



# Nutraceutici come trattamenti di supporto nella sindrome metabolica

---

**Francesco Visioli**

*Dept. of Molecular Medicine, University of Padova, Italy*

---

# **Sindrome Metabolica**

Obesità centrale e almeno due dei seguenti quattro fattori:

- Trigliceridi alti, bassi livelli di colesterolo HDL (HDL-C), pressione alta, o elevata glicemia a digiuno

# **Sindrome Metabolica**

Qualsiasi tre dei cinque fattori di rischio  
(Obesita' centrale, trigliceridi alti, bassi livelli  
di colesterolo HDL (HDL-C), pressione alta, o  
elevata glicemia a digiuno)

# **Importante**

Proteina C reattiva (CRP) elevata in SM -  
> infiammazione come «fil rouge»

Obesita' viscerale,  
inattivita' fisica, genetica,  
eta'



Resistenza insulinica



Patologia CV



Ipertensione, diabete  
tipo II, infiammazione,  
dislipidemia,  
microalbuminuria,  
quadro pro-trombotico

# **Cause**

**FATTORI AMBIENTALI – STILI DI VITA**

- **Calorie, indice glicemico, esercizio fisico**

# Cause

Meccanismi ormonali

- Leptina, resistina, adiponectina, glucocorticoidi (?)

