

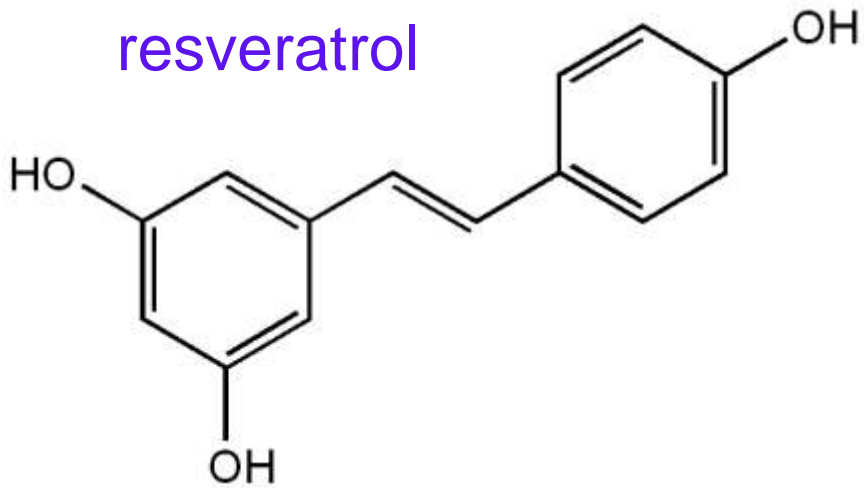
# Benefit of Wine Drinking



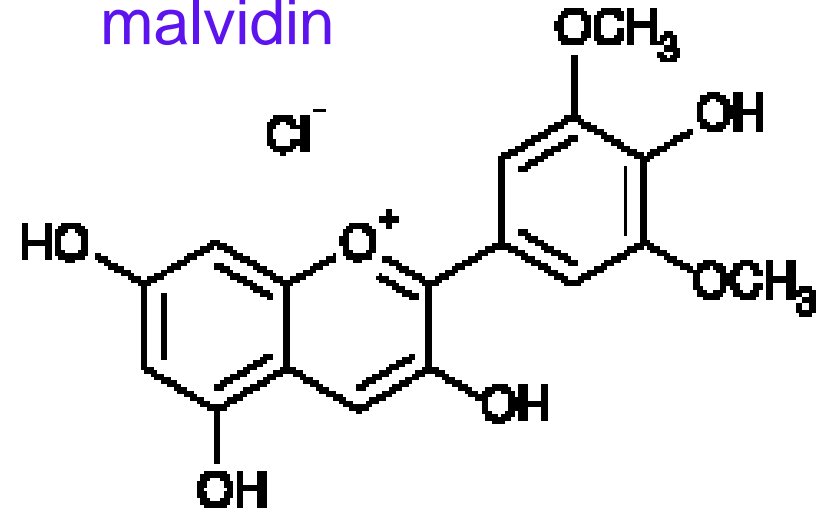
**Prof. Balázs Sümegi**  
**Department of Biochemistry and**  
**Medical Chemistry and Szentágothai**  
**Research Center, University of Pécs,**  
**Hungary.**

# Chemical structure of the best known red wine polyphenols

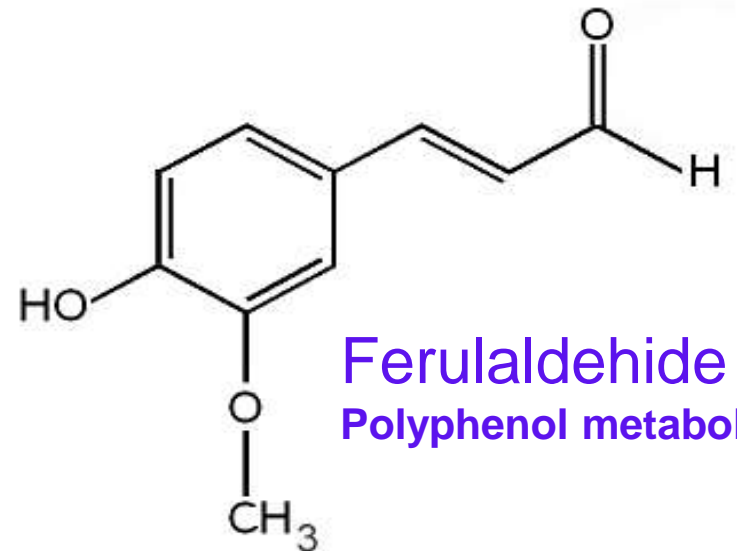
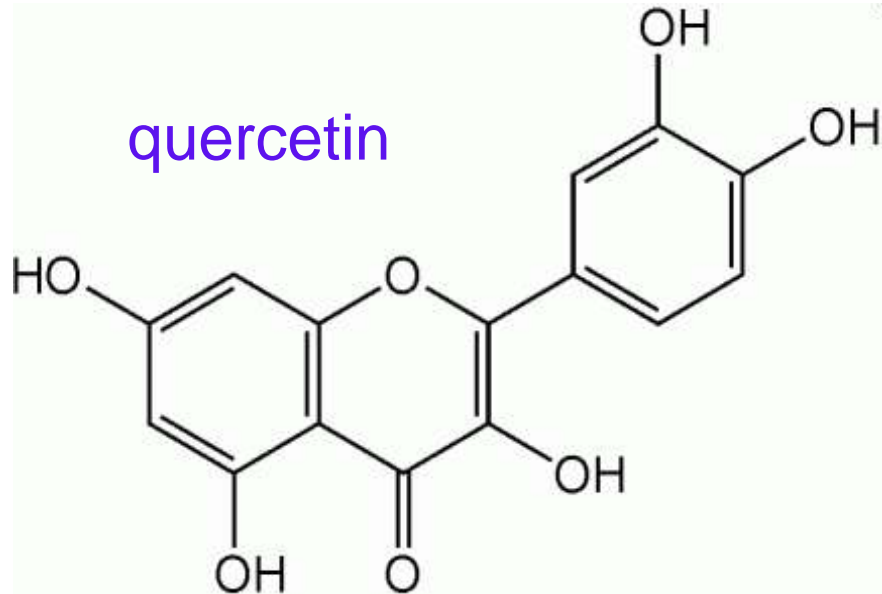
resveratrol



