>**

*Stintzing et al., **2005**; Journal of agricultural and food chemistry, 53(2), 442–451*

Table 1. Distribution and contents of phenols and flavonoids in the various parts of *O. ficus-indica*.

Plant tissue	Main Component Identified	Content in mg/100 g	References
Flower	Gallic acid	1630–4900	[20,25–27]
	Quercetin 3-*O*-Rutinoside	709	
	4 Kaempferol 3-*O*-Rutinoside	400	
	5 Quercetin 3-*O*-Glucoside	447	
	6 Isorhamnetin 3-*O*-Robinobioside	4269	
	7 Isorhamnetin 3-*O*-Galactoside	979	
	8 Isorhamnetin 3-*O*-Glucoside	724	
	9 Kaempferol 3-*O*-Arabinoside	324	
Pulp	Total phenolic acid	218.8	[13,28,29,31,32,38]
	Quercetin	9	
	Isorhamnetin	4.94	
	Kaempferol	0.78	
	Luteolin	0.84	
	isorhamnetin glycosides	50.6	
	Kaempferol	2.7	
Seed	Total phenolic acid	48–89	[33]
	Feruloyl-sucrose isomer 1	7.36–17.62	
	Feruloyl-sucrose isomer 2	2.9–17.1	
	Sinapoyl-diglucoside	12.6–23.4	
	Total Flavonoids	1.5–2.6	
	Total Tannins	4.1–6.6	
Skin fruits	Total phenolic acid	45,700	[5,30,34]
	Total Flavonoid	6.95	
	Kaempferol	0.22	
	Quercetin	4.32	
	Isorhamnetin	2.41–91	
Cladode	Gallic acid	0.64–2.37	[4,29,35–37]
	Coumaric	14.08–16.18	
	3,4-dihydroxybenzoic	0.06–5.02	
	4-hydroxybenzoic	0.5–4.72	
	Ferulicacid	0.56–34.77	
	Salicylicacid	0.58–3.54	
	Isoquercetin	2.29–39.67	
	Isorhamnetin-3-*O*-glucoside	4.59–32.21	
	Nicotiflorin	2.89–146.5	
	Rutin	2.36–26.17	
	Narcissin	14.69–137.1	

El-Mostafa et al., Molecules ***2014****, 19*

Malattia	Effetto del fico d'India (varie prove effettuate su animali o persone)
Sindromi dismetaboliche	Riduzione del contenuto glicemico e del diabete (Alarcon-Aguilar et Al., 2003; Luo et Al., 2010; Becerra-Jiménez e Andrade-Cetto A., 2012). Riduzione del colesterolo (Oh e Lim, 2006). Aumento di enzimi antiossidanti (Perfumi e Tacconi, 1996).
Problemi renali	Diuretico e antiuricemico (Park et Al., 2001). Aumento della escrezione di sodio e potassio nelle urine (Galati et Al., 2002).
Malattie infiammatorie	Azione anti-infiammatoria in sindromi croniche (Palevitch, 1993; Park et Al., 2001).
Malattie neoplastiche	Effetti antiproliferativi, chemiopreventivi, apoptosi delle cellule tumorali (Sreekanth et Al., 2007; Chavez-Santoscoy et Al., 2009; Lee et Al., 2011).
Malattie neurologiche	Protezione da danni neurologici (Wie, 2000; Dok-Go et al., 2003). Miglioramento post-ischemico (Kim et al., 2006) Aumento della memoria a lungo termine (Kim et al., 2010). Funzione antidepressiva (Park et Al., 2010).
Sintomi da stress ossidativo	Vari effetti antiossidativi (Fernández-López et Al., 2010; Kuti, 2004; Brahmi et al., 2011; 2012).
Danni da alcool	Prevenzione dell'ubriachezza e riduzione dei sintomi successivi (Wiese et Al., 2004; Pittleret Al., 2005).