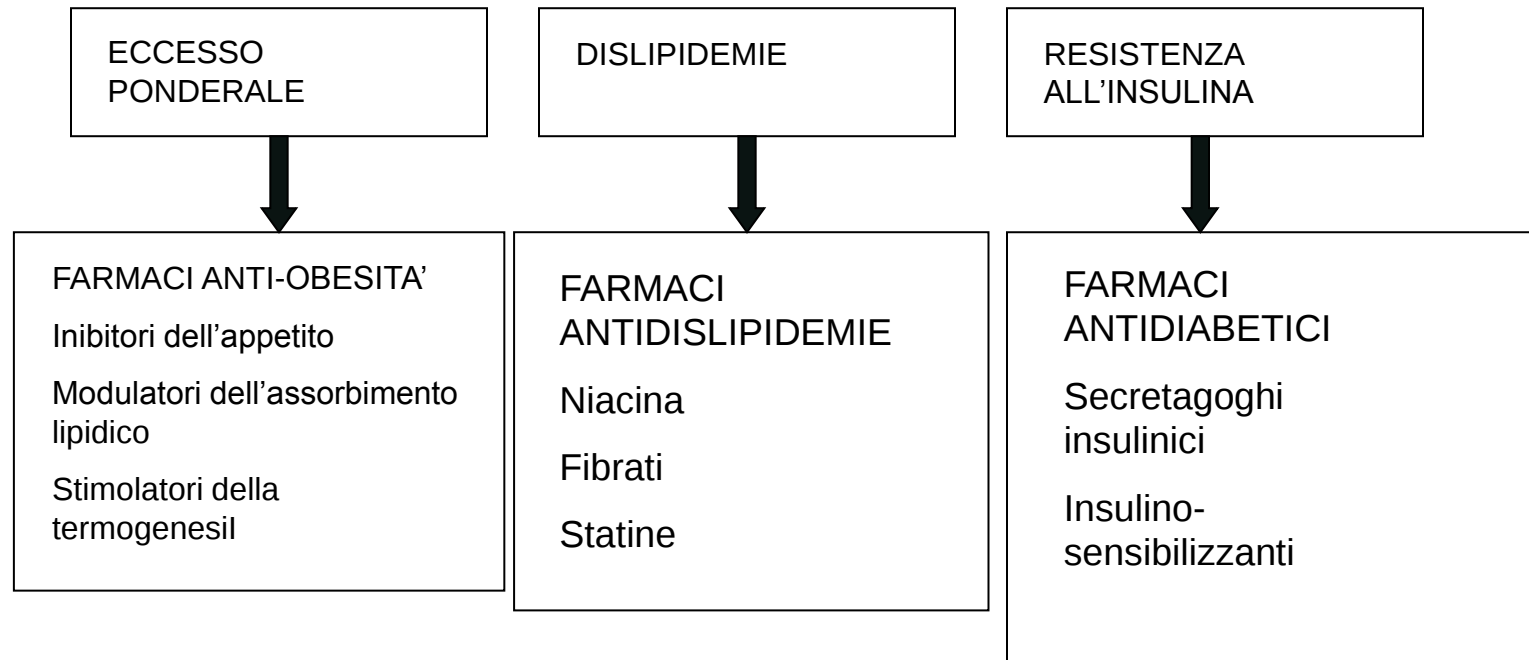
# **Cause**

Meccanismi metabolici

- Insulino-resistenza

# Rimedi

## Trattamento farmacologico della sindrome metabolica



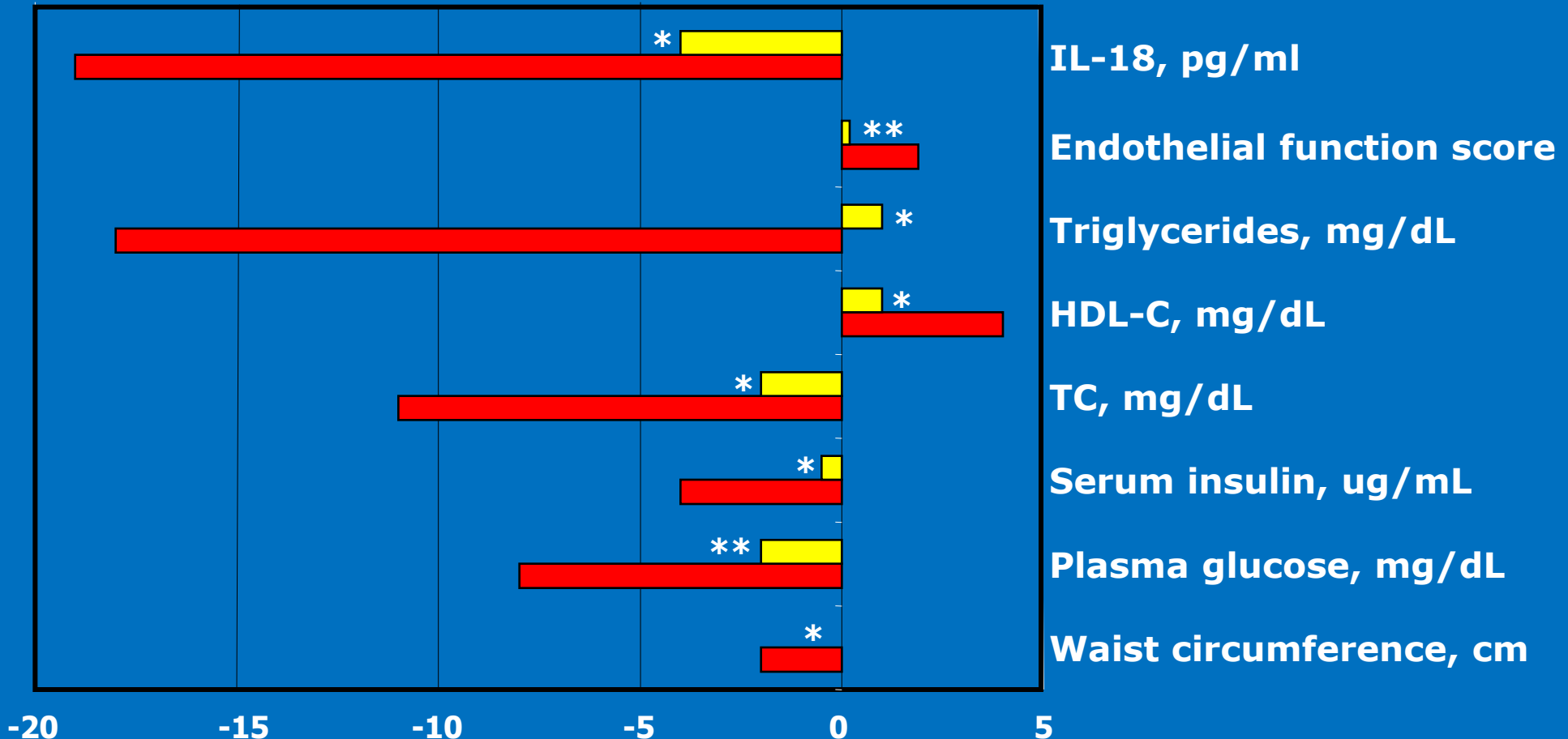
**Rimedi**

PREVENZIONE

# Mediterranean-Style Diet and Metabolic Syndrome

- **Subjects:** 180 patients (99 males and 81 females) with the metabolic syndrome as defined by the ATPIII.
- **Intervention:** Mediterranean-style diet with increased amounts of whole grain, fruits, vegetables, nuts and olive oil.
- **Main outcome measures:** nutrient intake, endothelial function score, lipid and glucose parameters, insulin sensitivity, CRP and interleukins.

# Changes in assessed variables after 2 years of intervention (n=90) and control (n=90) diet, in patients with metabolic syndrome



\*:  $p \leq 0.01$

\*\* :  $p \leq 0.001$

■ Intervention diet ■ Control diet

*Esposito., JAMA 2004*

## Changes in CRP levels (mg/dL) after 2 years of intervention (n=90) and control (n=90) diet, in patients with metabolic syndrome

|                   | Baseline | 2 years |
|-------------------|----------|---------|
| Control diet      | 2.9      | 2.8     |
| Intervention diet | 2.8      | 1.7* §  |

\*  $p \leq 0.01$  2y vs baseline

§  $p \leq 0.01$  intervention vs control diet at 2 y

# Nutraceuticals

# Nutraceuticals - examples

- Omega 3 fatty acids (long chain EPA and DHA, maybe short chain ALA)



