



# Nutraceutici come trattamenti di supporto nella sindrome metabolica

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**Francesco Visioli**

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

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# **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**

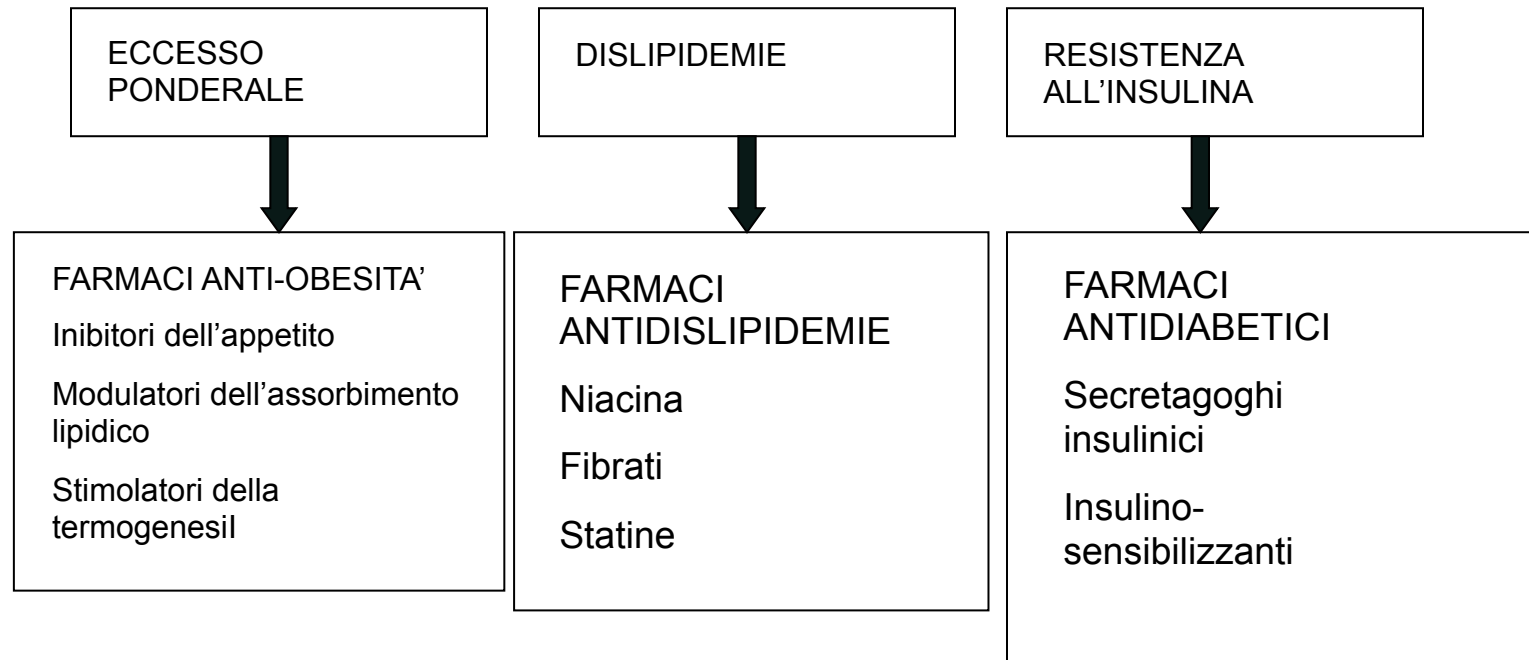
Meccanismi metabolici

- Insulino-resistenza



# Rimedi

## Trattamento farmacologico della sindrome metabolica



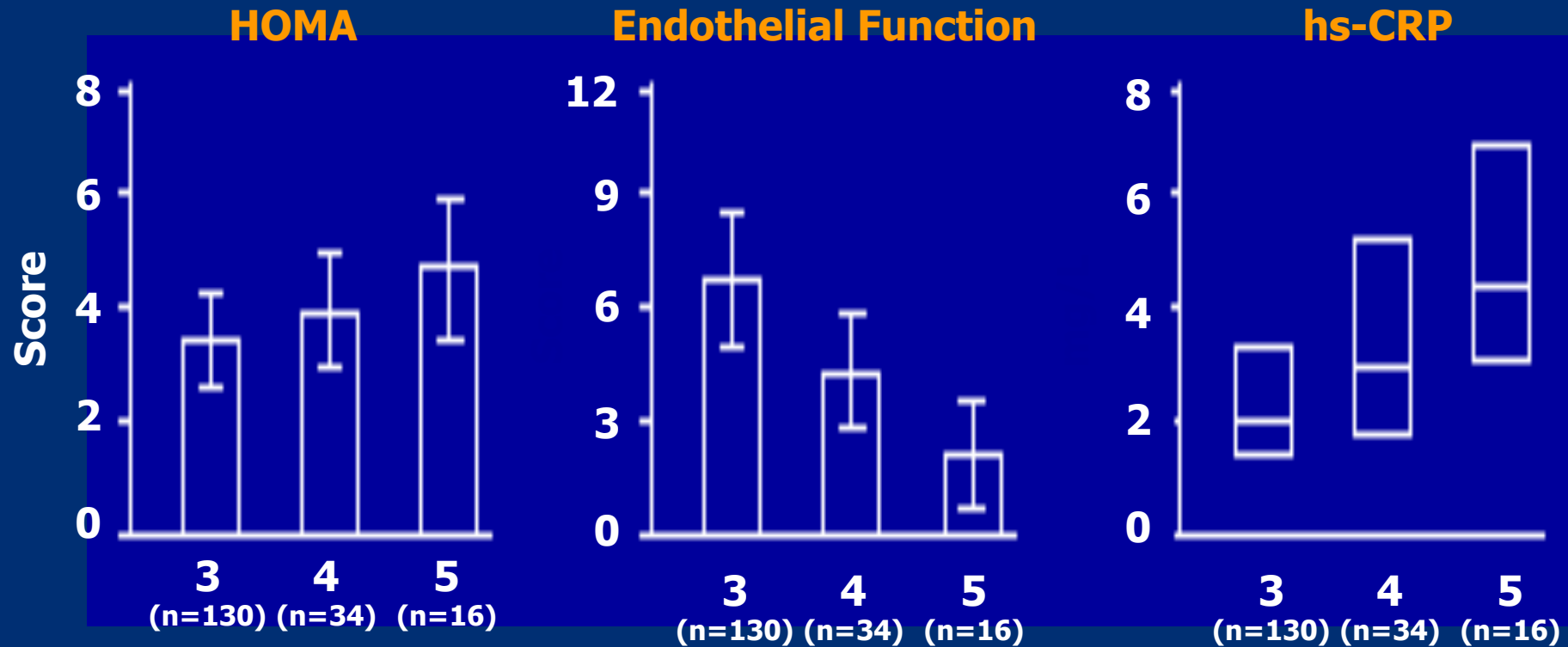
