Tornata Accademia Vite e Vino, 7 dicembre 2013, Biblioteca la Vigna – Vicenza
*A ricordo e onore di **Francesco Orlandi**, Consigliere e Coordinatore del Gruppo di Lavoro Umberto Pallotta "Vino e Salute"*

Azione ed effetti benefici dell'etanolo e dei polifenoli del vino

Chiara Cerletti

Laboratorio di Nutraceutica

Dipartimento di Epidemiologia e Prevenzione,
IRCCS, Istituto Neurologico Mediterraneo NEUROMED, Pozzilli (IS)

CERLETTI, Giovanni Battista
(1846-1906)

Enologo italiano, volontario garibaldino nel 1866.

Nel 1873 fondò le prime stazioni sperimentali di viticoltura su basi scientifiche, e nel 1876, **a Conegliano, la prima scuola di viticoltura ed enologia in Italia**.

Si occupò molto del problema delle bonifiche, per le quali elaborò piani originali, che, attuati in Lombardia e nell'Agro romano, fecero risorgere l'agricoltura in molte plaghe abbandonate.

Treccani.it
L'ENCICLOPEDIA ITALIANA

Spedizione in a.p. - 45% - art. 2 comma 20/b legge 662/96 - Filiale di Milano
In caso di mancato recapito si restituisca al mittente che si impegna a pagare la relativa tassa

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NUTRITION, METABOLISM AND CARDIOVASCULAR DISEASES

Volume 11
Suppl. to No. 4
August 2001

HEALFO Conference

FOOD and NUTRITION for BETTER HEALTH
Highlights from EC research programmes

Wine and cardiovascular disease

G. de Gaetano[1], and C. Cerletti[2], on behalf of the FAIR CT 97 3261 Project participants

Moderate consumption of red wine, but not gin, decreases erythrocyte superoxide dismutase activity: A randomised cross-over trial☆

R. Estruch [a,b,*], E. Sacanella [a,b], F. Mota [a], G. Chiva-Blanch [a], E. Antúnez [a], E. Casals [c], R. Deulofeu [c], D. Rotilio [d], C. Andres-Lacueva [e,f], R.M. Lamuela-Raventos [b,e], G. de Gaetano [d], A. Urbano-Marquez [a]

Nutrition, Metabolism & Cardiovascular Diseases (2011) 21, 46–53

Decreased tumor necrosis factor–induced adhesion of human monocytes to endothelial cells after moderate alcohol consumption[1–3]

Am J Clin Nutr 2004;80:225–30.

Eva Badía, Emilio Sacanella, Joaquim Fernández-Solá, José Maria Nicolás, Emilia Antúnez, Domenico Rotilio, Gaetano, Alvaro Urbano-Márquez, and Ramon Estruch

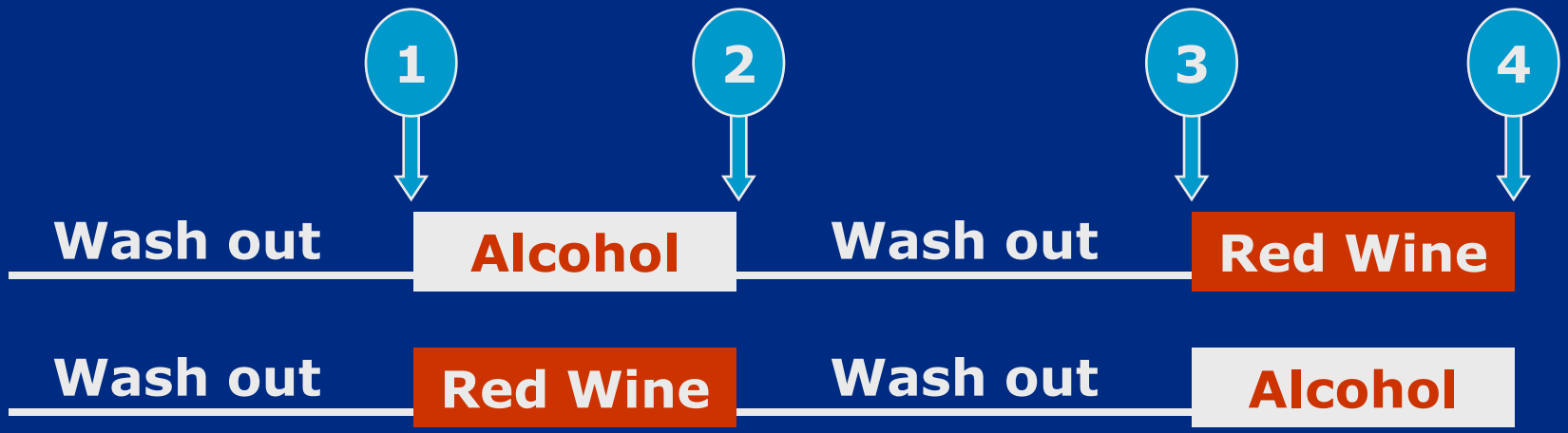
Different effects of red wine and gin consumption on inflammatory biomarkers of atherosclerosis: a prospective randomized crossover trial Effects of wine on inflammatory markers

Ramon Estruch [a], Emilio Sacanella [a], Eva Badia [a], Emilia Antúnez [a], José Maria Nicolás [a], Joaquim Fernández-Solá [a], Domenico Rotilio [b], Giovanni de Gaetano [c], Emanuel Rubin [d,*], Alvaro Urbano-Márquez [a]

Atherosclerosis 175 (2004) 117–123

Main Results

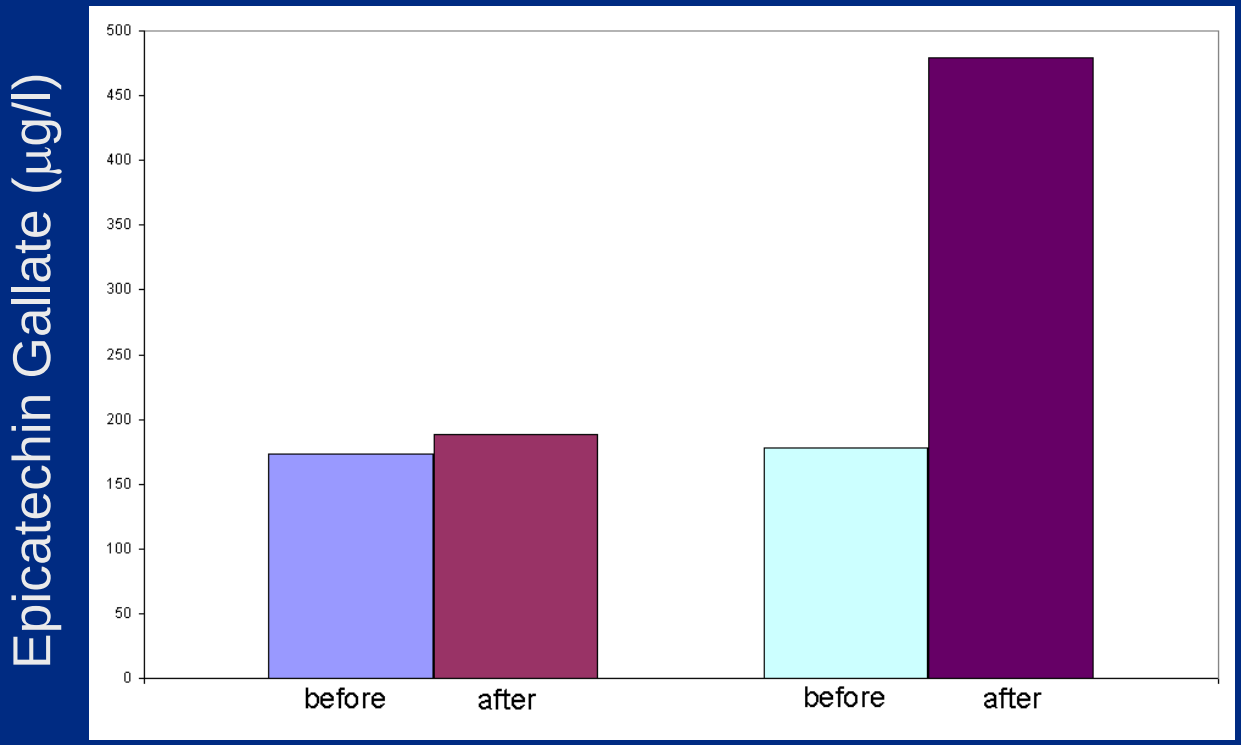
A controlled, prospective, randomized, cross-over study in 40 healthy Spanish volunteers