# Curcumin



# Hydroxytyrosol as anti-inflammatory agent

## 1. In vitro

### INHIBITION OF LEUKOCYTE LEUKOTRIENE B<sub>4</sub> PRODUCTION BY AN OLIVE OIL-DERIVED PHENOL IDENTIFIED BY MASS-SPECTROMETRY

Anna Petroni, Milena Blasevich, Nadia Papini, Marco Salami, Angelo Sala  
and Claudio Galli

Institute of Pharmacological Sciences, University of Milan. Milan. Italy

*Thrombosis Research*, Vol. 87, No. 3, pp. 315–322, 1997

### Inhibition of Leukocyte 5-Lipoxygenase by Phenolics from Virgin Olive Oil

Rocio de la Puerta,\*† Valentina Ruiz Gutierrez‡ and J. Robin S. Hoult\*§

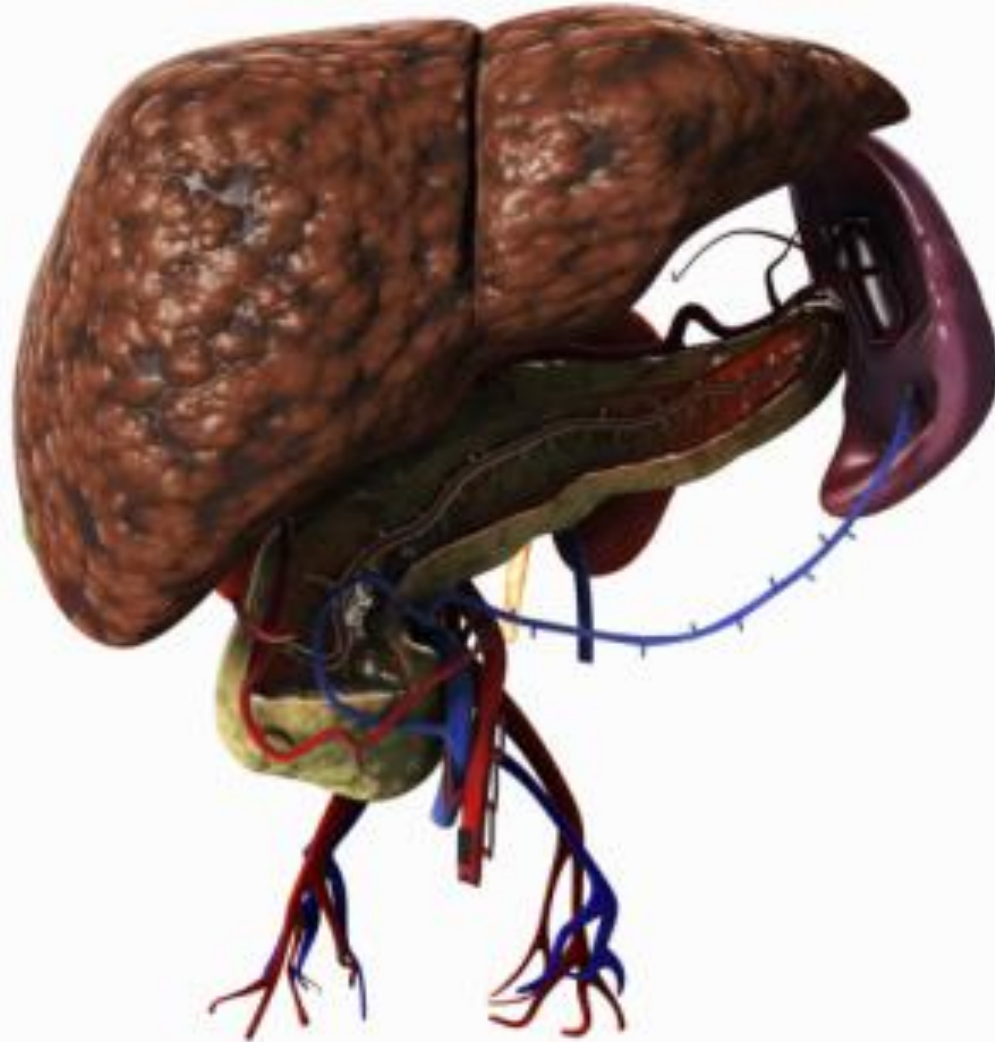
*Biochemical Pharmacology*, Vol. 57, pp. 445–449, 1999.

### Inhibition of Arachidonate Lipoxygenase Activities by 2-(3,4-Dihydroxyphenyl)ethanol, a Phenolic Compound from Olives

Noriko KOHYAMA, Tadahiro NAGATA,\* Shin-ichi FUJIMOTO, and Keizo SEKIYA†

*Biosci. Biotech. Biochem.*, 61 (2), 347–350, 1997

N.B.