malvidin



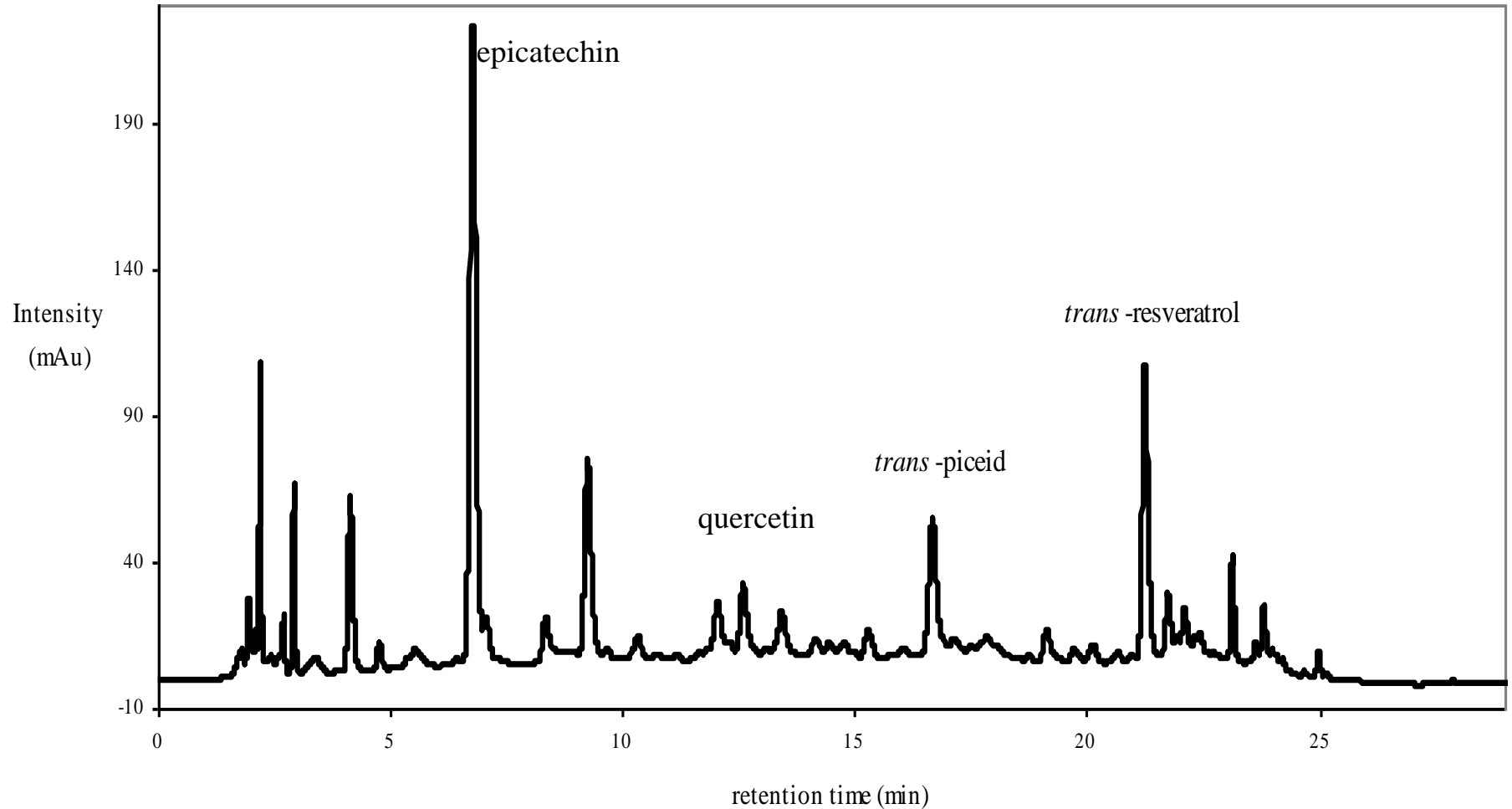
quercetin



Ferulaldehyde  
Polyphenol metabolit

# Polgár Merlot (2002) HPLC spectra

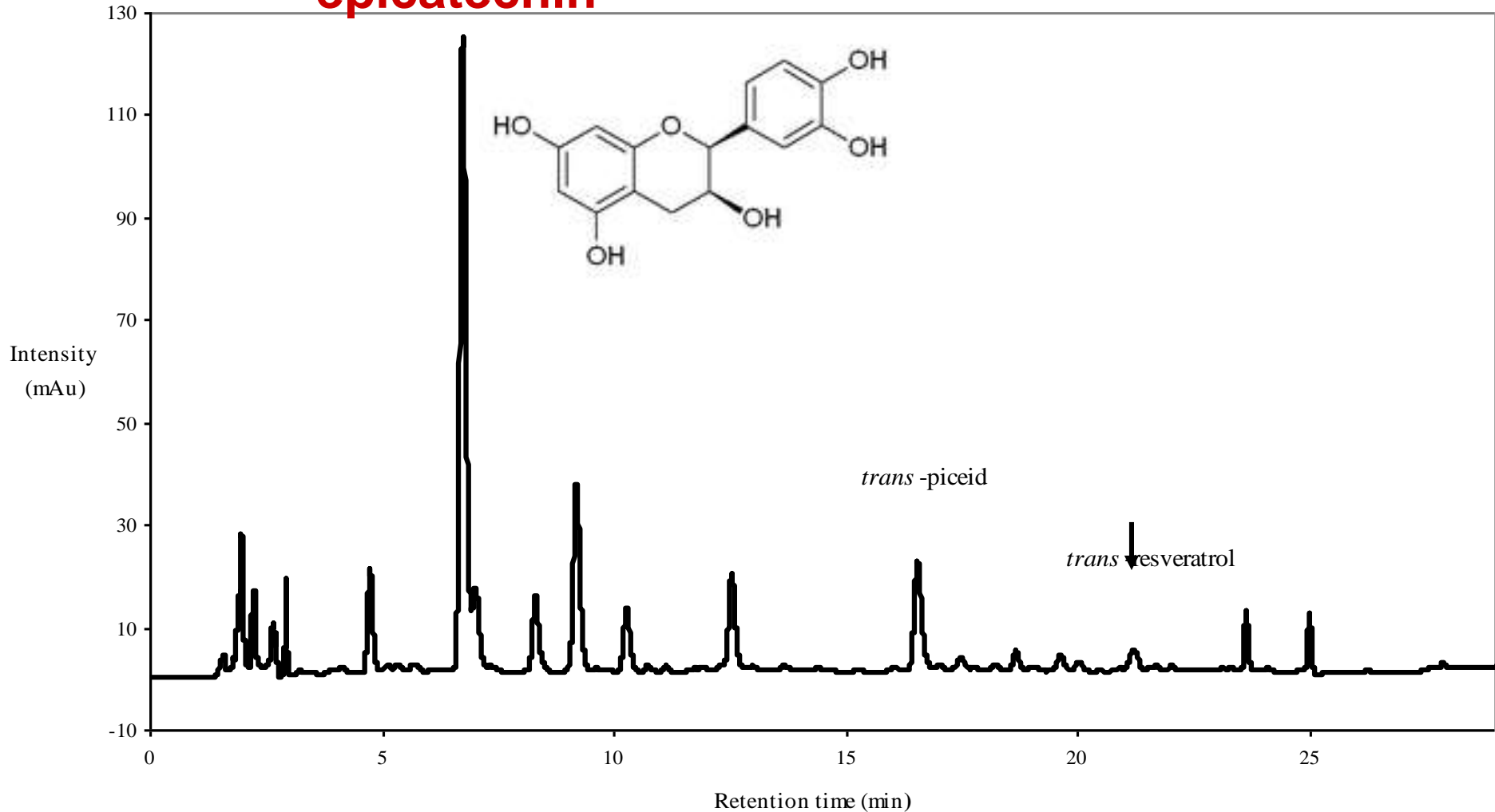
Food Chemistry 98 (3): 453-462 2006



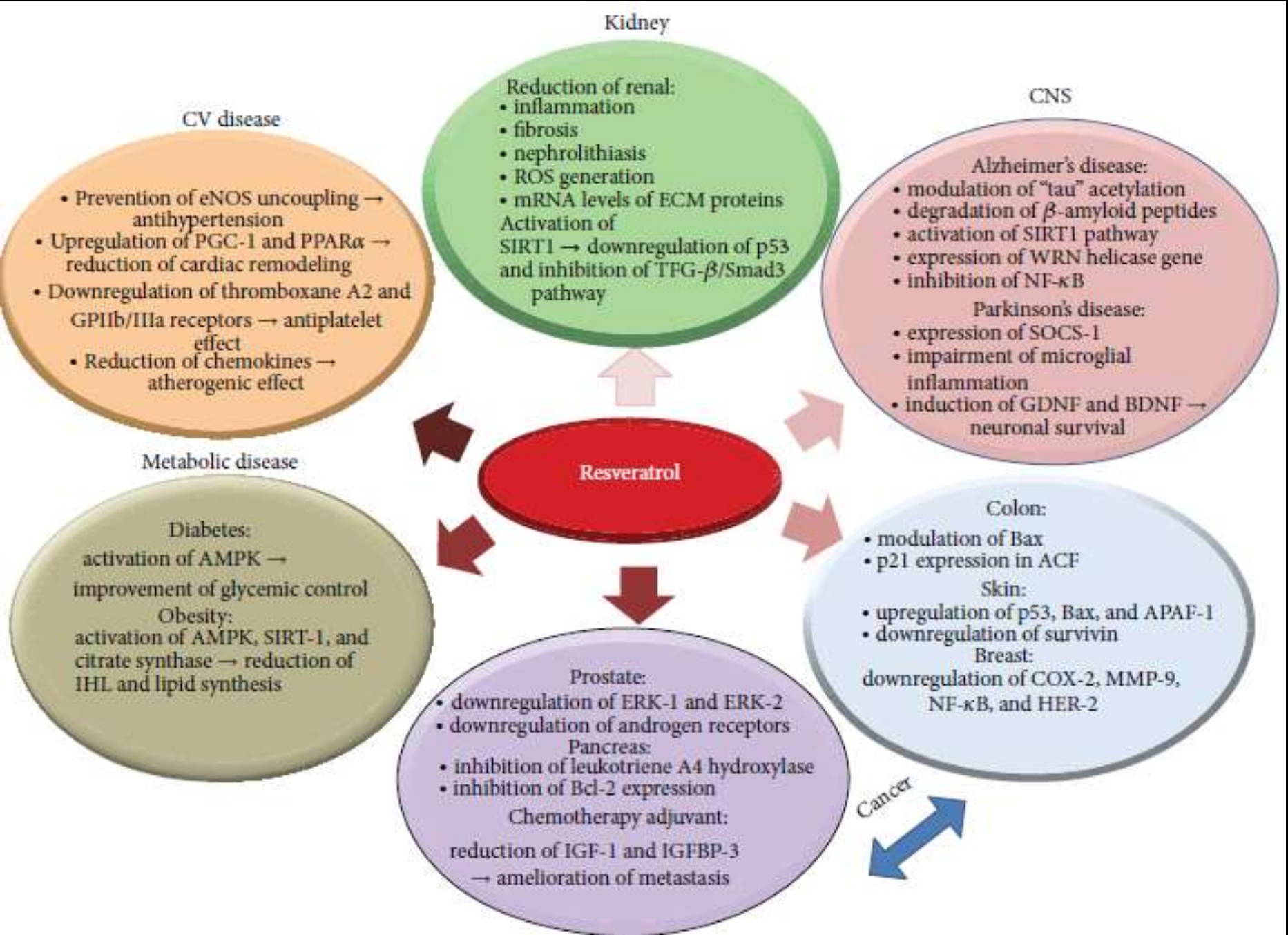