30 g alcohol/day – 28 days supplement and 14 days wash-out

Main Results

Effects on blood polyphenols levels



Main Results

Effects on cholesterol

Both alcohol and red wine

- ↑ HDL cholesterol (the "good" one)
- ↓ LDL cholesterol (the "bad" one) oxidation rate
- ↓ LDL/HDL ratio

Main Results

Effects on adhesion molecules

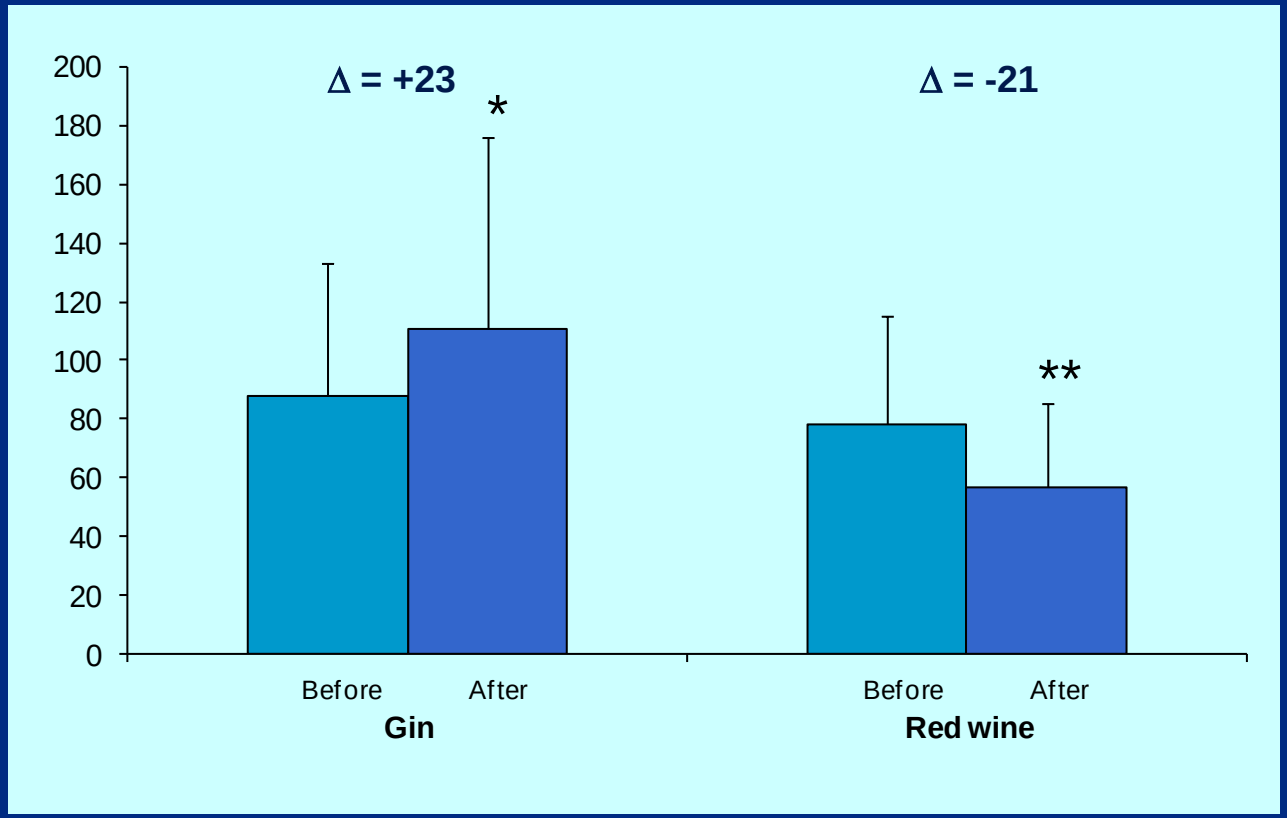
Red wine but not alcohol

↓ MONOCYTE ADHESION MOLECULES
LFA1, MAC-1, VLA-4, MCP-1

↓ SOLUBLE ADHESION MOLECULES
VCAM, ICAM-1

The adhesive molecule MAC-1 (CD11b/CD18) plays a crucial role in platelet-leukocyte interaction

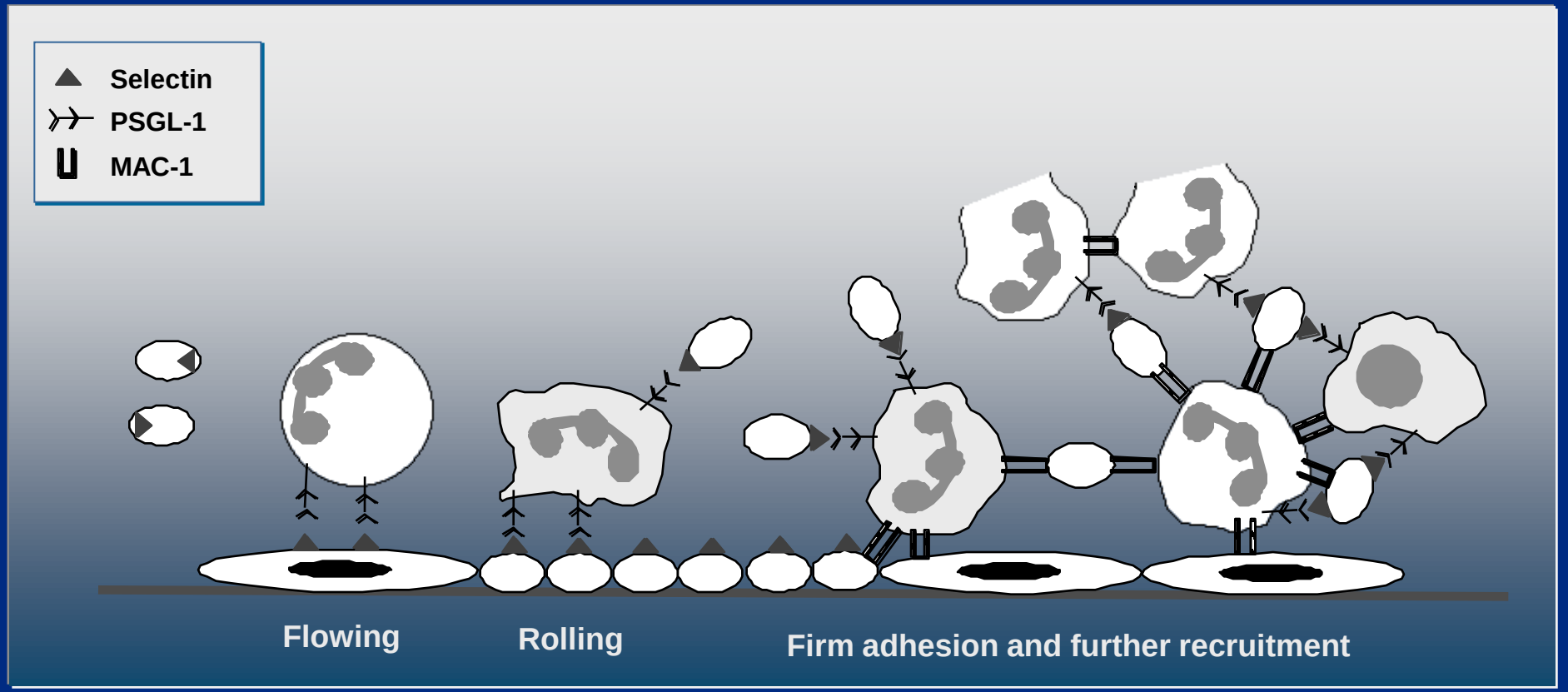
Effect of red wine and gin on MAC-1 expression on human monocytes