# In vitro studies with parent compound

**>10  $\mu\text{M}$**



# Hydroxytyrosol as anti-inflammatory agent

## 1. In vivo

### Hydrolyzed Olive Vegetation Water in Mice Has Anti-Inflammatory Activity<sup>1</sup>

Catherine M. Bitler,<sup>2</sup> Tiffany M. Viale, Bassam Damaj,<sup>\*</sup> and Roberto Crea

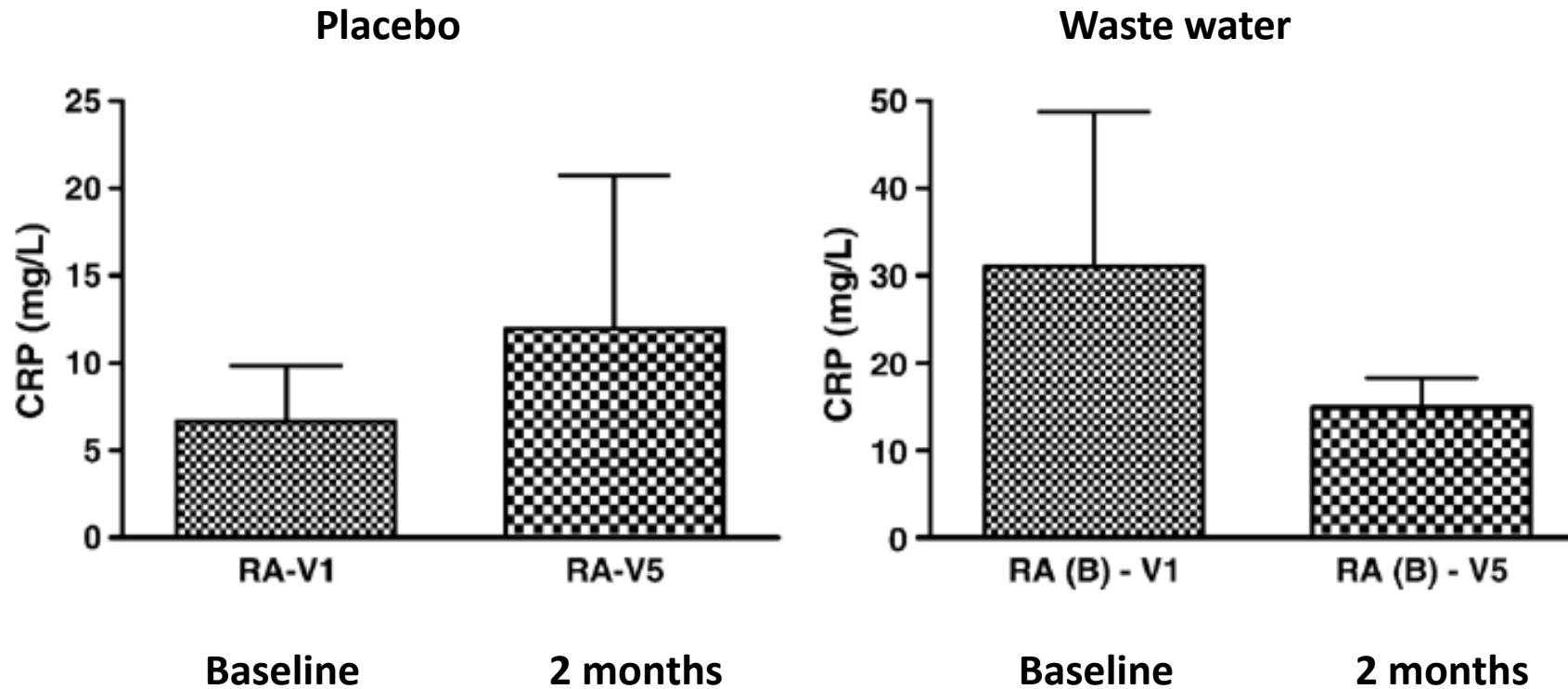
J. Nutr. 135: 1475–1479, 2005.

Olive extract supplement decreases pain and improves daily activities  
in adults with osteoarthritis and decreases plasma homocysteine  
in those with rheumatoid arthritis<sup>☆</sup>

Catherine M. Bitler<sup>b,\*</sup>, Kathleen Matt<sup>a</sup>, Mary Irving<sup>a</sup>, Ginger Hook<sup>a</sup>, Joseph Yusen<sup>a</sup>,  
Forrest Eagar<sup>a</sup>, Ken Kirschner<sup>a</sup>, Brian Walker<sup>a</sup>, Roberto Crea<sup>b</sup>

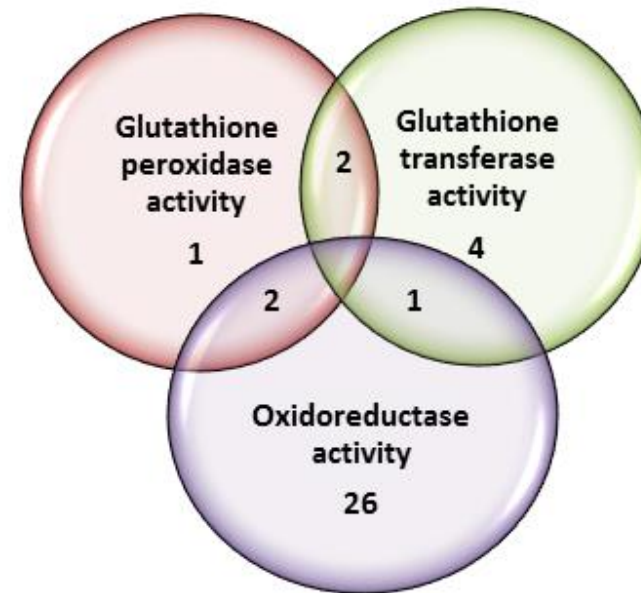
Nutrition Research 27 (2007) 470–477

# CRP levels in rheumatoid arthritis patients



# Chronic hydroxytyrosol feeding modulates glutathione-mediated oxido-reduction pathways in adipose tissue: A nutrigenomic study