**Rimedi**

**PREVENZIONE**

# Mediterranean-Style Diet and Metabolic Syndrome

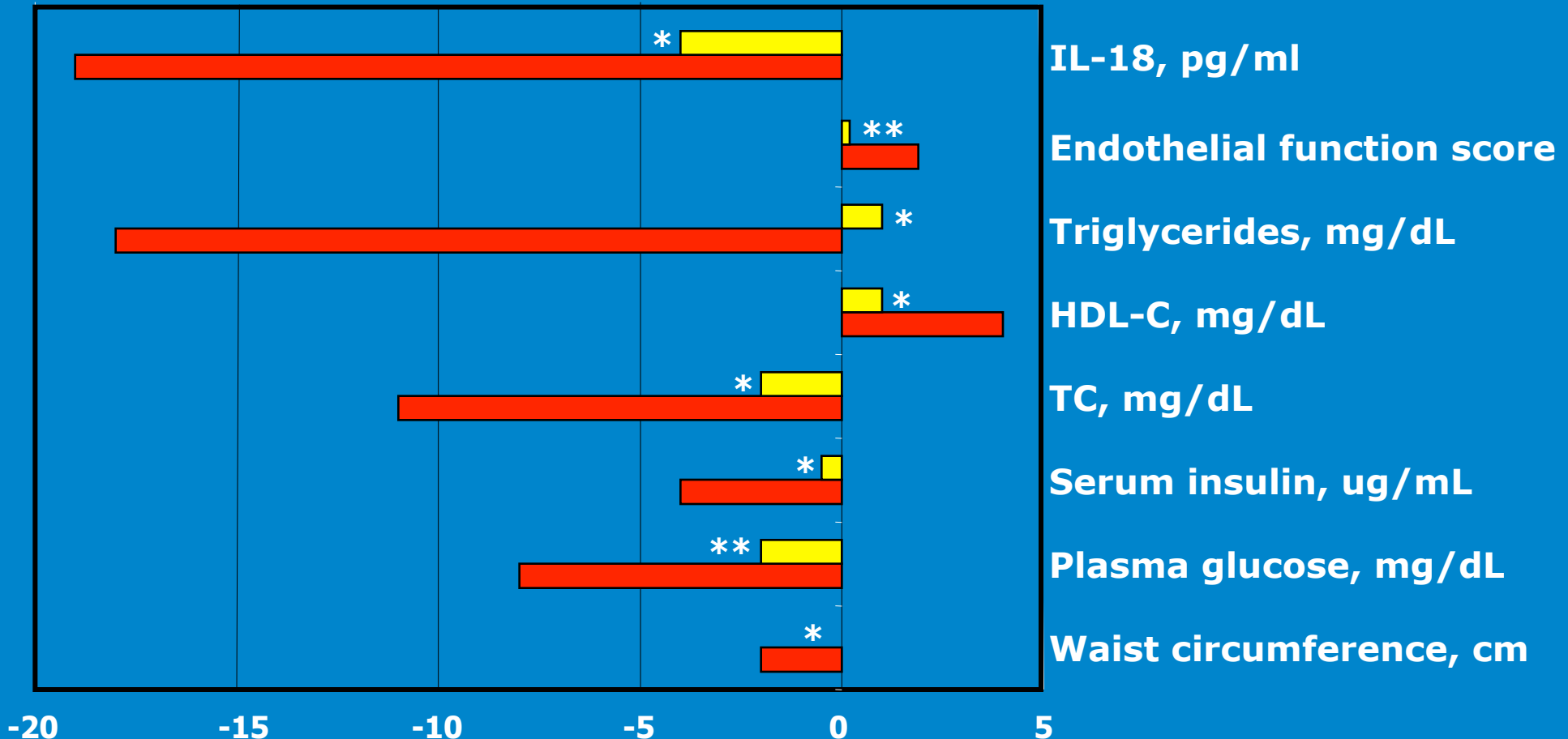
- **Subjects:** 180 patients (99 males and 81 females) with the metabolic syndrome as defined by the ATPIII.
- **Intervention:** Mediterranean-style diet with increased amounts of whole grain, fruits, vegetables, nuts and olive oil.
- **Main outcome measures:** nutrient intake, endothelial function score,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

# Distribution of HOMA Score, Endothelial Function Score and hs-CRP Levels among the 180 Patients at Baseline, by Presence of 3, 4 and 5 Components of the MS



No. Of Components of the Metabolic Syndrome

# 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

# **Nutraceutici**

# 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

# Hydroxytyrosol as anti-inflammatory agent

## 1. In vitro

**Hydroxytyrosol inhibits pro-inflammatory cytokines, iNOS, and COX-2 expression in human monocytic cells**

Xiaomei Zhang • Jun Cao • Laifu Zhong

Naunyn-Schmied Arch Pharmacol

N.B.