A. Pardini, monografia, 2018

Principali proprietà:

1. **Antiulcera/gastroprotettive**
2. **Ipoglicemizzanti**: correlate alla componente fibrosa (solubile) e a pectine e mucillagini → effetto meccanico di binding zuccheri → ↓ assorbimento ↑ escrezione fecale
3. **Ipolipemizzanti/Antiaterogene**: non azione meccanica ma metabolica → interazione con pathway del metabolismo del colesterolo (pectine/polifenoli)
4. **Antiossidanti/Antinfiammatorie: ↓** citochine proinfiammatorie
5. **Obesità:** capacità di ↓ accumulo di lipidi e adipogenesi

*El-Mostafa et al., Molecules **2014**, 19*
*Diaz MS et al., Oxid. Med. And Cell. Long. **2017***

he effects of Prickly Pear fruit and cladode (*Opuntia spp.*) consumption on lood lipids: A systematic review

aroline Gouws, Reza Mortazavi, Duane Mellor, Andrew McKune, Nenad Naumovski

A B S T R A C T

Background: The current dietary recommendations for cardiovascular disease (CVD) risk reduction include increased fruit and vegetable consumption. The *Opuntia spp.*, Prickly Pear (PP) fruit is rich in dietary fiber and may have lipid-lowering effects but it is often confused with the PP stem/leaf (Cladode (CLD)), or not identified. The efficacy of the PP fruit and CLD in reducing CVD risk is a growing area of research.
Methods: This systematic review (PROSPERO: CRD42018110643), examined the effects of consuming the *Opuntia spp.* components (PP or CLD) on CVD risk factors, specifically total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG). The review, performed from February through September 2019, used resources available through Food Science and Technology Abstracts (EBSCO), Medline, Scopus, CINAHL, Web of Science and Cochrane databases.
Results and Discussion: Eleven articles met the inclusion criteria, which *characterised Opuntia spp.* products as either PP ($n = 6$), CLD ($n = 4$) or commercial products' ($n=1$). Effects were investigated in healthy and obese populations as well as those with metabolic illnesses, specifically type 2 diabetes and metabolic syndrome. PP consumption was associated with significant reductions in TC ($p < 0.05$) in all but one included study, whereas in the remaining studies ($n=6$), LDL-C levels decreased ($p < 0.05$). Separately, the effect of CLD consumption on lipids was small with one study reporting a significant increase in plasma HDL-C in a subgroup of participants (> 45 years of age) following consumption of a patented CLD powder product. It is plausible, that differences in overall effect may be due to compositional distinctions between CLD and PP, such as fiber composition. Care must be taken in future studies to accurately report the identity of the selected components of *Opuntia spp*.

Gouws, C., et al; **2020**. *Complementary therapies in medicine, 50, 102384.*

14° CONGRESSO NAZIONALE SINut

Clinical research

Lipid disorders

SINut Società Italiana di Nutraceutica

12-14 settembre 2024

Bologna

Comparative effect of a nutraceutical compound based on a flavonoid complex from bergamot on plasma lipids, glucose metabolism, and liver enzymes: a 3-arm, double-blind, placebo-controlled, randomized clinical trial

Federica Fogacci, Valentina Di Micoli, Maddalena Veronesi, Arrigo F.G. Cicero

Table II. Effect of different nutraceutical regimens on investigated laboratory parameters