E. Giordano, A. Dávalos, F. Visioli\*





≠



# Ortho molecular medicine

*Linus Pauling*

# Tè verde



# Weight and plasma lipid control by decaffeinated green tea

Doriane Richard<sup>a,\*</sup>, Kaouthar Kefi<sup>a</sup>, Ullah Barbe<sup>a</sup>, Andrea Poli<sup>b</sup>, Pedro Bausero<sup>a</sup>, Francesco Visioli<sup>a</sup>

Pharmacological Research 59 (2009) 351–354

# Strong points

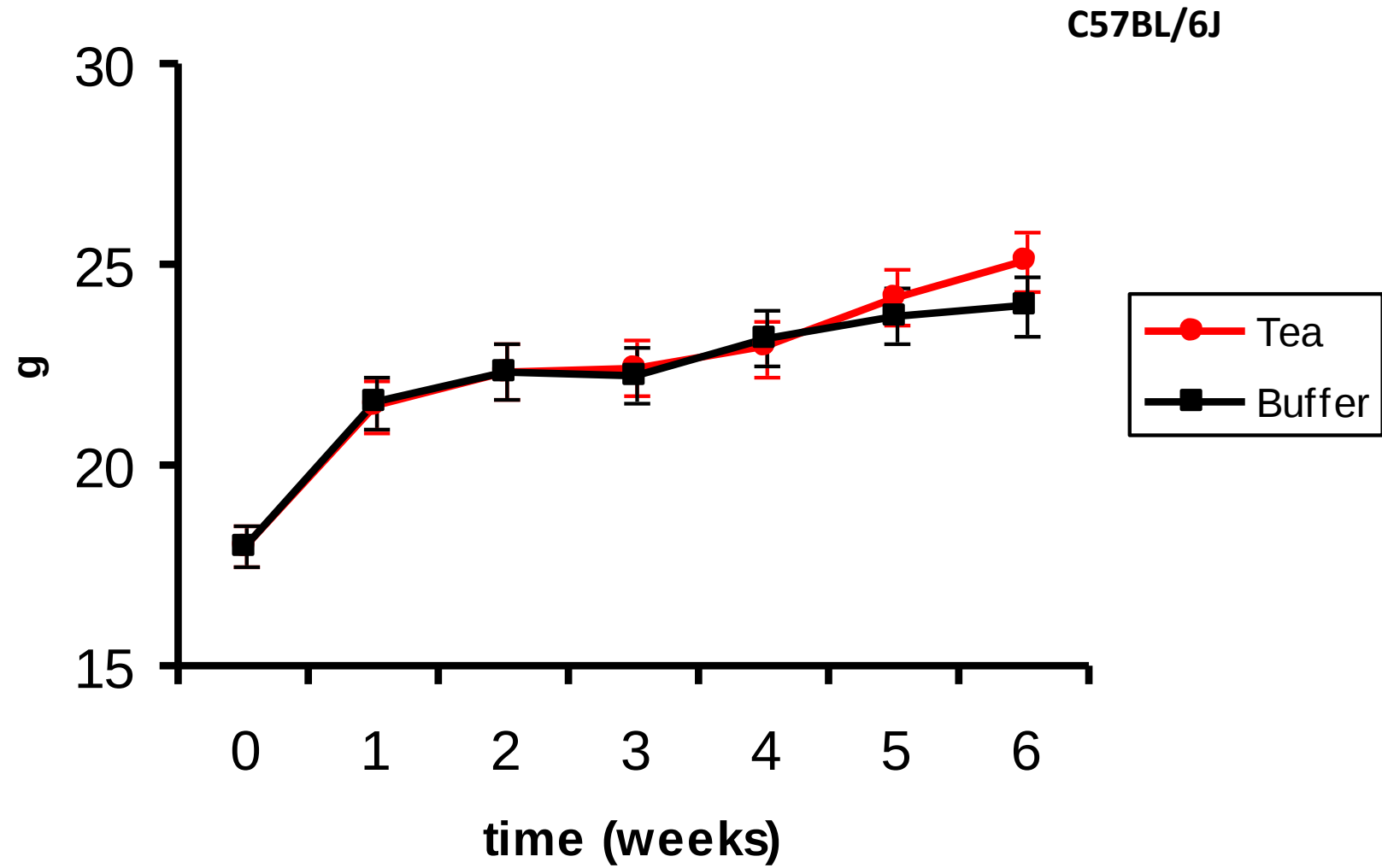
- Tea, not extracts.
- No caffeine  $\Rightarrow$  distinguish the effects of catechins from those of caffeine.
- No caffeine  $\Rightarrow$  no excitatory effects.