# Bock Chardonnay (2003) HPLC spectra

J Chromatogr Sci. 2005 Oct;43(9):445-9.

**epicatechin**



# Beneficial effects of resveratrol with the potential molecular mechanisms

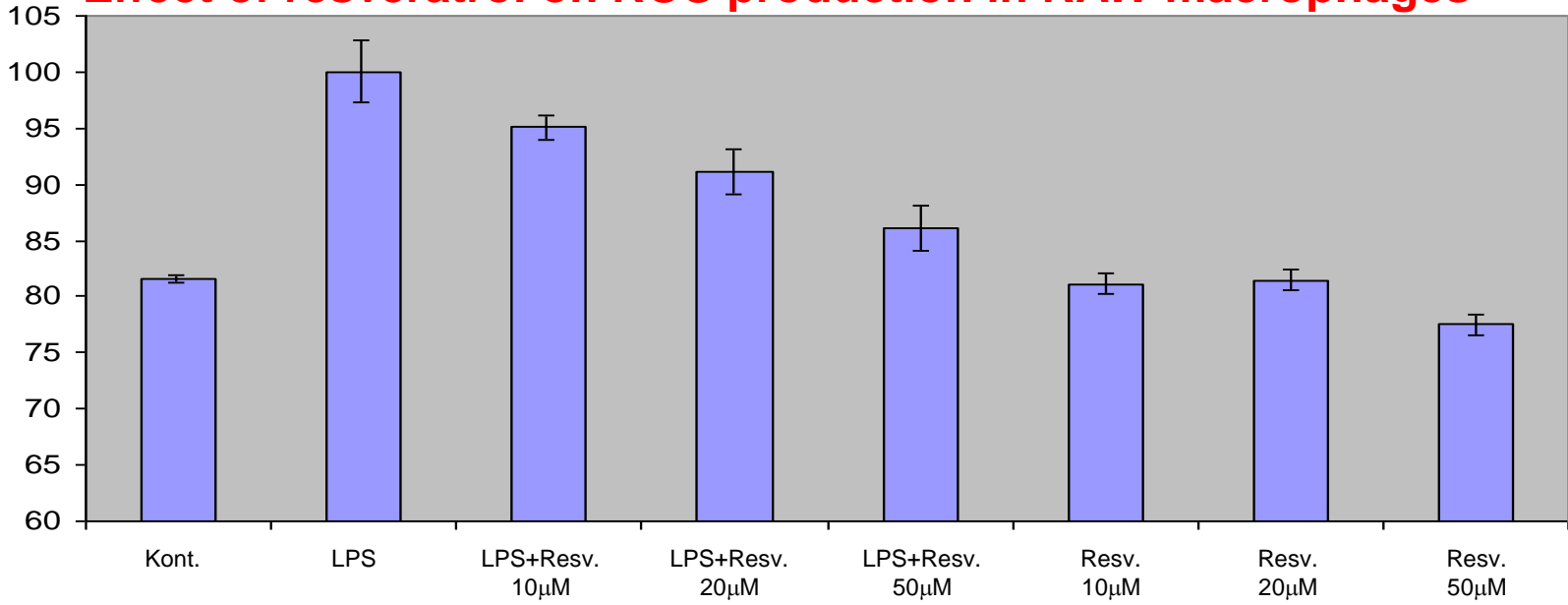




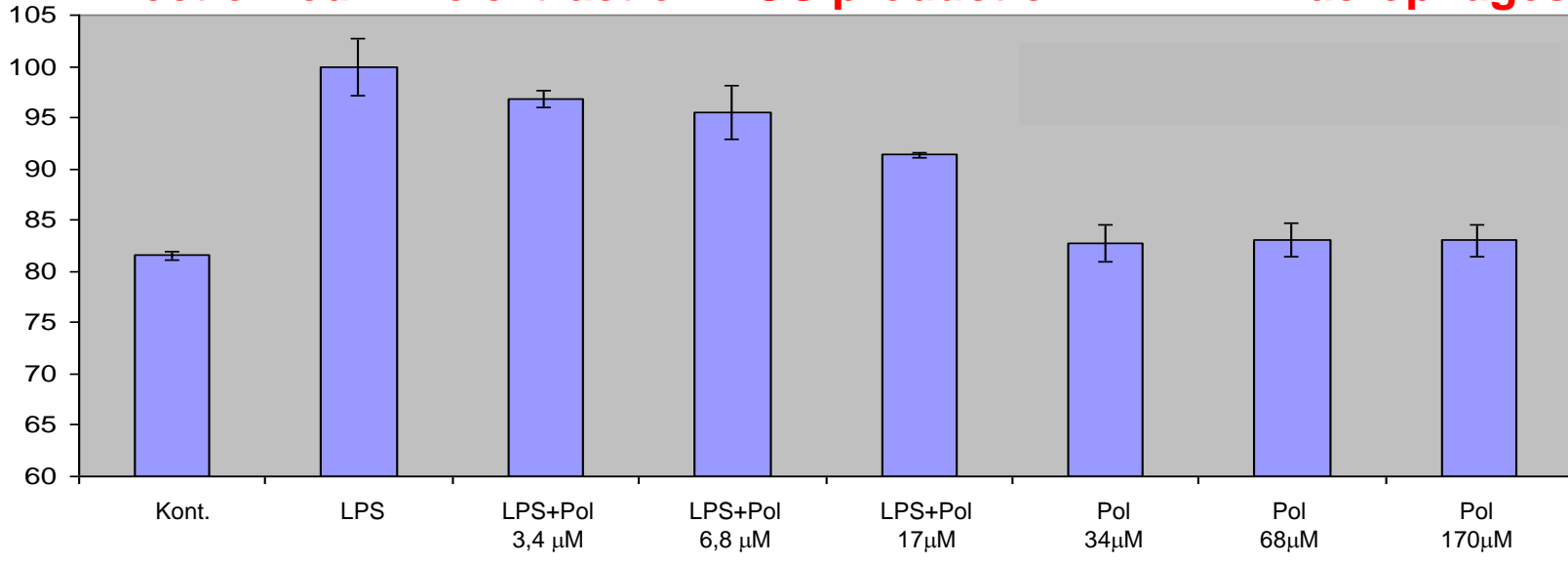
# Effects of red wine polyphenols on cytokines expression