# In vitro studies with parent compound

**>10 mM**



# 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

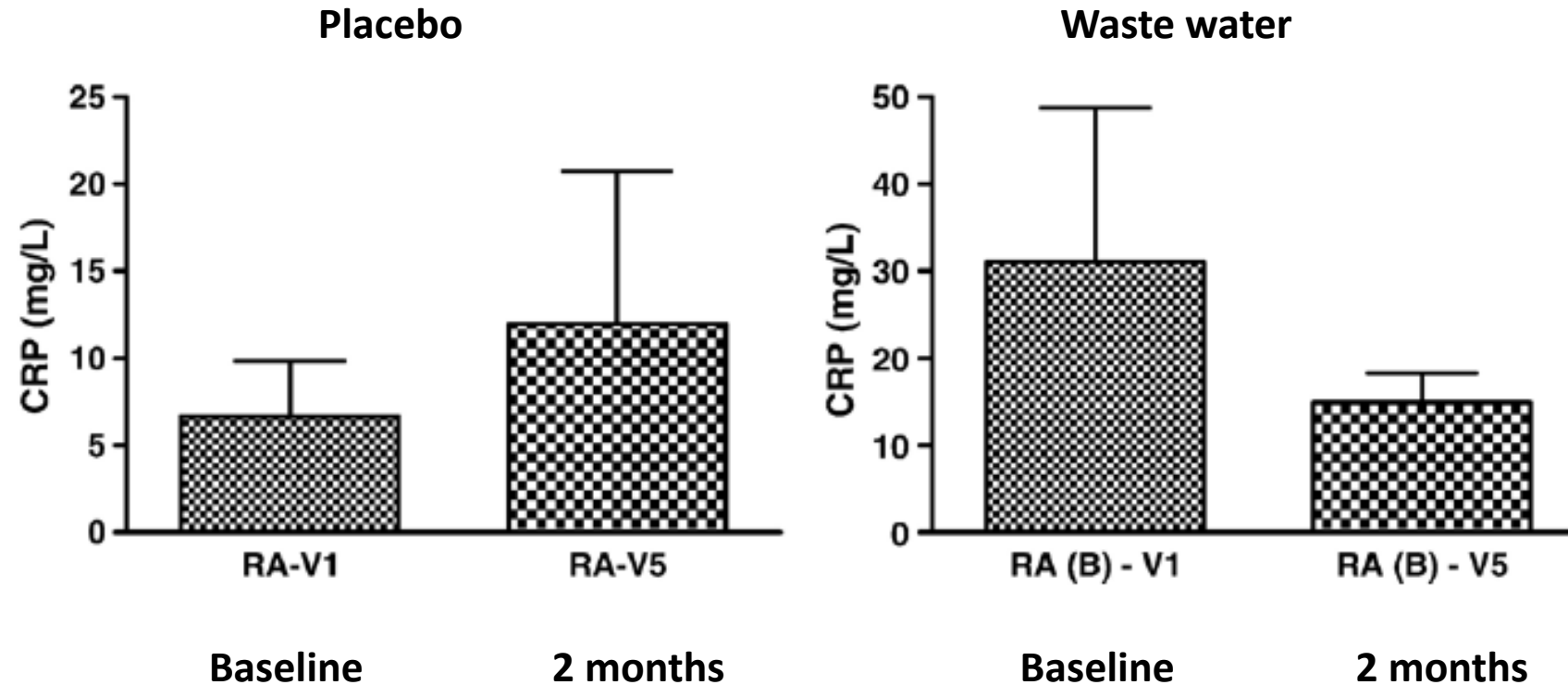
*J. Nutr.* 135: 1475–1479, 2005.

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>

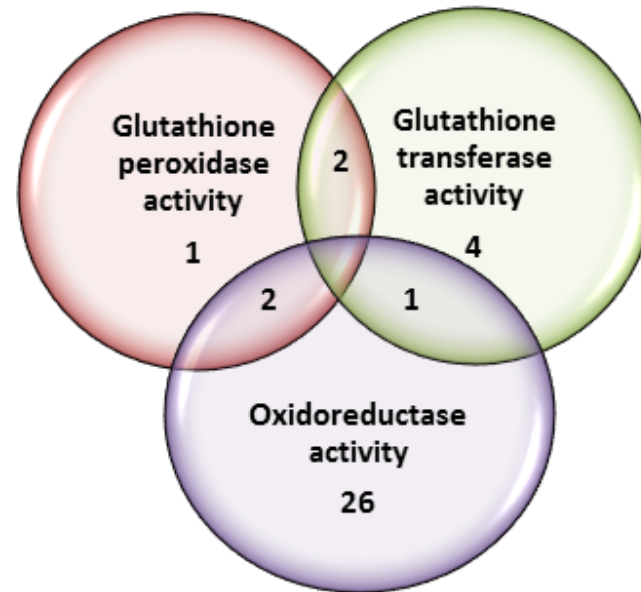
*Nutrition Research* 27 (2007) 470–477

# 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  distinguish the effects of catechins from those of caffeine.
- No caffeine  no excitatory effects.