Parameter	Pre-run-in	Baseline			T1		
		Placebo	Verum low dose	Verum full dose	Placebo	Verum low dose	Verum full dose
TC [mg/dl]	248 ±13.0	239.8 ±11.7	246 ±7	238 ±13	241 ±13	210 ±12*°	205 ±13*°
HDL-C [mg/dl]	44 ±3	46.5 ±3	46 ±2	44 ±3	44 ±3	49 ±1*°	50 ±2*°
LDL-C [mg/dl]	161 ±8	150.7 ±10	159 ±6	155 ±8	157 ±9	127 ±9*°	125 ±8*°
Non-HDL-C [mg/dl]	204 ±11	197.4 ±10	207 ±8	198 ±11	197 ±12	161 ±11*°	155 ±12*°
TG [mg/dl]	216 ±19	205.4 ±14	195 ±23	197 ±16	198 ±18*	170 ±16*°	156 ±12*°#
ApoB [mg/dl]	146 ±9	140.1 ±8	143 ±7	143 ±7	141 ±7	120 ±9*°	119 ±9*°
ApoAI [mg/dl]	118 ±12	101.9 ±12	113 ±14	114 ±16	118 ±14	137 ±13*°	139 ±11*°
FPG [mg/dl]	88 ±3	89.5 ±3	89 ±3	90 ±3	88 ±3	84 ±2*	83 ±4*
GOT [U/l]	23 ±3	24.5 ±3	24 ±2	25 ±4	25 ±3	22 ±2*	21 ±3*
GPT [U/l]	22 ±3	21.9 ±2	22 ±2	22 ±3	22 ±3	20 ±4*	20 ±4*
gGT [mg/dl]	32 ±2	34.6 ±2	37 ±2	33 ±2	33 ±2	24 ±3*	23 ±4*
CPK [U/ml]	104 ±19	101.3 ±21	118 ±19	95 ±15	120 ±25	106.8 ±24.4	96.1 ±18.6

**p < 0.05 vs. baseline; °p < 0.05 vs. placebo; #p < 0.05 vs. placebo and verum low-dose. SBP – systolic blood pressure, DBP – diastolic blood pressure, TC – total cholesterol, LDL-C – low-density lipoprotein cholesterol, HDL-C – high-density lipoprotein cholesterol, TG – triglycerides, Apo – apolipoprotein, FPG – fasting plasma glucose, GOT – glutamic-oxaloacetic transaminase, GPT – glutamate-pyruvate transaminase, gGT – γ-glutamyl transferase, CPK – creatine phosphokinase.*

Introduction: Bergamot and opuntia (prickly pear cladodes) standardized extracts have been demonstrated to have positive metabolic effects in pre-clinical and clinical models.

Material and methods: The aim of this study was to evaluate the metabolic effect of a combined nutraceutical containing 150 mg of *Opuntia ficus* Indica extract, 400 mg of plant sterols, 12.5 mg of thiamine, and 200 mg of Brumex® a phytocomplex from bergamot fruit (*Citrus bergamia* Risso et Poiteau, fructus) standardized 40% in total flavonoids and min 5% in 3-hydroxy-3-methylglutaryl-flavanones. Thus, we carried out a randomized, double-blind, placebo-controlled clinical trial on 75 hypercholesterolaemic subjects randomized to take the active compound (2 tablets per day), placebo (2 tablets per day), or both (1 per product per day).

Results: After 12 weeks of treatment with 1 tablet per day, we observed a significant reduction of a number of metabolic parameters: total cholesterol (TC) (–14.6%), low-density lipoprotein cholesterol (LDL-C) (–19.9%), non-high-density lipoprotein cholesterol (non-HDLC) (–22.1%), triglycerides (TG) (–13.1%), Apolipoprotein B (–16%) (all $p < 0.05$ both versus baseline and versus placebo), fasting plasma glucose (–5.1%), glutamate oxaloacetate transaminase (–7.8%), glutamate pyruvate transaminase (–7.3%), and γ-glutamyl transferase (–34.4%) (all $p < 0.05$ versus baseline). High-density lipoprotein cholesterol (HDL-C) was increased 6.9% by the use of 1 tablet per day ($p < 0.05$ versus baseline). All parameters were reduced to the same extent when taking the full dose (2 tablets), beyond TG.

Conclusions: the tested nutraceutical compound based on a flavonoid complex from bergamot and opuntia showed a short-term positive impact on plasma lipids, fasting plasma glucose, and liver enzyme in overall healthy subjects affected by hypercholesterolaemia with low cardiovascular risk.

*Fogacci F., et al; **2023**. Arch. Med Sci, 19(5):1180-1185.*

TAKE HOME MESSAGE

- Cardioprotezione: modifica fattori di rischio cardiovascolari

  ↓

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- Necessità di ulteriori studi clinici
- Possibilità di riutilizzo di alimenti e scarti alimentari derivanti dalla catena alimentare con promozione dell'economia circolare

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Grazie per l’attenzione