**Studies: LPS-induced cytokines and TNF- $\alpha$  synthesis in macrophages**

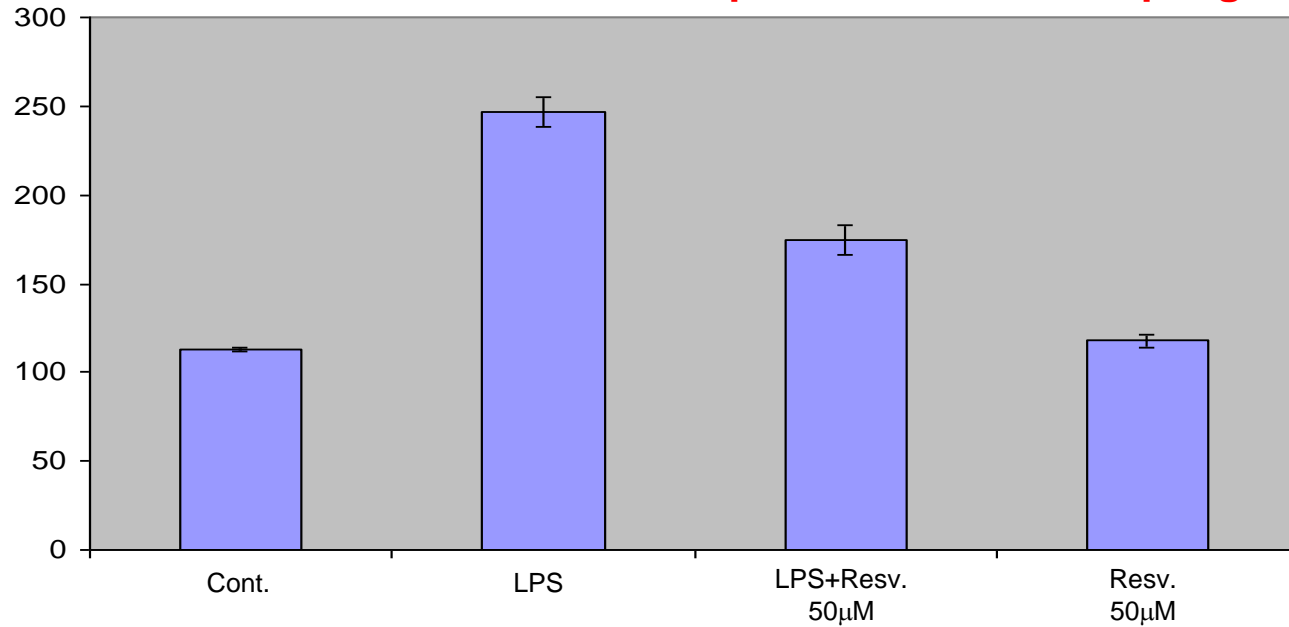
## LPS% **Effect of resveratrol on ROS production in RAW macrophages**



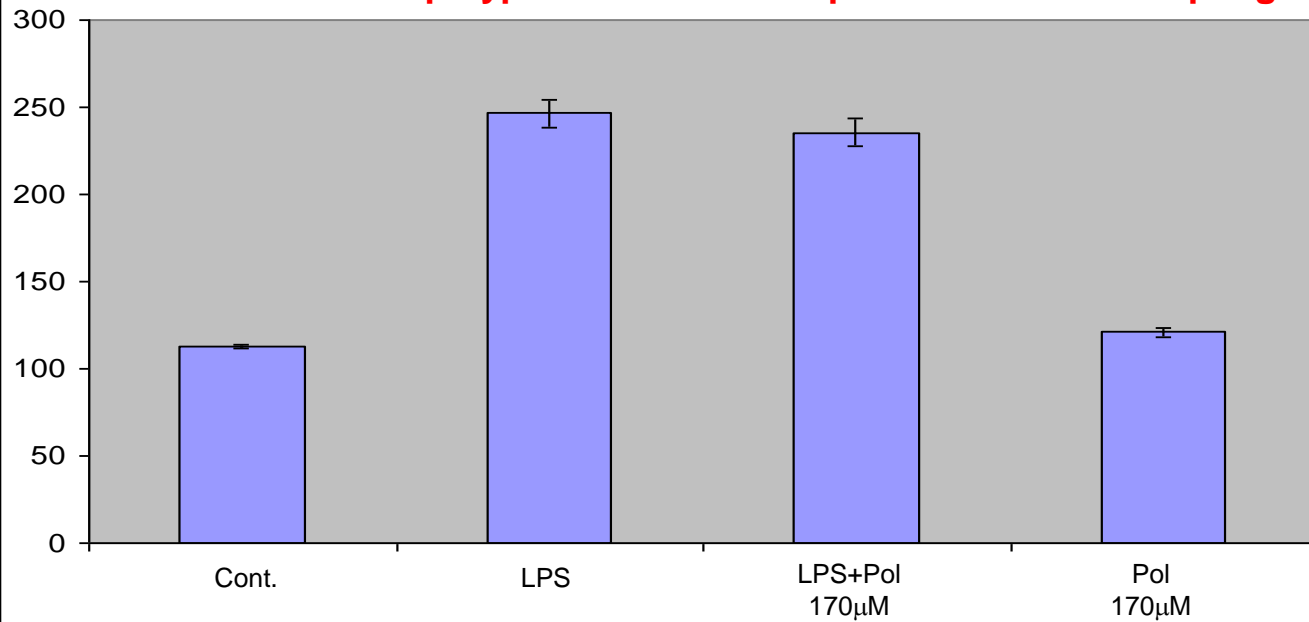
## LPS% **Effect of red wine extract on ROS production in RAW macrophages**



**OD450** **Effect of resveratrol on TNF- $\alpha$  production in macrophages**



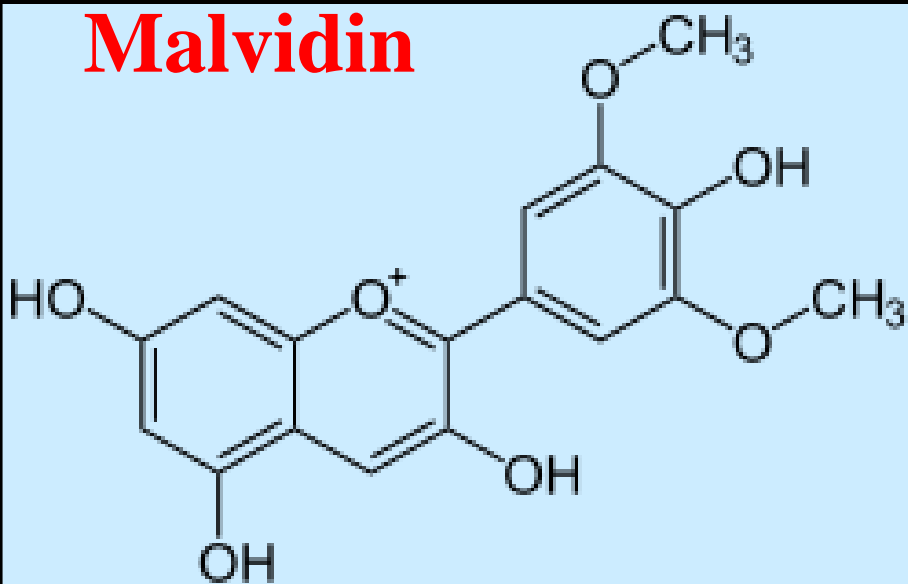
**OD450** **Effect of red wine polyphenols on TNF- $\alpha$  production in macrophages**



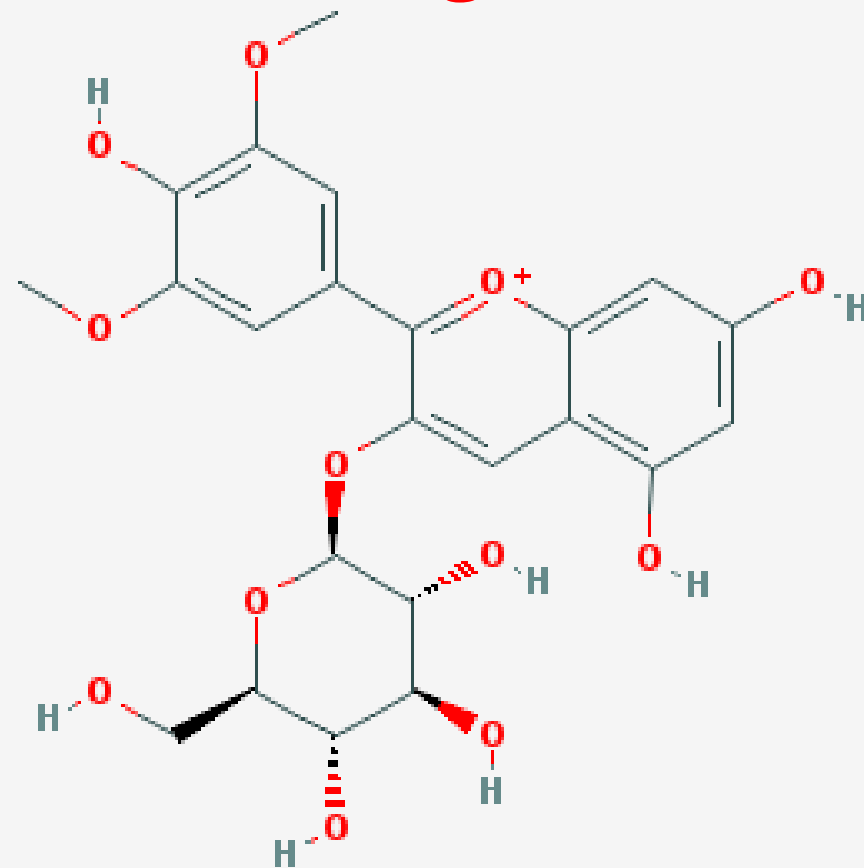


**Malvidin and its glucoside occur in much higher concentration in red wine than resveratrol, and suppress oxidative stress, inflammation and protect mitochondria**