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

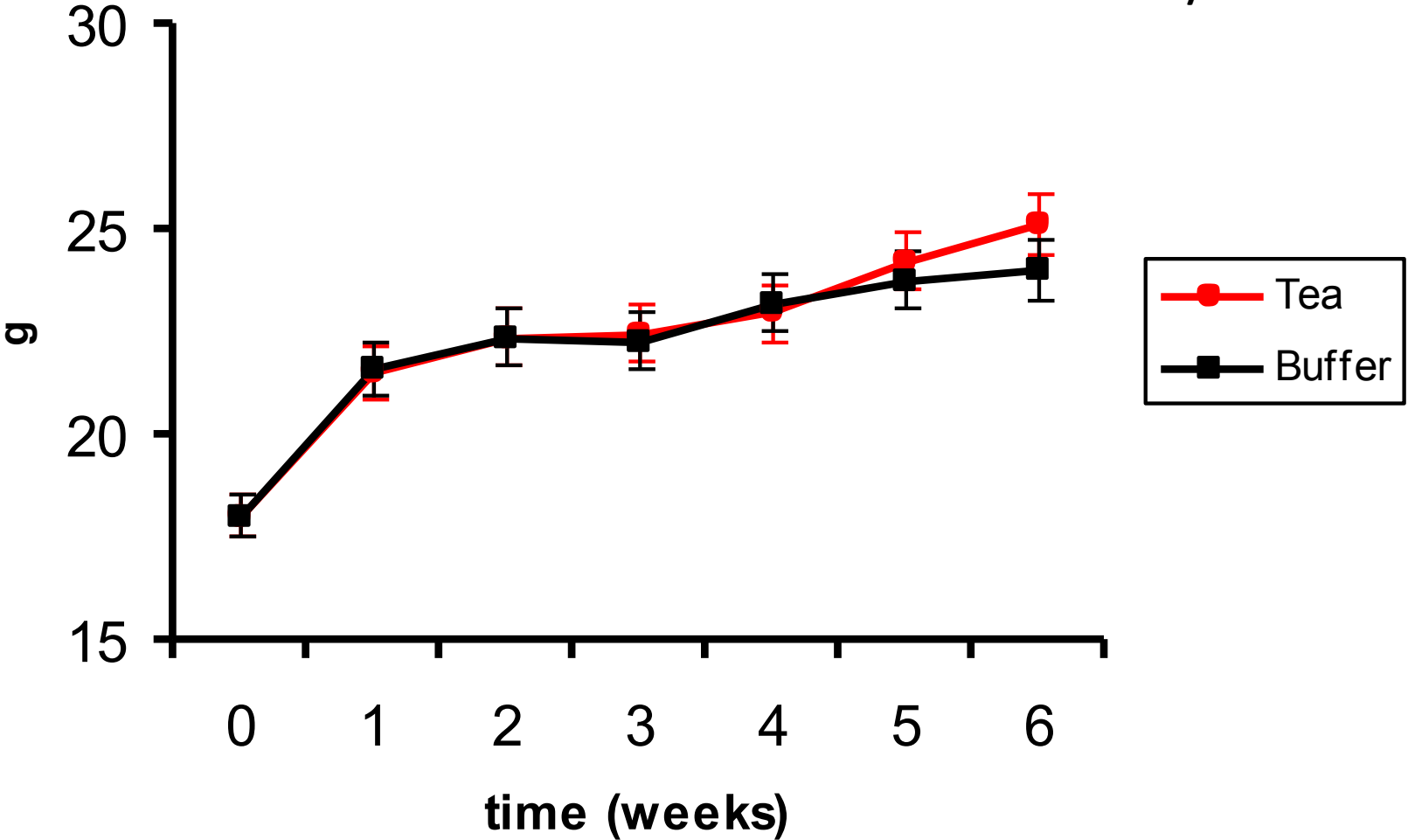
# Decaffeinated green tea composition

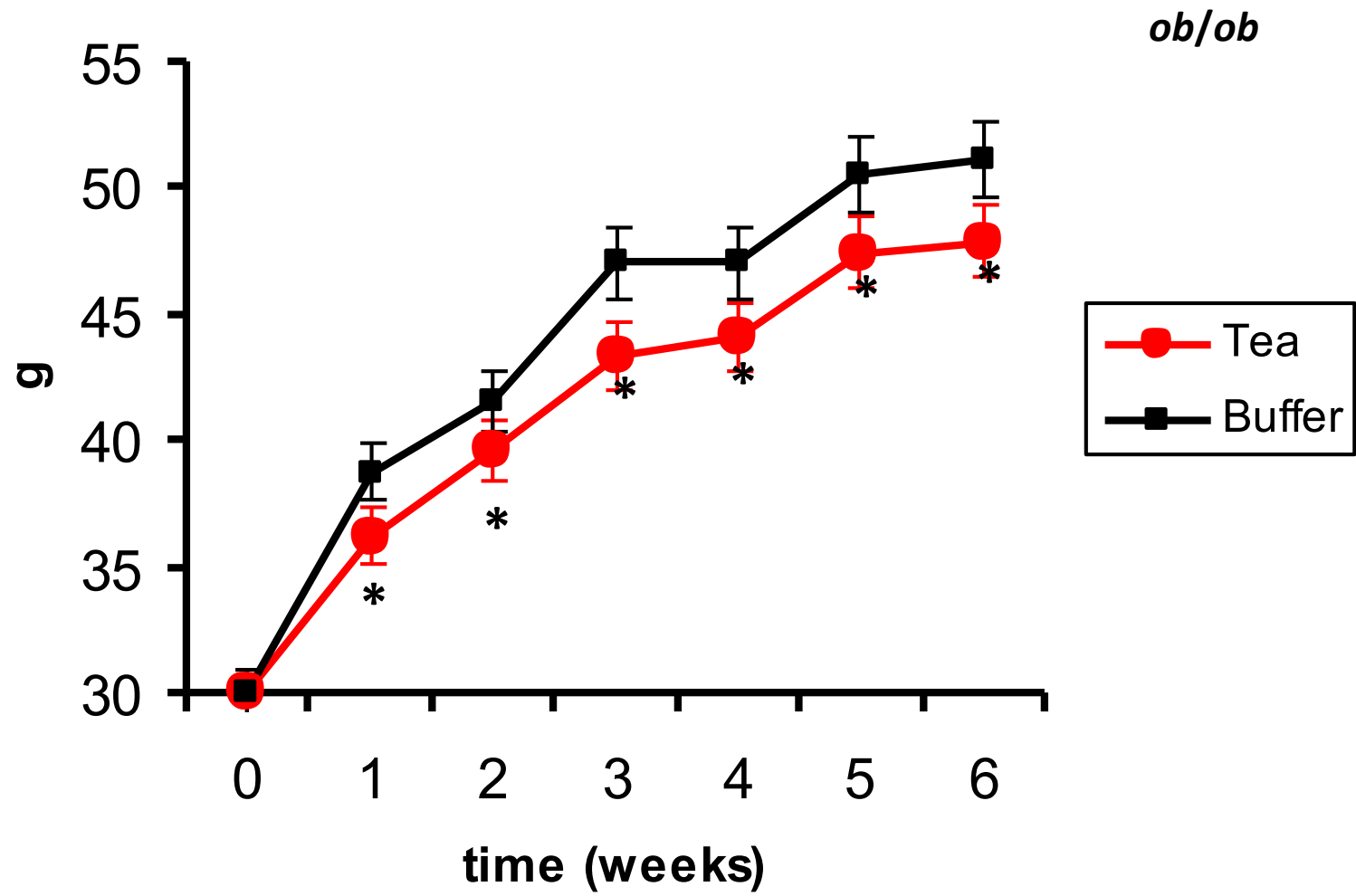
**71.75 mg total catechins per g** of leaves (1.38 mg were catechin, 6.77 mg epicatechin, 4.45 mg gallocatechin, 32.21 mg epigallocatechin, 21.04 mg epigallocatechin gallate, 0.39 mg gallocatechin gallate, 5.51 mg epicatechin gallate, catechin gallate n.d.