* p<0.05
**p<0.01

Hypothetical sequence of interactions between PMN leukocytes and activated platelets or injured endothelial cells

Role of MAC-1



de Gaetano et al. Trends Pharmacol Sci 2003

Alcohol-free red wine prevents arterial thrombosis in dietary-induced hypercholesterolemic rats: experimental support for the 'French paradox'

A. DE CURTIS, S. MURZILLI,* A. DI CASTELNUOVO, D. ROTILIO, M. B. DONATI, G. DE GAETANO and L. IACOVIELLO

Table 2 Lipid plasma levels (mean ± SE) with or without cholesterol-rich diet (with or without 5 months' alcohol-free red wine)

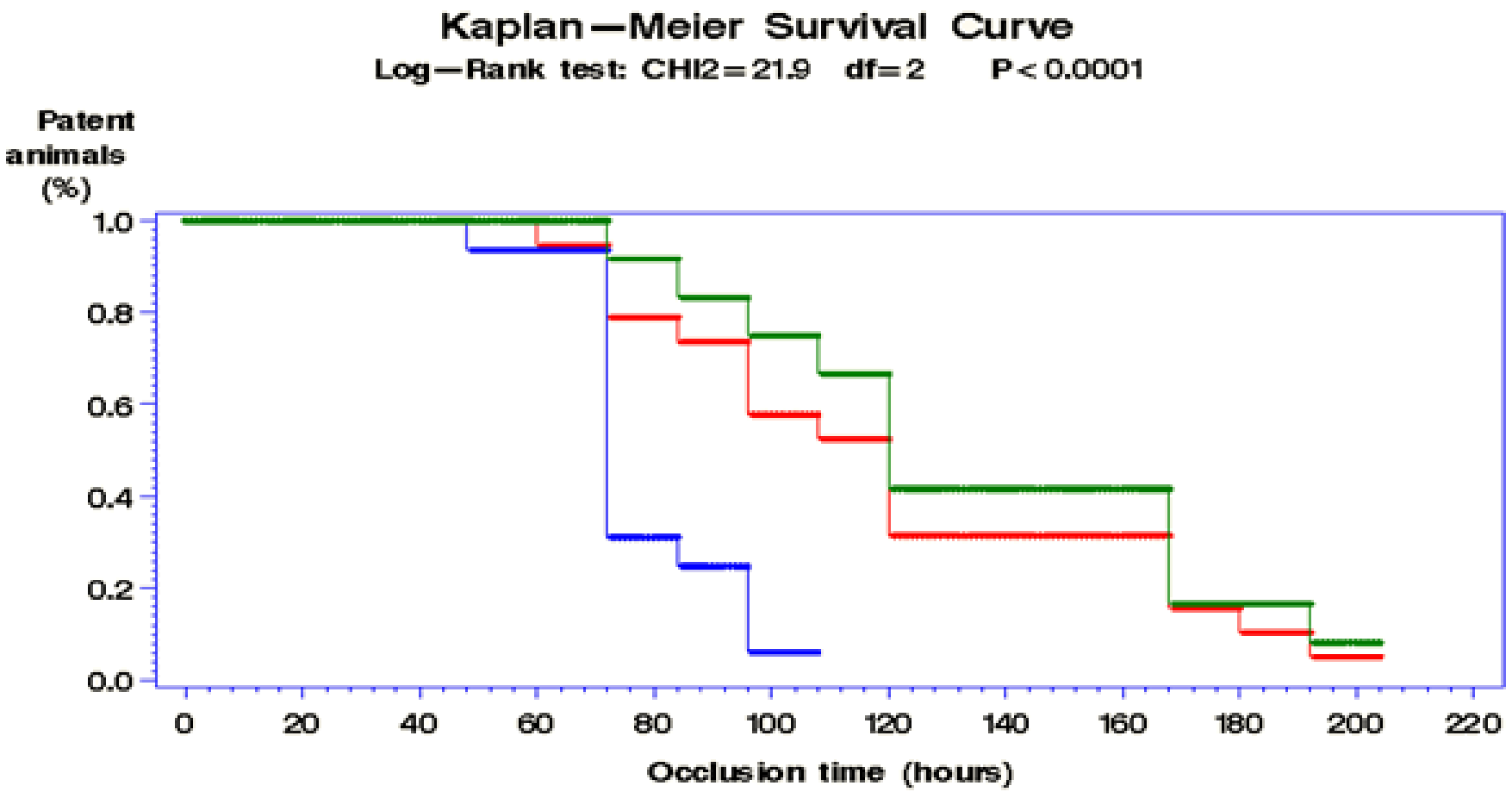
	contr-diet	Chol-diet	Chol-diet+ W
Cholesterol (mg dL^{-1})	54 ± 3	538 ± 32*	693 ± 43
HDL Cholesterol (mg dL^{-1})	33 ± 3	87 ± 4*	107 ± 7†
Triglycerides (mg dL^{-1})	70 ± 4	231 ± 24*	393 ± 29†
Occlusion time (h)	174 ± 20	70 ± 9*	125 ± 23†

*$P < 0.001$ vs. FNL; †$P < 0.01$ vs. FNL + diet.

FNL=normolipidemic rats

J Thromb Haemost 2005

Effect of wine on experimental arterial thrombosis in rats fed a hypercholesterolemic diet