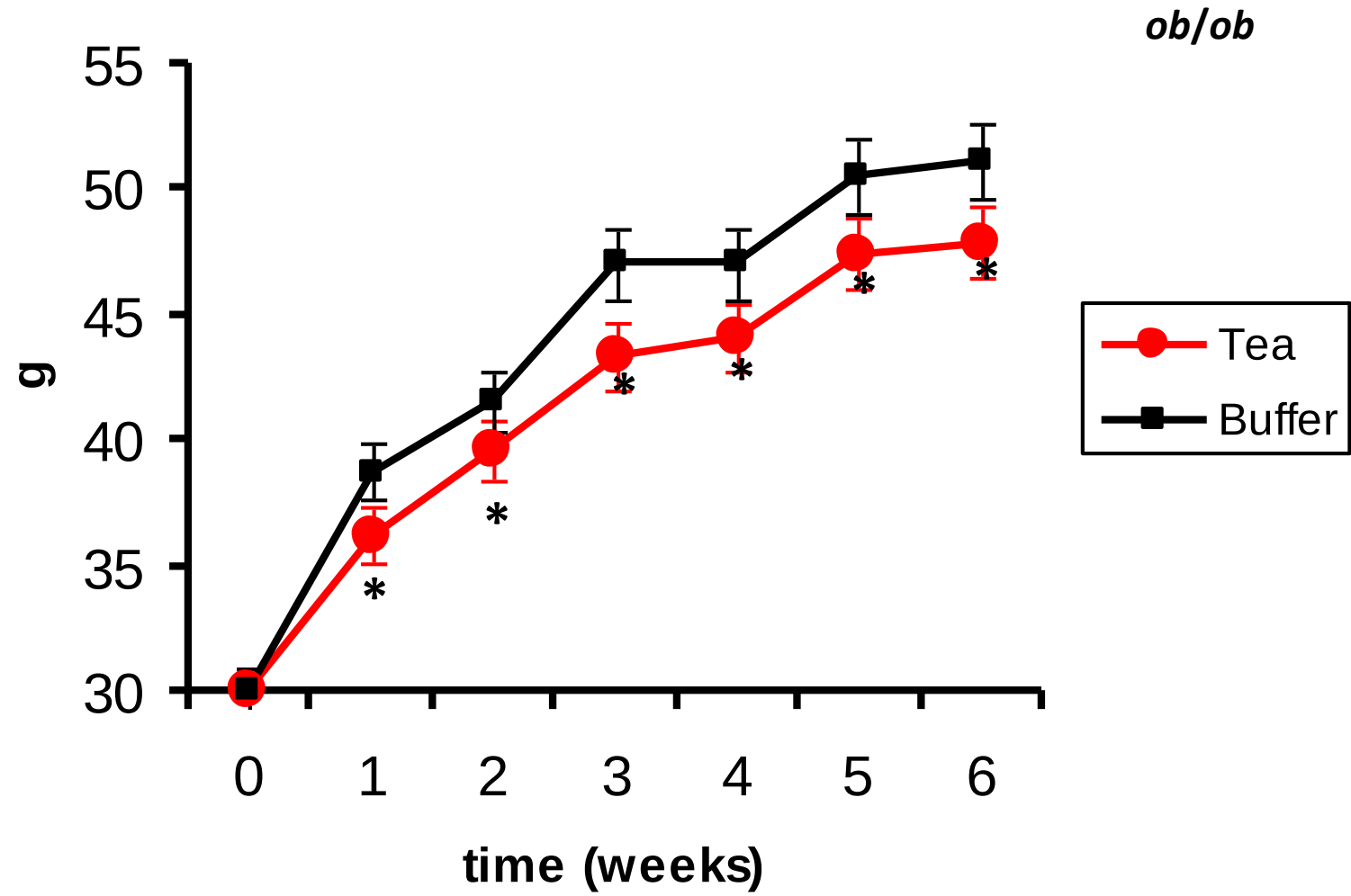
- 20 mice/group
- Leptin-deficient (*ob/ob*)
- C57BL/6J lean littermates
- 2% decaffeinated green tea, ad libitum

# Decaffeinated green tea composition

**71.75 mg total catechins per g** of leaves (1.38 mg were catechin, 6.77 mg epicatechin, 4.45 mg gallocatechin, 32.21 mg epigallocatechin, 21.04 mg epigallocatechin gallate, 0.39 mg gallocatechin gallate, 5.51 mg epicatechin gallate, catechin gallate n.d.