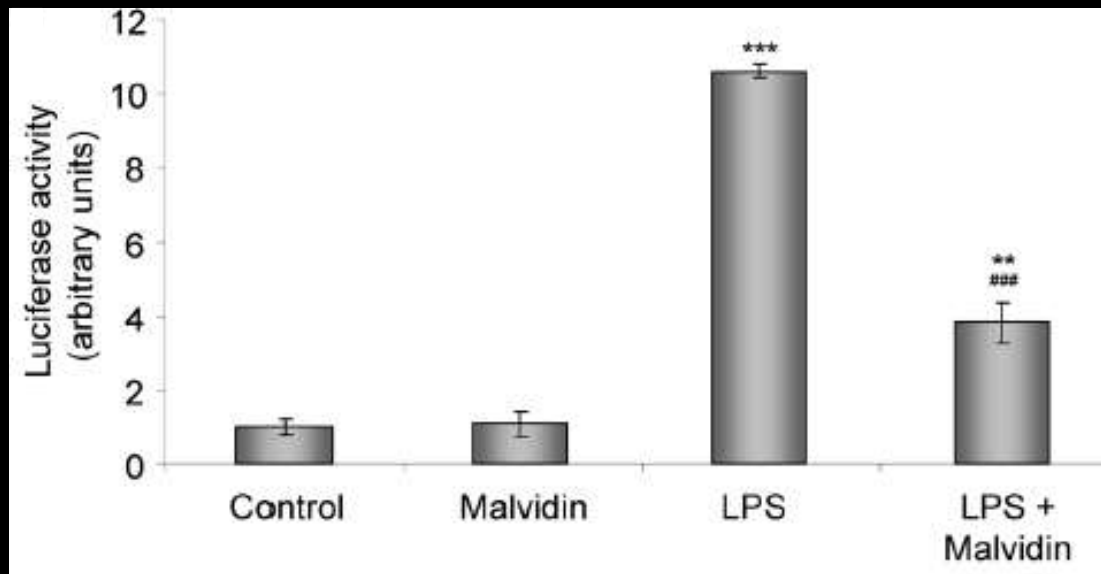
**Malvidin**



**Malvidin-3-glucoside**

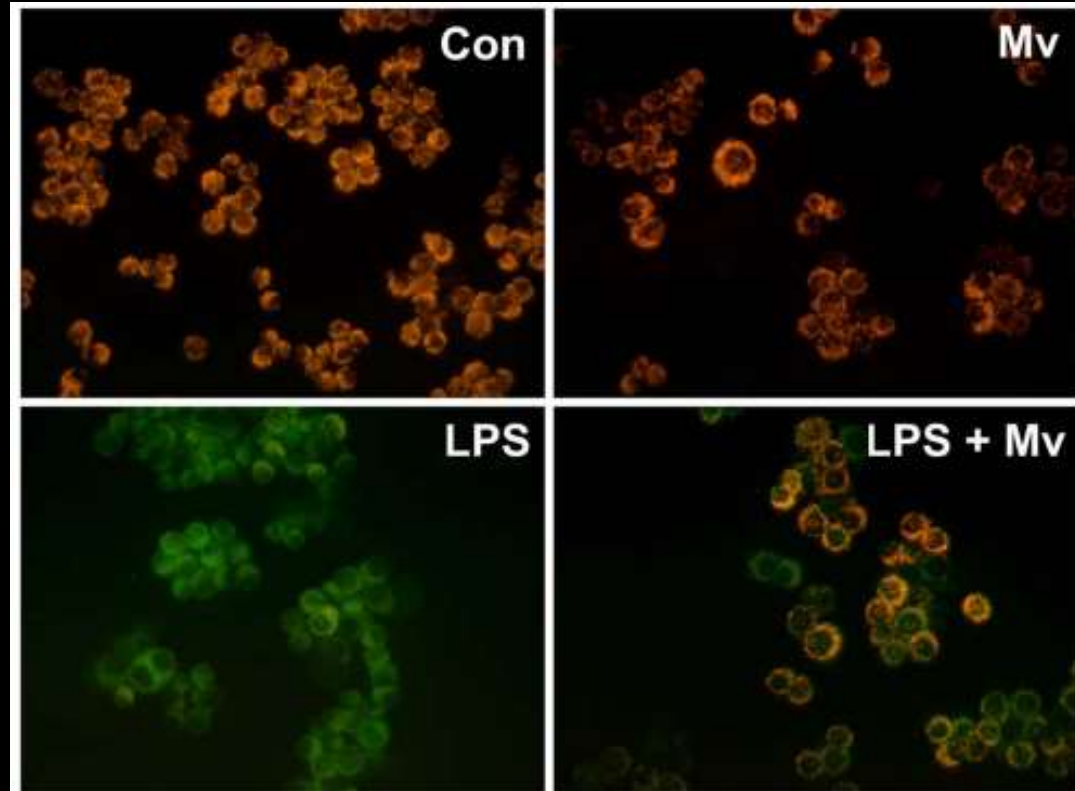


Effect of malvidin on LPS induced activation of NF $\kappa$ B by luciferase reporter assay after 1 mg/mL LPS exposure for 24 hours in RAW 264.7 cells