De Curtis et al, J Thromb Haemost 2005

Alcohol-free red wine reduce platelet adhesion to fibrillar collagen

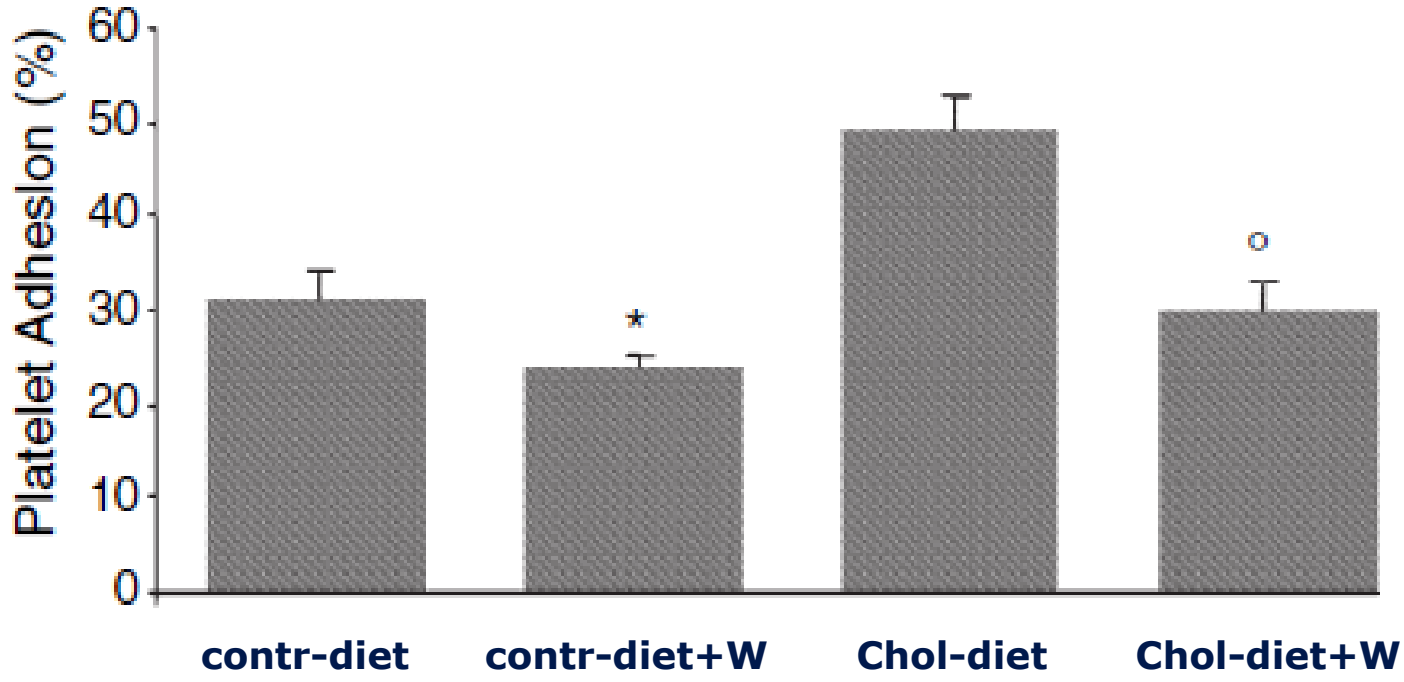


Fig. 2. Platelet adhesion to fibrillar collagen (mean ± SE) (mean in animals fed standard diet, or standard diet plus 5 months' 'alcohol-free' red wine or cholesterol-rich diet or cholesterol-rich diet plus 5 months' 'alcohol-free' red wine (*$P < 0.05$ vs. FNL; °$P < 0.05$ vs. FNL + D).

J Thromb Haemost 2005

Modulation of haemostatic function and prevention of experimental thrombosis by red wine in rats: a role for increased nitric oxide production

[1]Tomasz Wollny, [1]Luca Aiello, [2]Donata Di Tommaso, [2]Vincenzo Bellavia, [2]Domenico Rotilio, [1]Maria Benedetta Donati, [1]Giovanni de Gaetano & *,[1]Licia Iacoviello

Table 1 Quantification of red and white wine antioxidant components

	Red wine (mg l^{-1})	*White wine* (mg l^{-1})
Total phenols*	1110±15	458±7
Total flavonoids†	462±5	75±4
Non coloured flavonoids†	336±8	<20
Total anthocyanins‡	56±3	<20
Free anthocyanins‡	36±3	<20
Tannins+	6.2±0.1	0.5±0.1

Expressed as *mg l^{-1} of Gallic Acid; †(+)-Catechin; ‡Cyanidin Chloride; +Tannic Acid; mean±s.d., $n=4$.

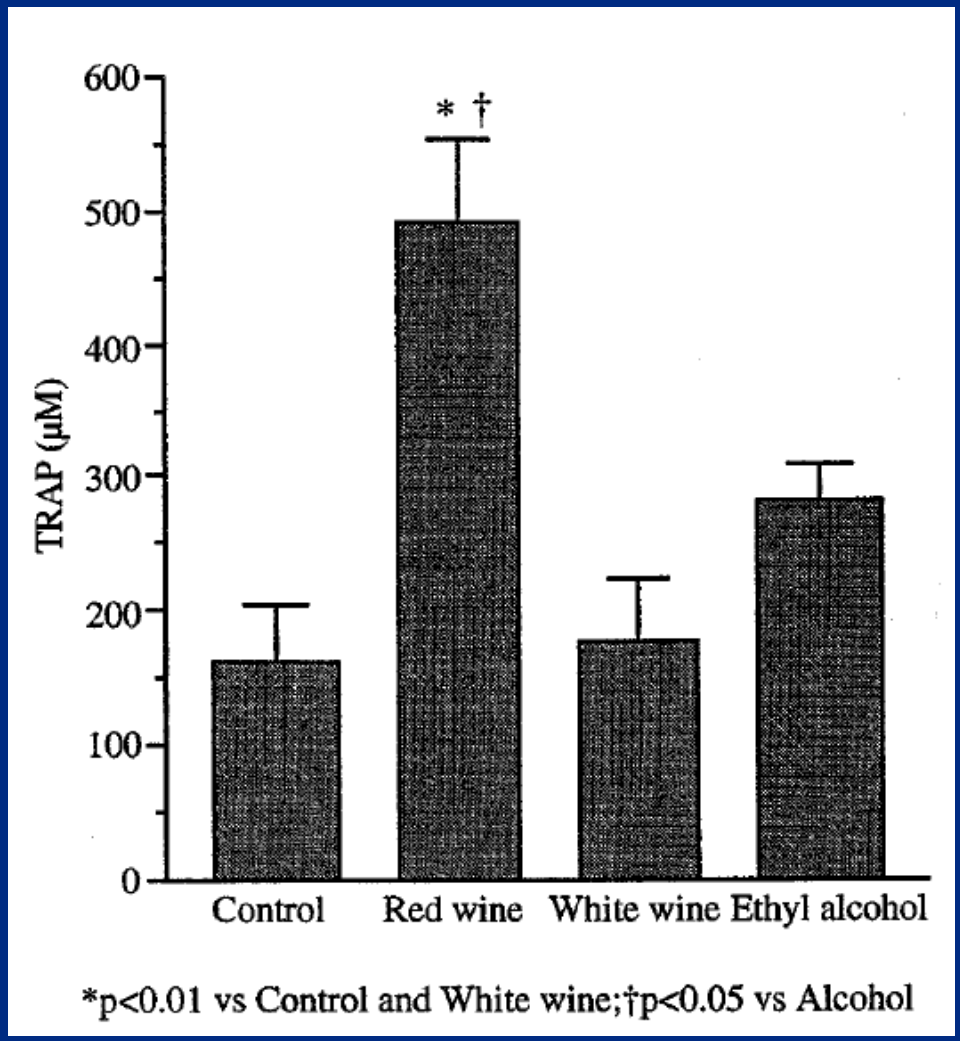
Br J Pharmacol 1999

Effect of red wine on platelet adhesion and thrombus formation

TREATMENT (supplement in drinking water)	Platelet adhesion	Thrombus weight
control	-	-
ethyl alcohol	=	=
white wine	=	=
red wine	↓	↓
alcohol-free red wine	↓	↓

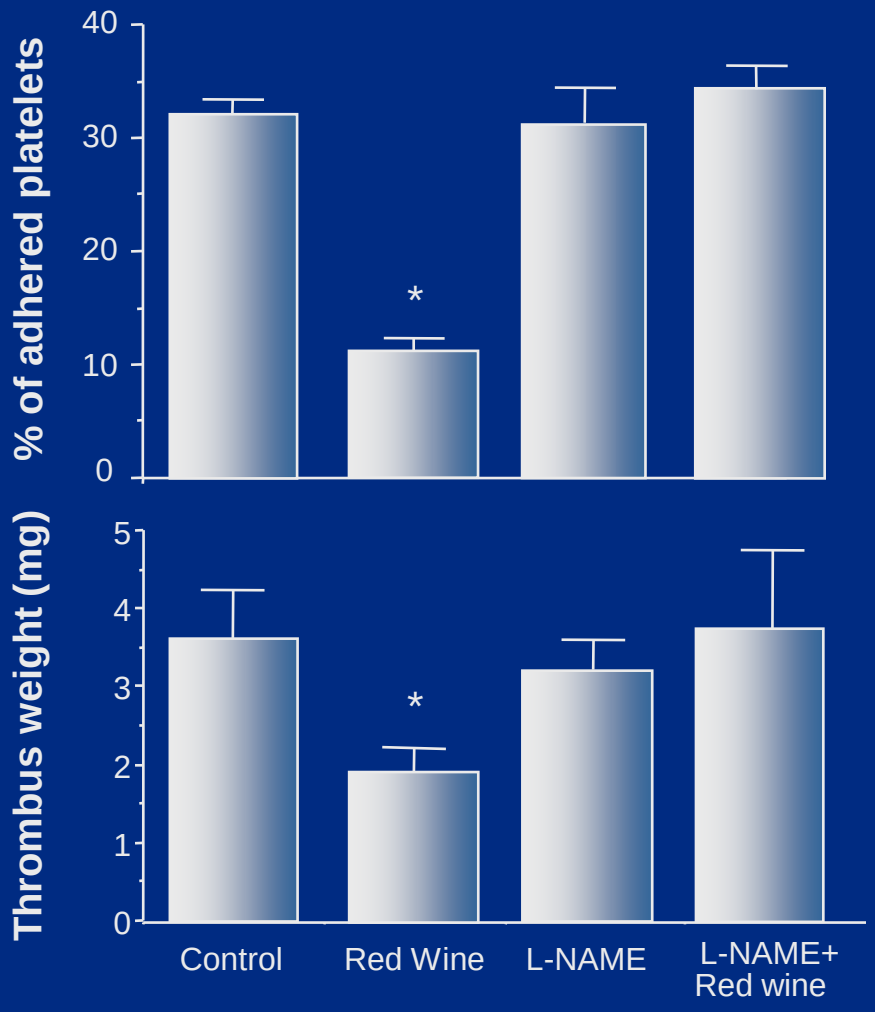
Wollny et al., Brit J Pharmacol, 1999

Total radical trapping antioxidant parameter (TRAP)