|                         | Adiponectine       | Cho                | TG                |
|-------------------------|--------------------|--------------------|-------------------|
|                         | ng/ml              | mg/dl              | mg/dl             |
| <b><i>ob/ob</i> eau</b> | 1,569±0,1754       | 156,36±10,08       | 35,68±5,32        |
| <b><i>ob/ob</i> thé</b> | <b>1,147±0,147</b> | <b>134,82±9,85</b> | <b>28,95±3,26</b> |
| C57BL/6J eau            | 0,761±0,437        | 84,77±9,83         | 23,68±9,61        |
| C57BL/6J thé            | 0,617±0,351        | 91,54±8,27         | 22,08±3,88        |





# Several mechanisms

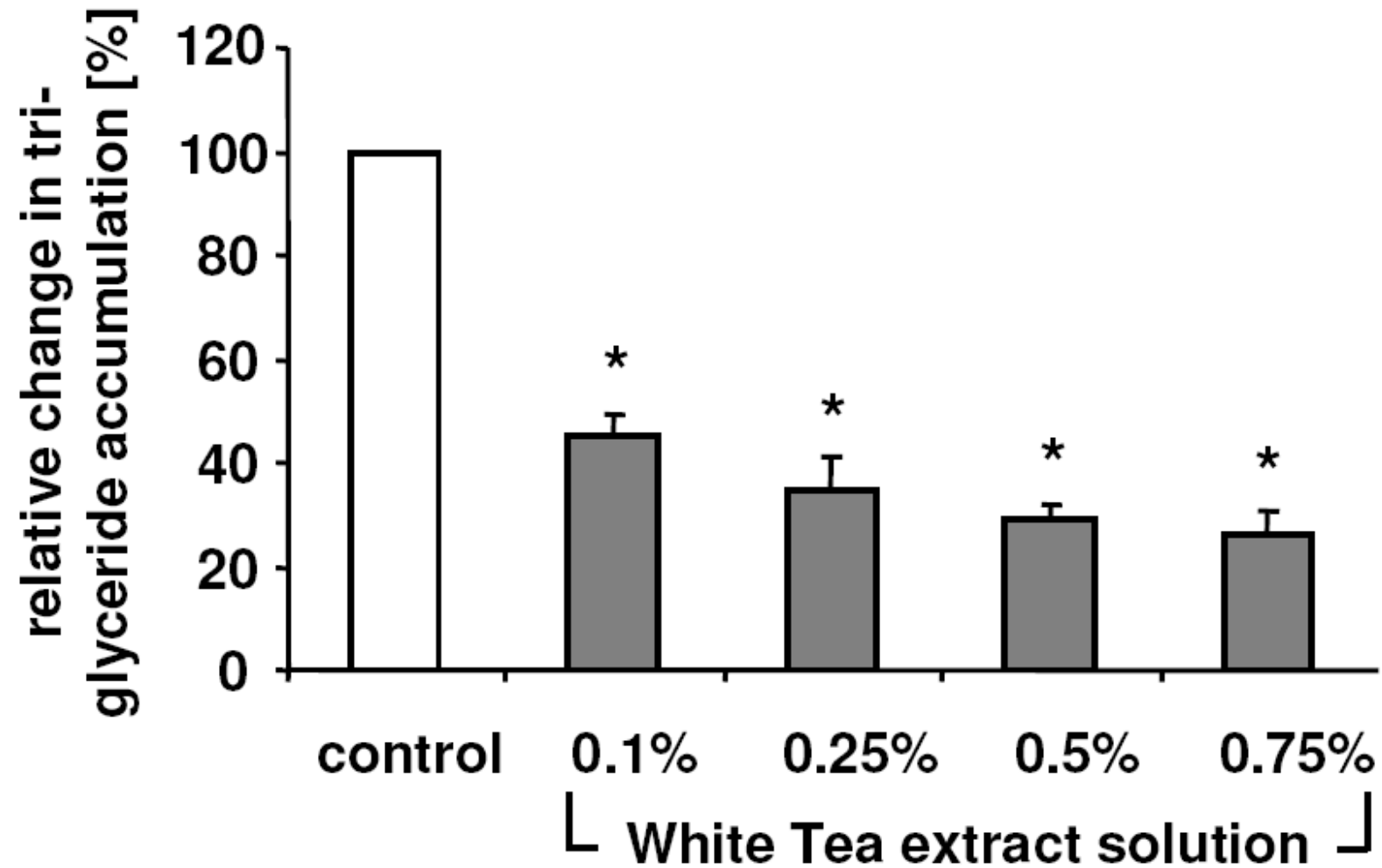
---

**White Tea extract induces lipolytic activity and inhibits adipogenesis in human subcutaneous (pre)-adipocytes**

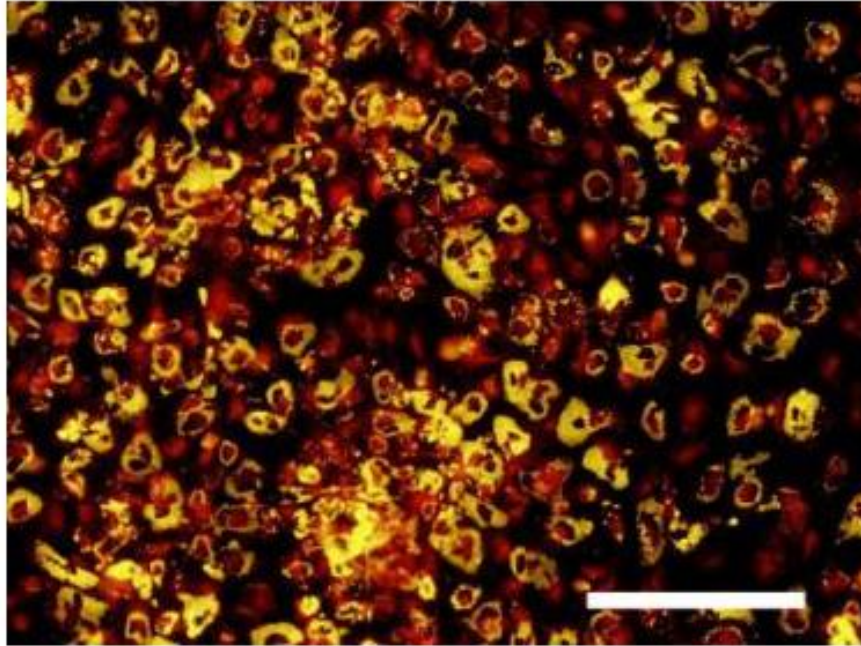
Jörn Söhle, Anja Knott, Ursula Holtzmann, Ralf Siegner, Elke Grönniger, Andreas Schepky, Stefan Gallinat, Horst Wenck, Franz Stäb and Marc Winnefeld\*

*Nutrition & Metabolism* 2009, **6**:20

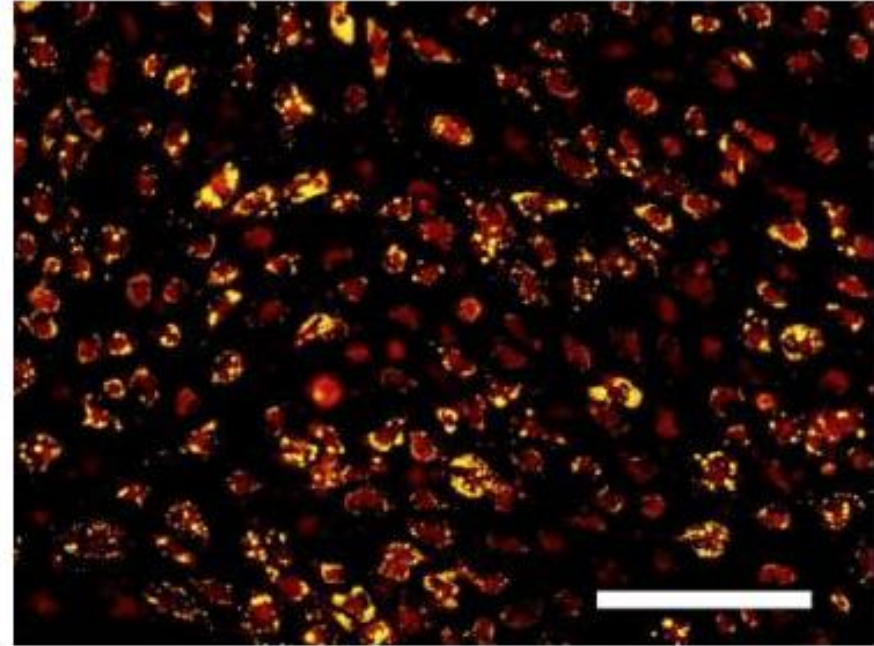
# Reduced accumulation of TG in adipocytes



**control**



**0.5% White Tea extract  
solution**