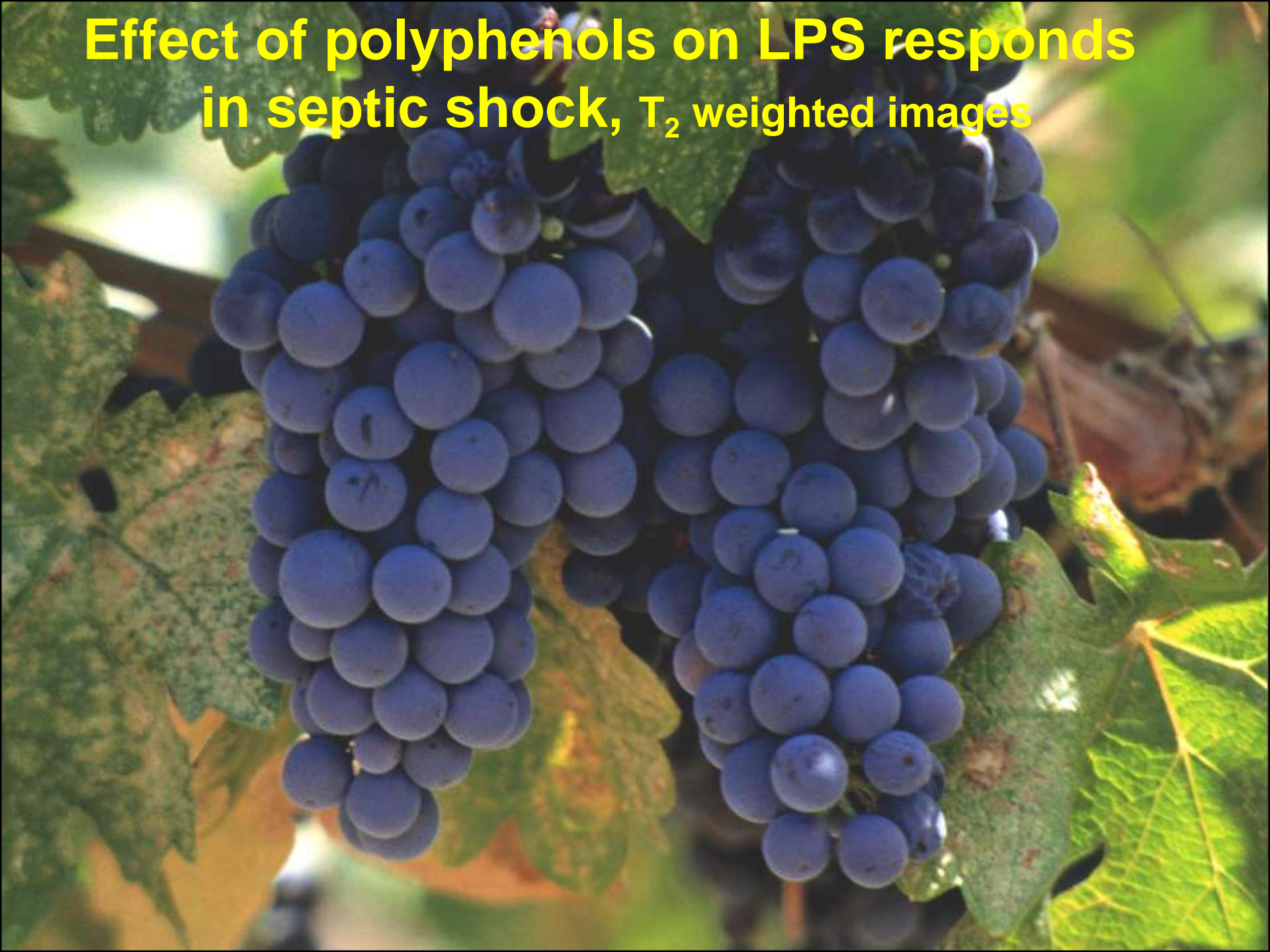


In red wines MALVIDIN and its glycoside are present at much higher concentrations than resveratrol!

Effect of LPS and malvidin on mitochondrial membrane potential of RAW 264.7 macrophages by JC-1. Mitochondria with normal membrane potential are red; mitochondria with collapsed membrane potential are green.

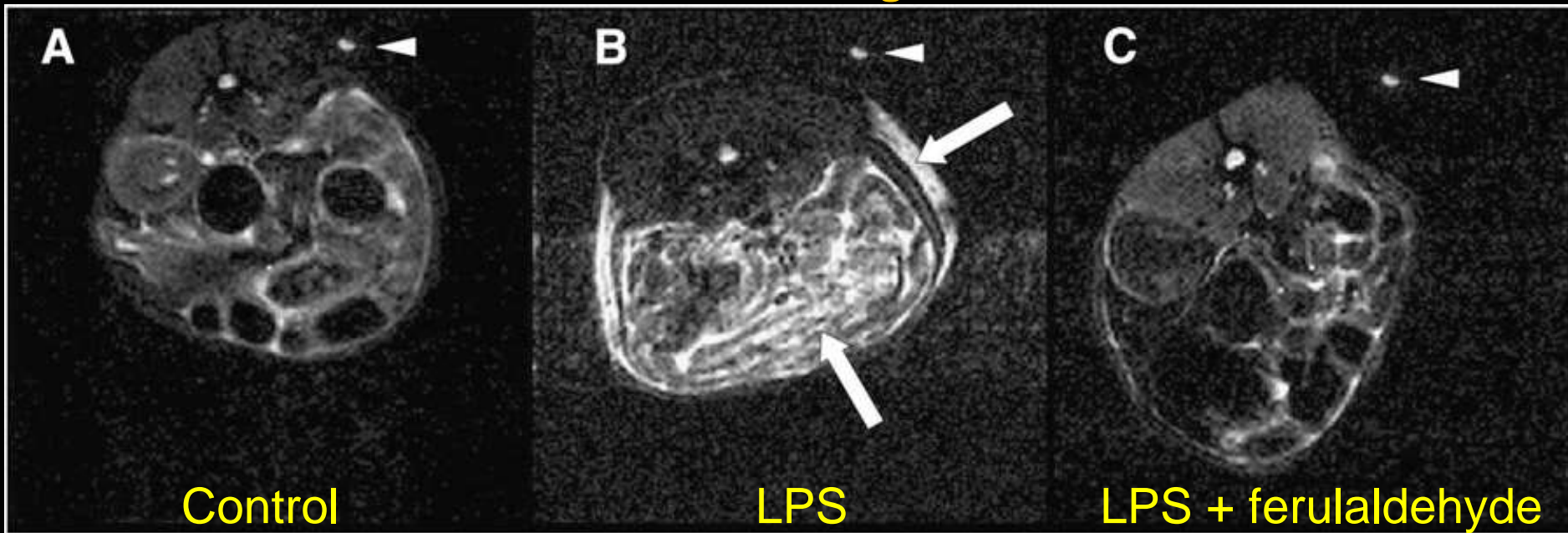


**Effect of polyphenols on LPS responds  
in septic shock, T<sub>2</sub> weighted images**

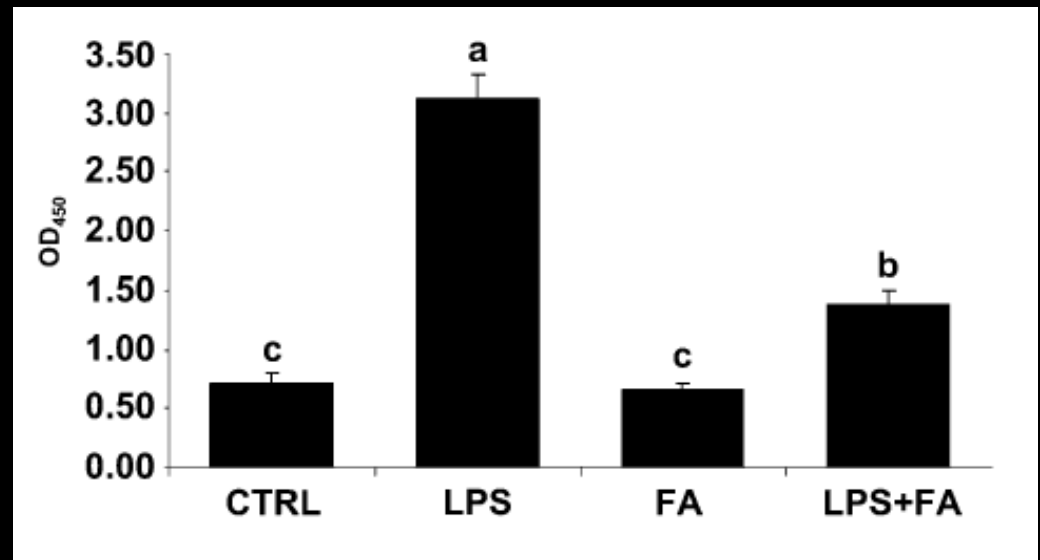


# Ferulaldehyde – a polyphenol metabolit – inhibits NF- $\kappa$ B activation and inflammation determined from T<sub>2</sub> weighted MRI imaging