Wollny et al., Brit J Pharmacol, 1999

NO inhibition by L-NAME abolishes the effect of red wine on platelet adhesion and thrombus formation



*p<0.001 vs control

Wollny et al., Brit J Pharmacol, 1999

Louis Ignarro

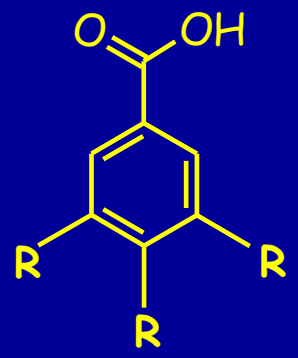
premio Nobel 1998 per la Fisiologia e la Medicina

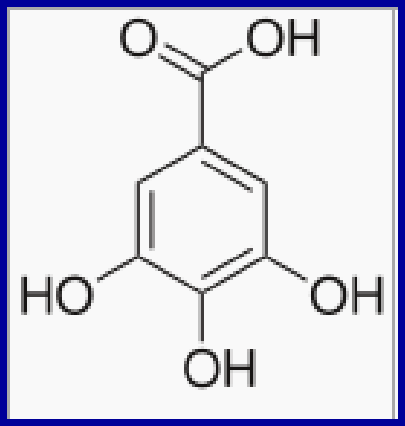
partecipò all'apertura del LXIII Anno Accademico dell'Accademia Italiana della Vite e del Vino - 23 marzo 2011, Firenze, Accademia dei Georgofili – con una Prolusione su "L'ossido nitrico e i meccanismi patogenetici coinvolti nello sviluppo delle malattie vascolari: il ruolo dei polifenoli".

"Cito sempre nelle conferenze che presento in giro per il mondo le vostre osservazioni sperimentali sull'effetto stimolante dei polifenoli del vino sull'ossido nitrico (NO) e sulla vasodilatazione NO-dipendente"

Da una lettera del prof. IGNARRO
a Giovanni de Gaetano

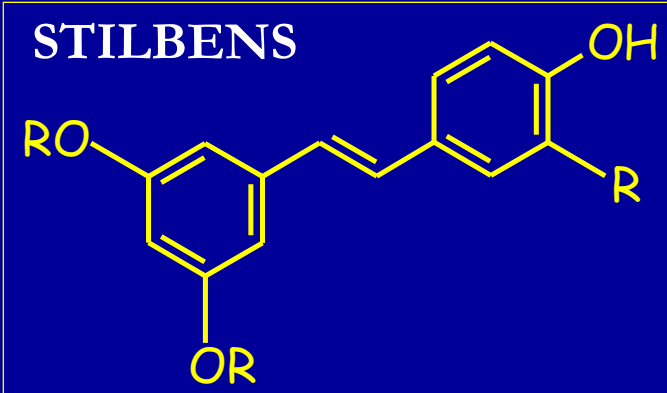
BENZOIC ACIDS





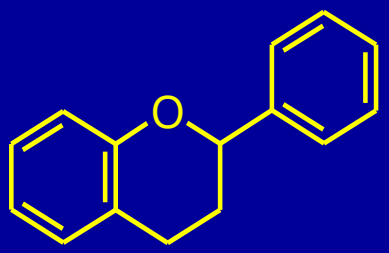
Gallic acid

STILBENS

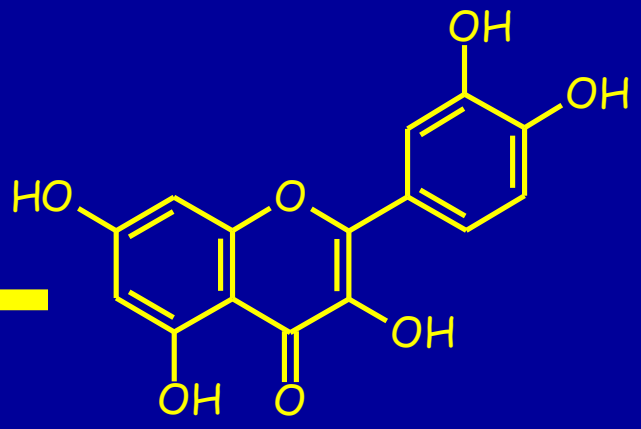


Resveratrol

FLAVONOIDS



- Flavan-3-ols
- Anthocyanins
- Proanthocyanidins
- Anthocyanidins
- Flavonols

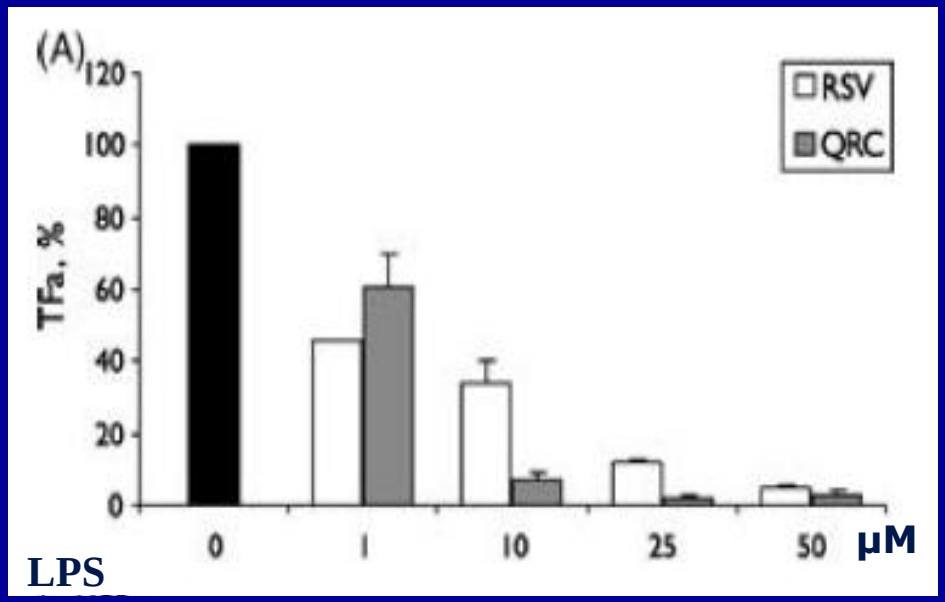


Quercetin

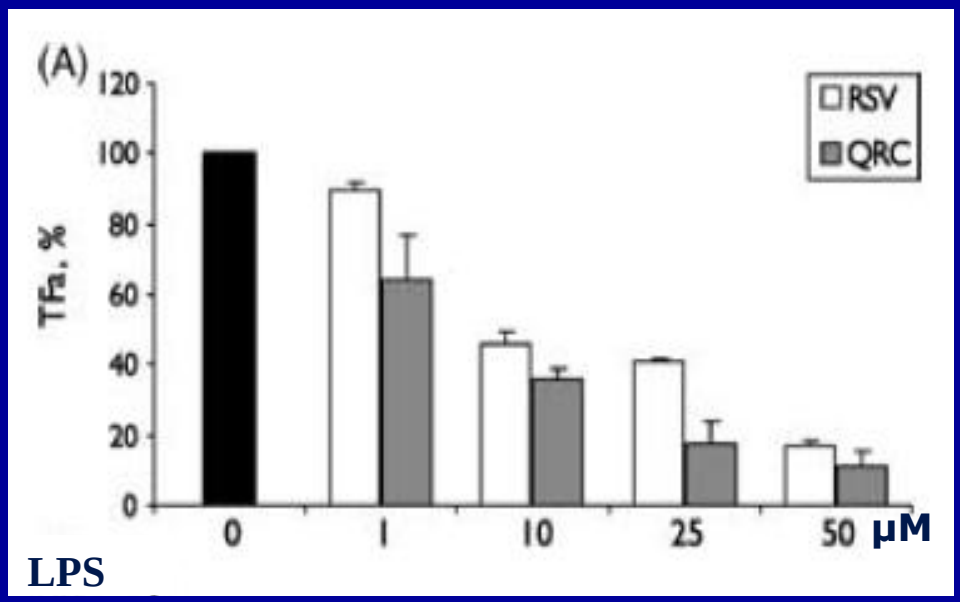
Resveratrol and quercetin down-regulate tissue factor expression by human stimulated vascular cells