# **Fibre solubili**

Beta-glucani, gomme, mucillagini (ad esempio, psillio), pectine, ed alcune emicellulose

**FDA:** prodotti alimentari contenenti almeno 0,75 g/porzione di fibra solubile da avena:  
"La fibra solubile da alimenti come crusca di avena, come parte di una dieta a basso contenuto di grassi saturi e colesterolo, può ridurre il rischio di infarto"

Una meta-analisi che ha combinato i risultati di 67 studi clinici controllati ha riportato che anche un aumento modesto (10 g al giorno) di assunzione di fibre viscosi comporta una riduzione media del colesterolo LDL di 22 mg/dL (0,57 mmol/L) e una riduzione media dei livelli di colesterolo totale di 17 mg/dL (0,45 mmol/L)

*Brown et al 1999*



Interazione tra fibre e biodisponibilità

# Conclusioni

SM diffusa (NHANES: 5% among the subjects of normal weight, 22% among the overweight, and 60% among the obese).

Prevenzione!

Terapia farmacologica affiancata a integrazione nutrizionale.

# The use of functional foods reduces drug therapy



# Conclusioni

Ricorda: Integratori  $\neq$  Farmaci

# **Conclusioni**

Utili complementi alla terapia farmacologica

Thank  
You!



[francesco.visioli@unipd.it]

 @visioli