## Abdominal region

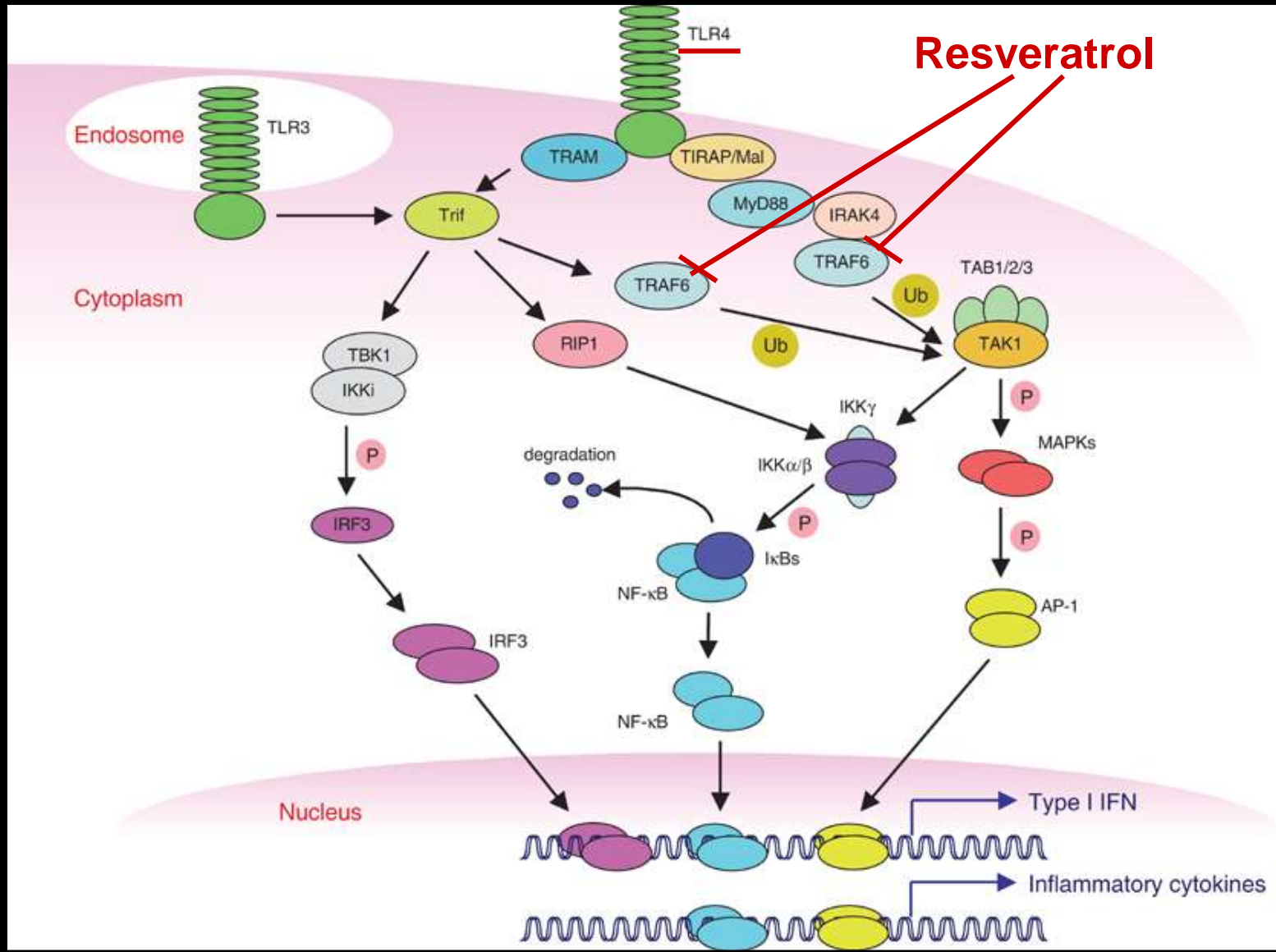


Resveratrol and its metabolit - Ferulaldehyde - suppresses LPS-induced binding to NF- $\kappa$ B to target sequences

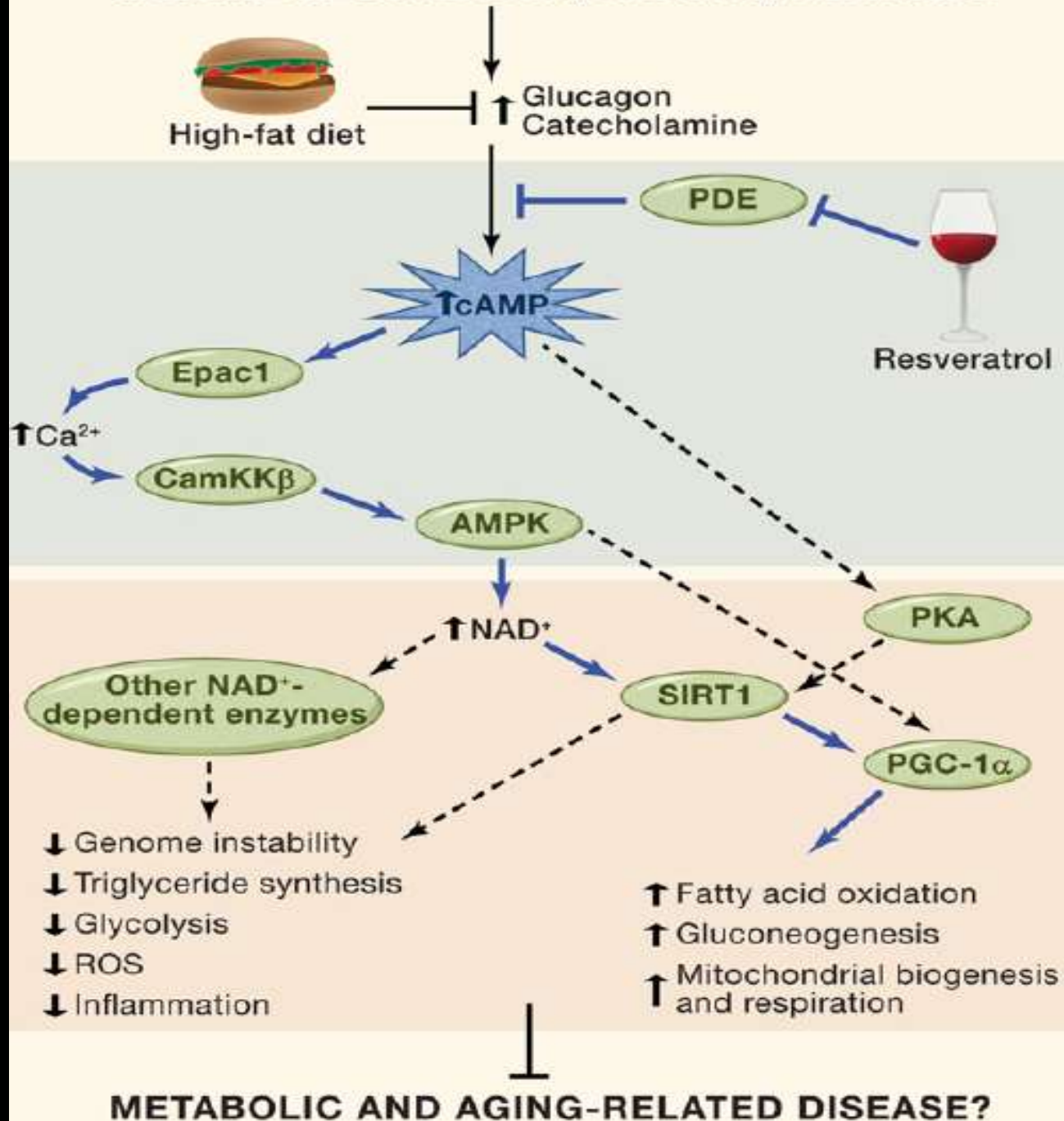


Resveratrol, by suppressing LPS-induced TRAF6 expression and ubiquitination, attenuates the LPS-induced TLR4-TRAF6-MAP kinase and Akt pathways that can be significant in its anti-inflammatory effects

*J Nutr Biochem.* 2013; 24,819-23.