	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



C57BL/6J





Several mechanisms

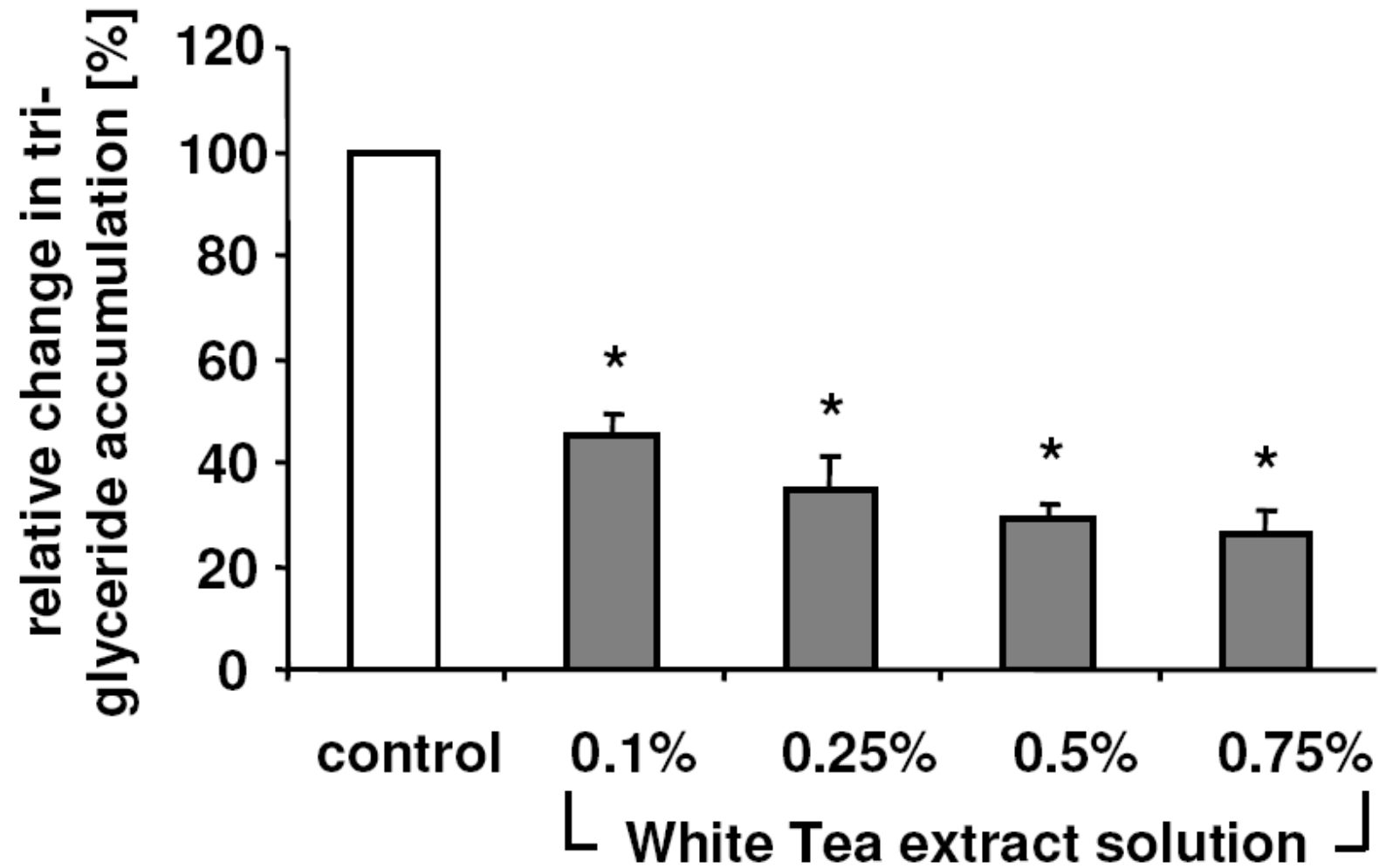
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**White Tea extract induces lipolytic activity and inhibits adipogenesis in human subcutaneous (pre)-adipocytes**