A. DI SANTO, A. MEZZETTI, E. NAPOLEONE, R. DI TOMMASO, M. B. DONATI,* G. DE GAETANO* and R. LORENZET

Endothelial cells



Mononuclear cells



J Thromb Haemost 2003

Interactions of gallic acid, resveratrol, quercetin and aspirin at the platelet cyclooxygenase-1 level

Functional and modelling studies

Marilena Crescente[1]; Gisela Jessen[2]; Stefania Momi[3]; Hans-Dieter Höltje[2]; Paolo Gresele[3]; Chiara Cerletti[1]; Giovanni de Gaetano[1]

[1]Research Laboratories, "John Paul II" Center for High Technology Research and Education in Biomedical Sciences, Catholic University, Campobasso, Italy; [2]Institut für Pharmazeutische und Medizinische Chemie, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany; [3]Department of Internal Medicine, Division of Internal and Cardiovascular Medicine, University of Perugia, Perugia, Italy

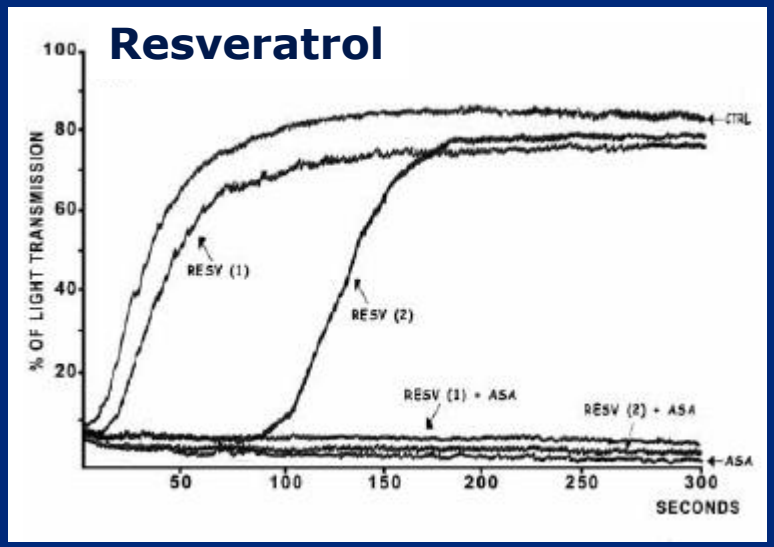
Table 1: Inhibition (μM, IC_{50}) by gallic acid, resveratrol and quercetin of platelet ROS production and platelet aggregation.

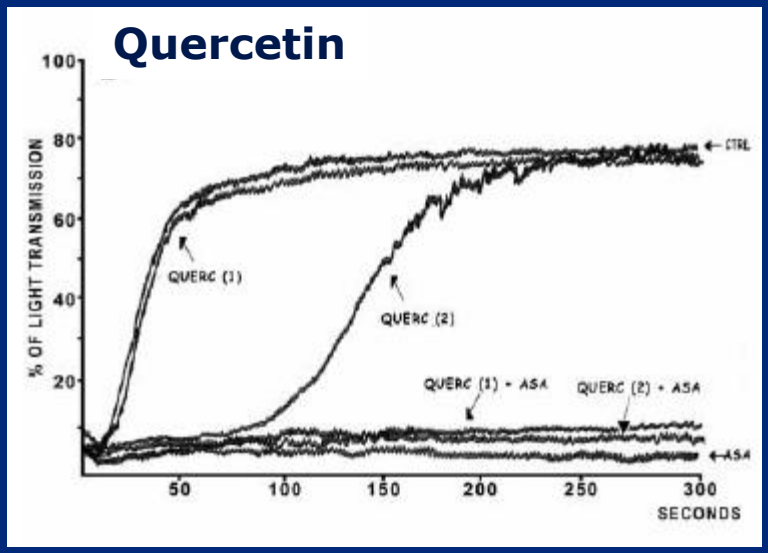
Polyphenol	ROS production	Aggregation	
		AA	TRAP
Gallic acid	35 ± 8	>1000	>1000
Resveratrol	10 ± 4	44 ± 18	270 ± 55
Quercetin	38 ± 1	130 ± 18	>400

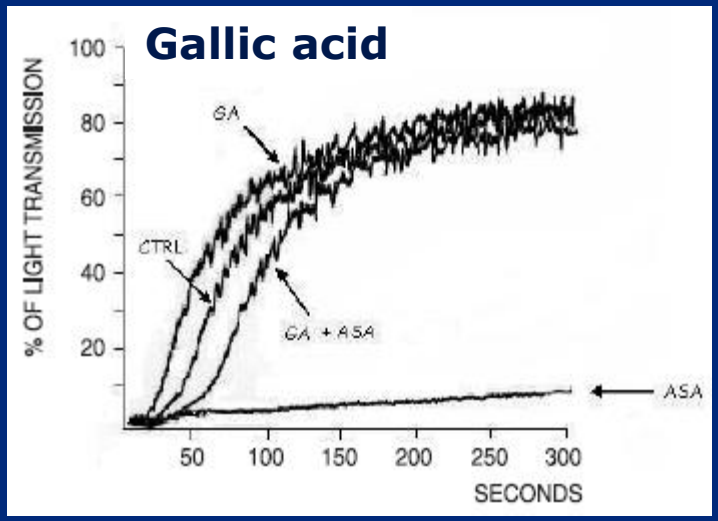
ROS production was induced in washed platelets by 2.5 μM arachidonic acid (AA); platelet aggregation was induced in PRP by AA (0.6–1 mM) or TRAP (10–20 μM). Data are reported as means ± SEM, n=3–6.