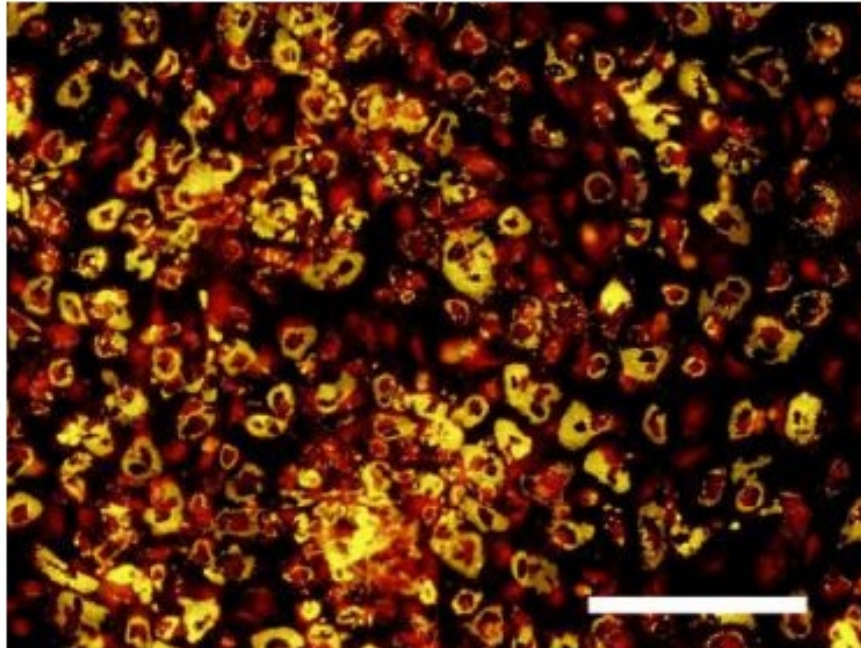
Jörn Söhle, Anja Knott, Ursula Holtzmann, Ralf Siegner, Elke Grönniger, Andreas Schepky, Stefan Gallinat, Horst Wenck, Franz Stäb and Marc Winnefeld\*

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

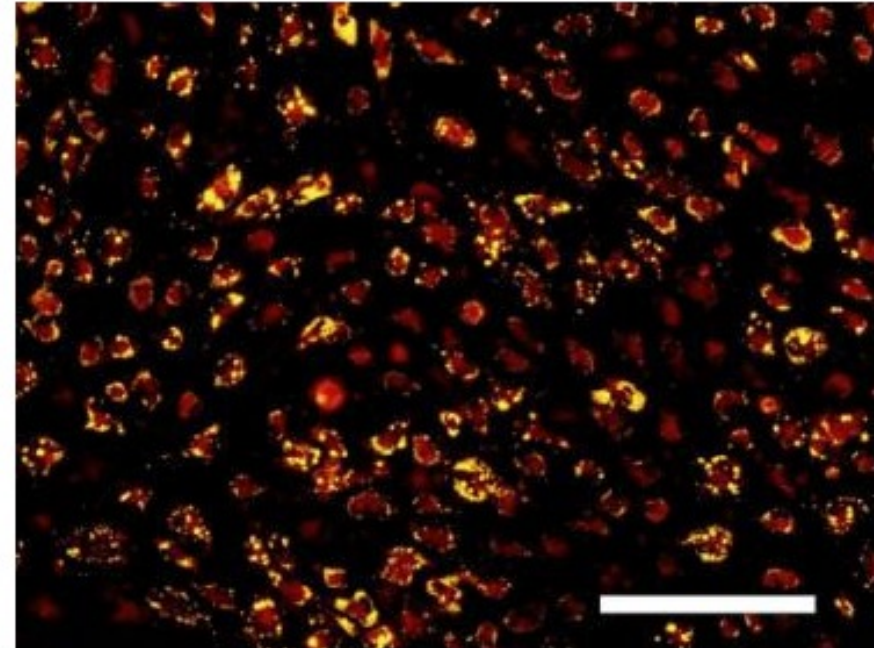
# Reduced accumulation of TG in adipocytes



**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 viscoso 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