Thromb Haemost 2009

Dietary polyphenols interact with platelet COX-1 and inhibit or preserve enzyme activity with mechanisms similar to that of aspirin

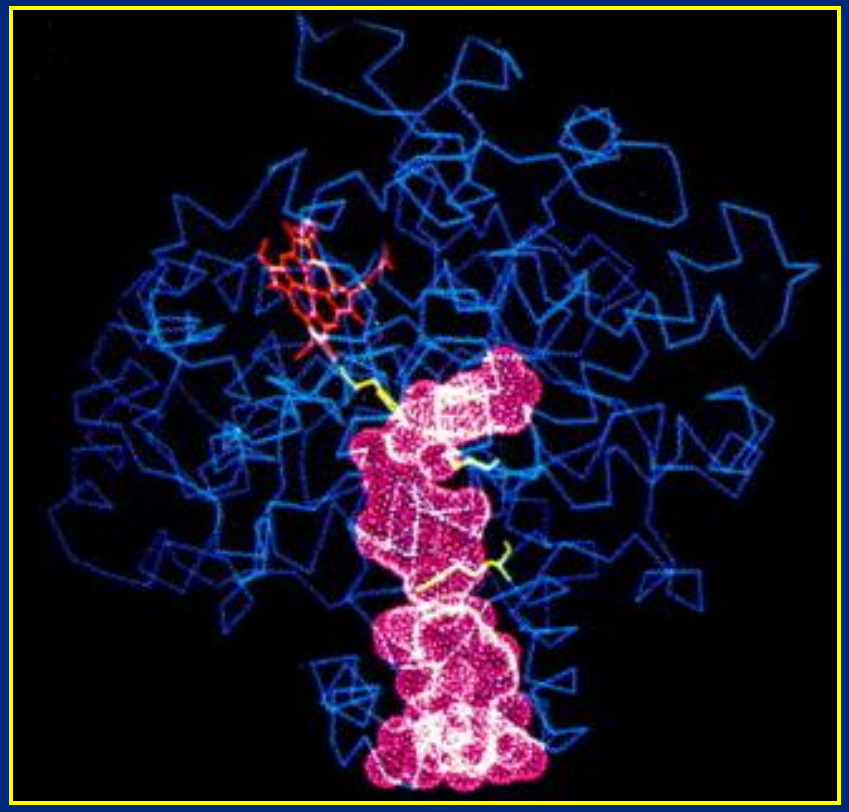


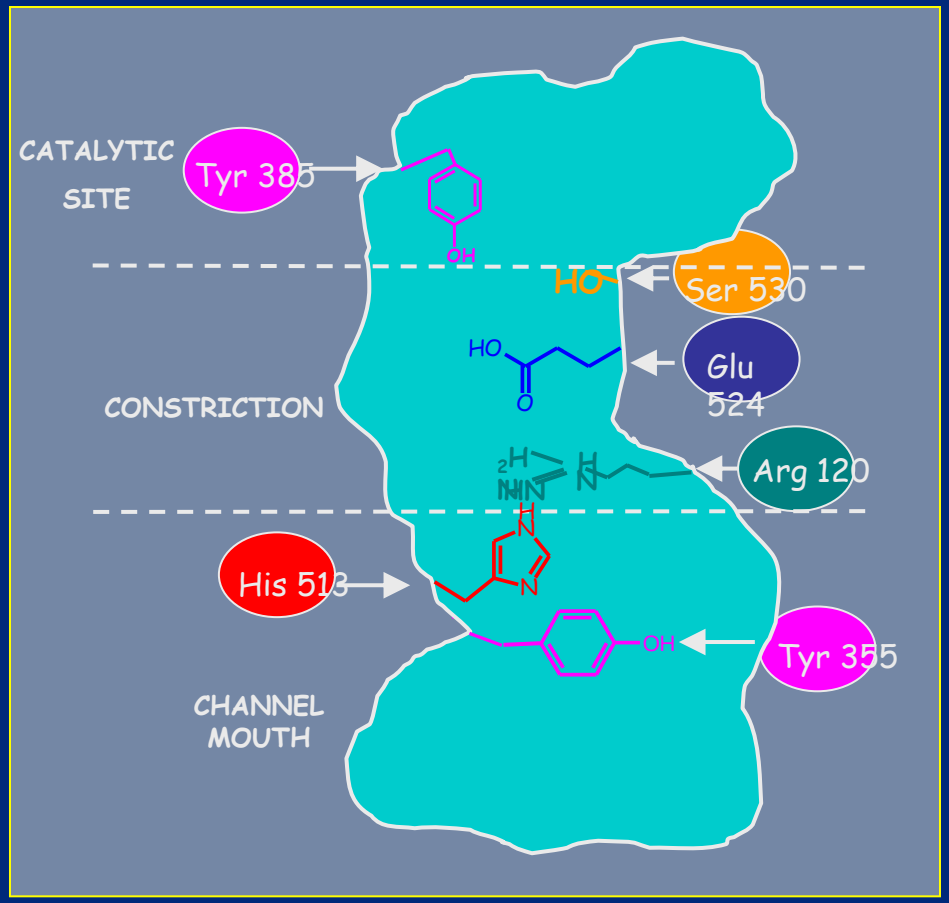




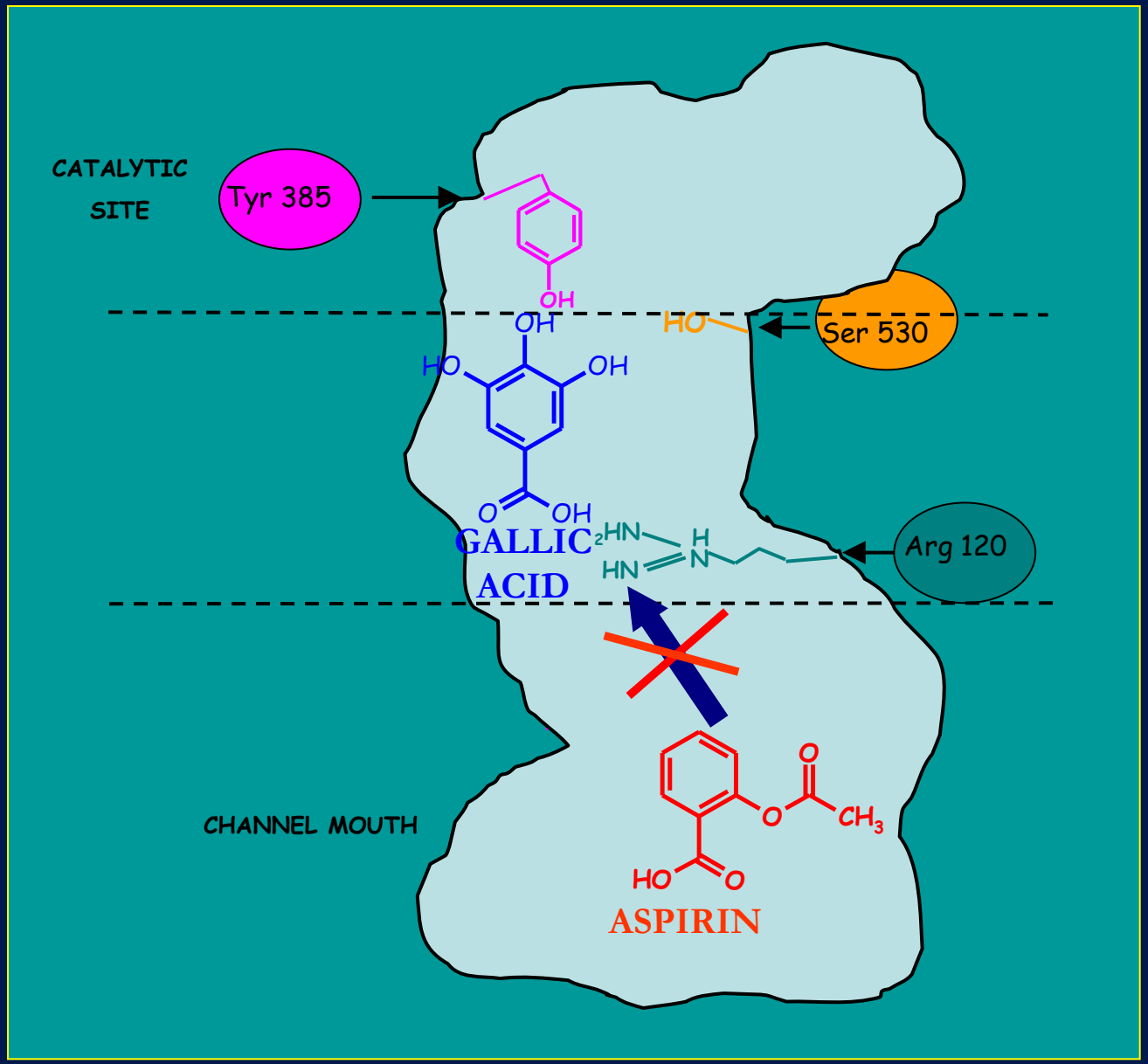
Thromb Haemost 2009

Molecular modelling: dietary polyphenols interact with the cristal structure of COX-1 and form stable complexes into the COX-1 channel, with functionally relevant interaction geometries and mechanisms similar to that of aspirin

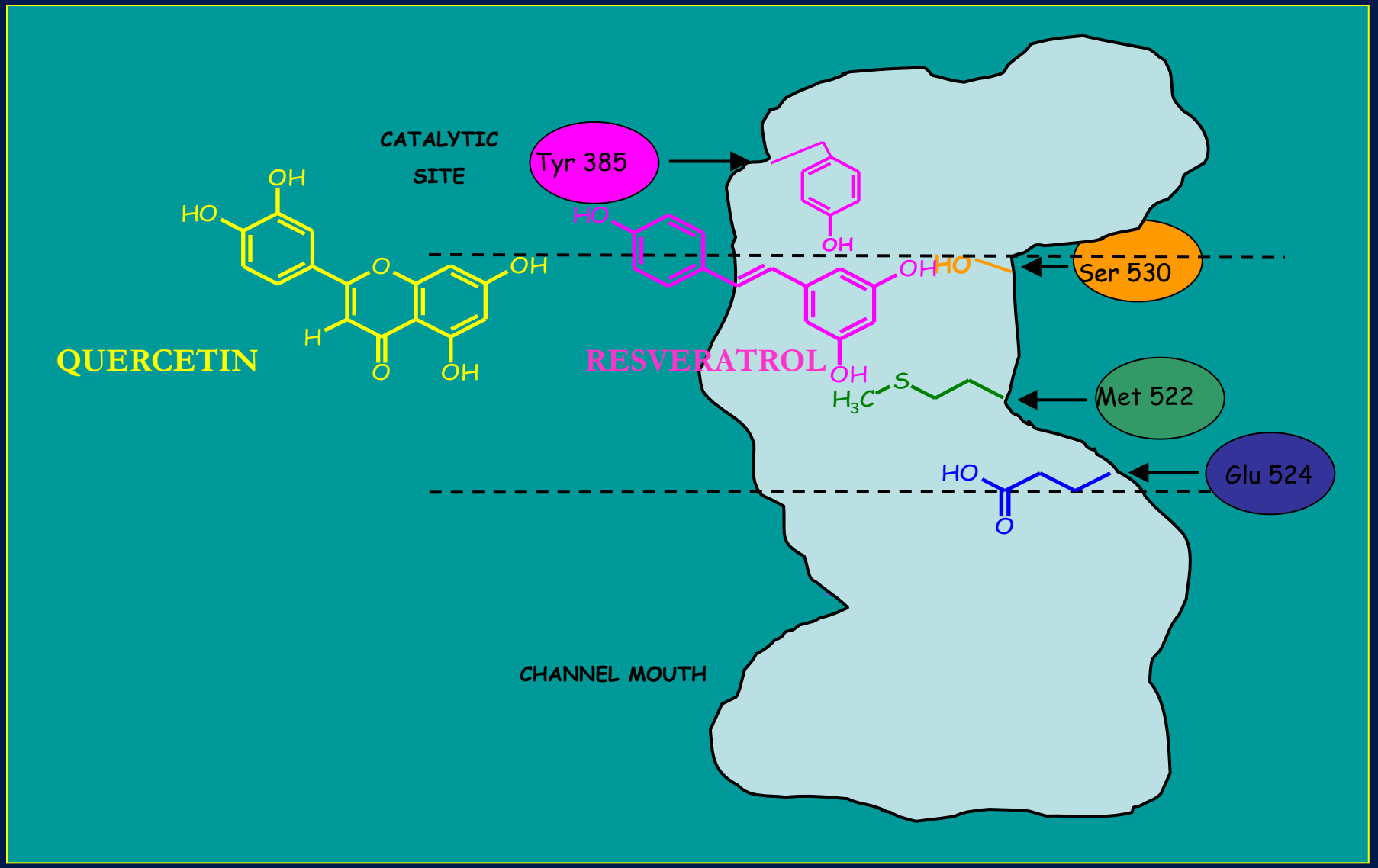




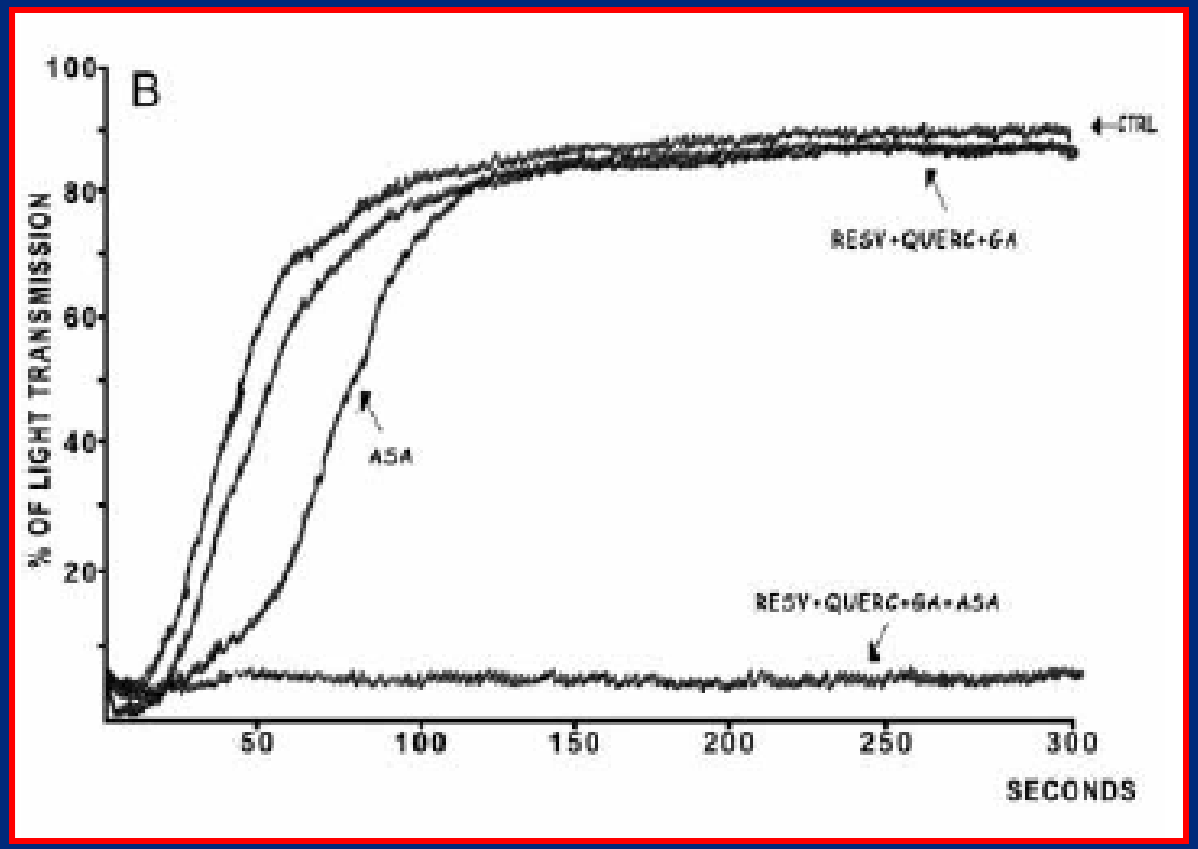
Gallic acid interaction with COX-1



Quercetin and resveratrol interaction with COX-1



"Red wine" polyphenol mixtures potentiate the platelet inhibitory effect of aspirin



Resveratrol 7.5 µM
Quercetin 15 µM
Gallic acid 120 µM

Aspirin ~10 µM

Thromb Haemost 2009

J Cardiovasc Pharmacol. 2006 Aug;48(2):1-5.

Resveratrol inhibits aggregation of platelets from high-risk cardiac patients with aspirin resistance.

Stef G, Csiszar A, Lerea K, Ungvari Z, Veress G.

State Hospital for Cardiology, Balatonfured, Hungary.

Omaggio a Francesco Orlandi