# CALORIE RESTRICTION, FASTING, EXERCISE



## One possible protective mechanism of resveratrol and red wine.

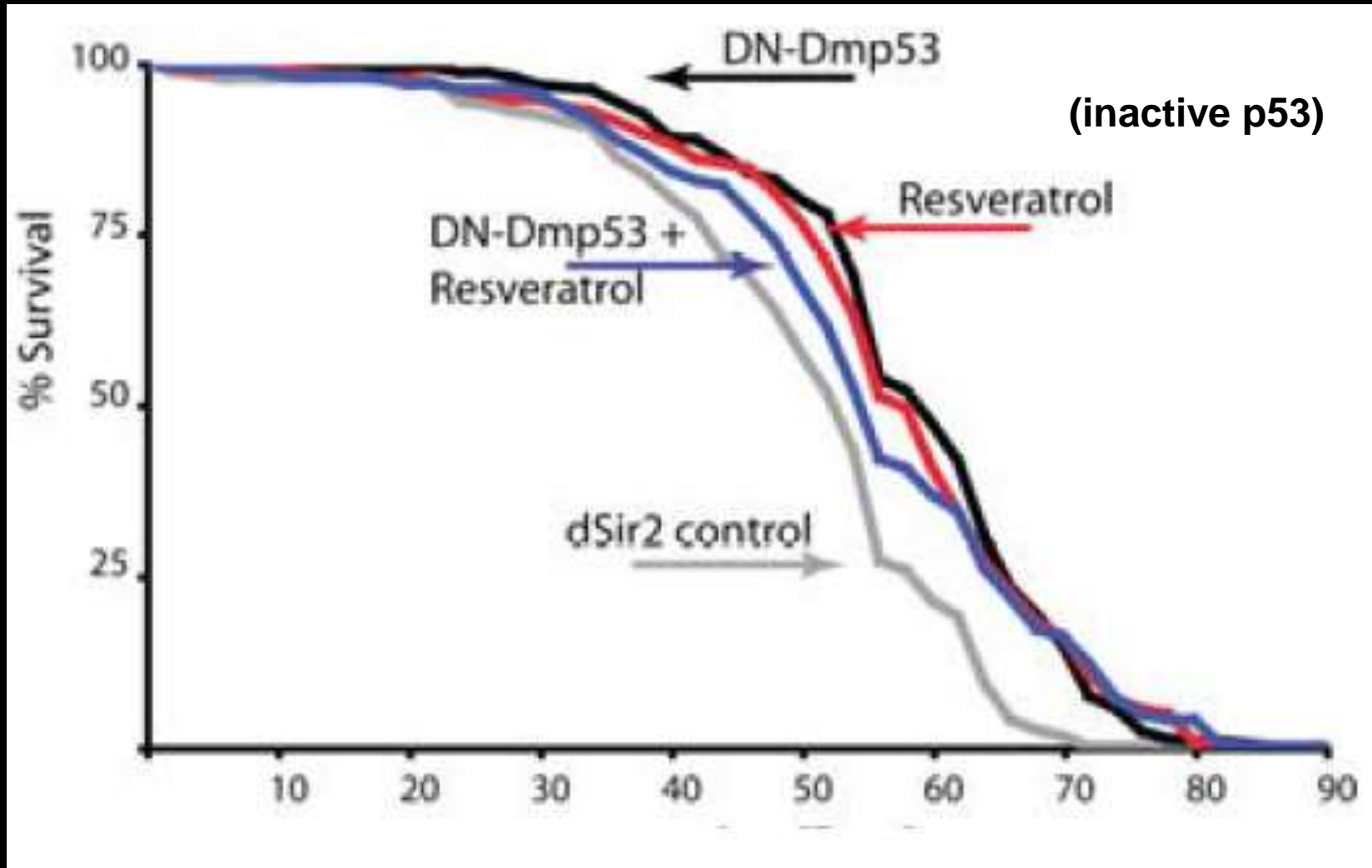
Dietary, Behavioral, and Pharmacologic Inputs Converge on cAMP-AMPK-SIRT1 Signaling to Produce Metabolic Benefits.

*Cell.* 2012 Feb 3;148(3):387-9.

Resveratrol and sildenafil synergistically improve diabetes-associated erectile dysfunction in streptozotocin-induced diabetic rats.

Bai & An. *Life Sci.* 2015 15;135:43-8.

# Resveratrol has minimal longevity effect on *D. melanogaster*



Moderate wine drinking increases the quantity of circulating endothelial progenitor cells in human. *Arterioscler Thromb Vasc Biol.* 2010 Apr;30(4):869-77.

***That is, wine drinking promotes regeneration in elderly!!!***

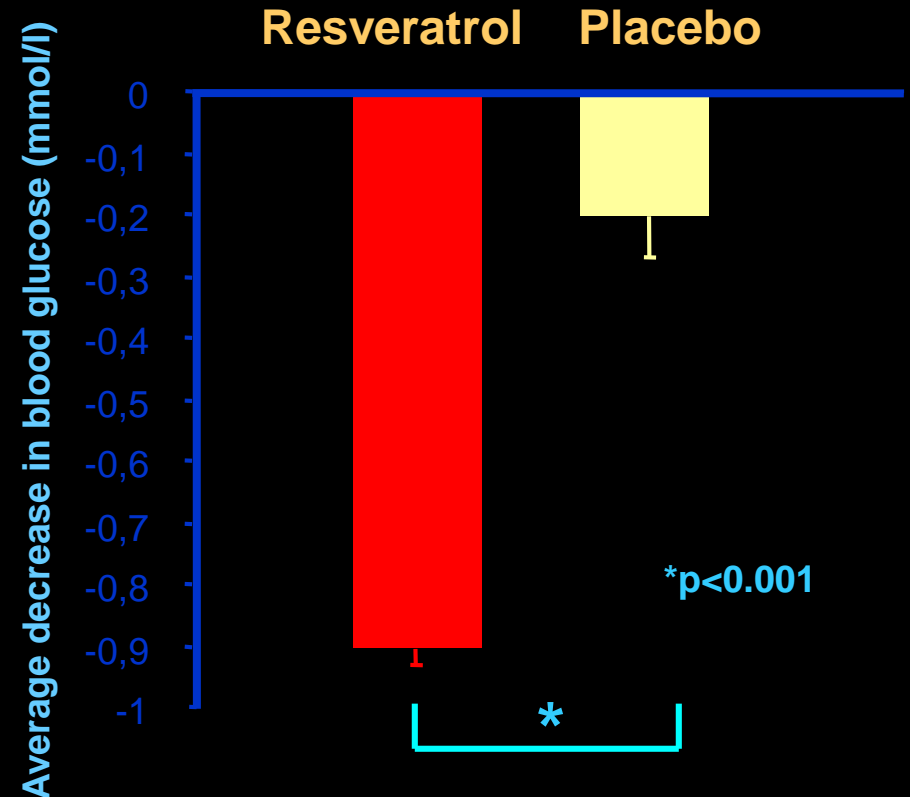
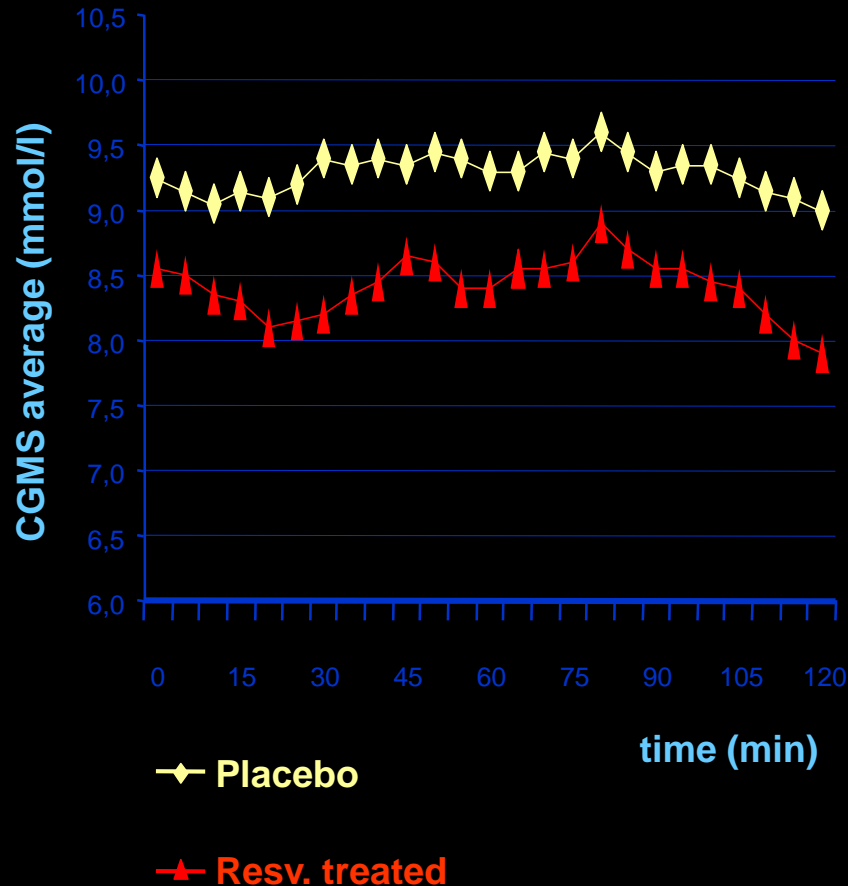
# **Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients**

**Br J Nutr. 2011 Aug;106(3):383-9. Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients. Brasnyó P, Molnár GA, Mohás M, Markó L, Laczy B, Cseh J, Mikolás E, Szijártó IA, Mérei A, Halmai R, Mészáros LG, Sümegi B, Wittmann I.**

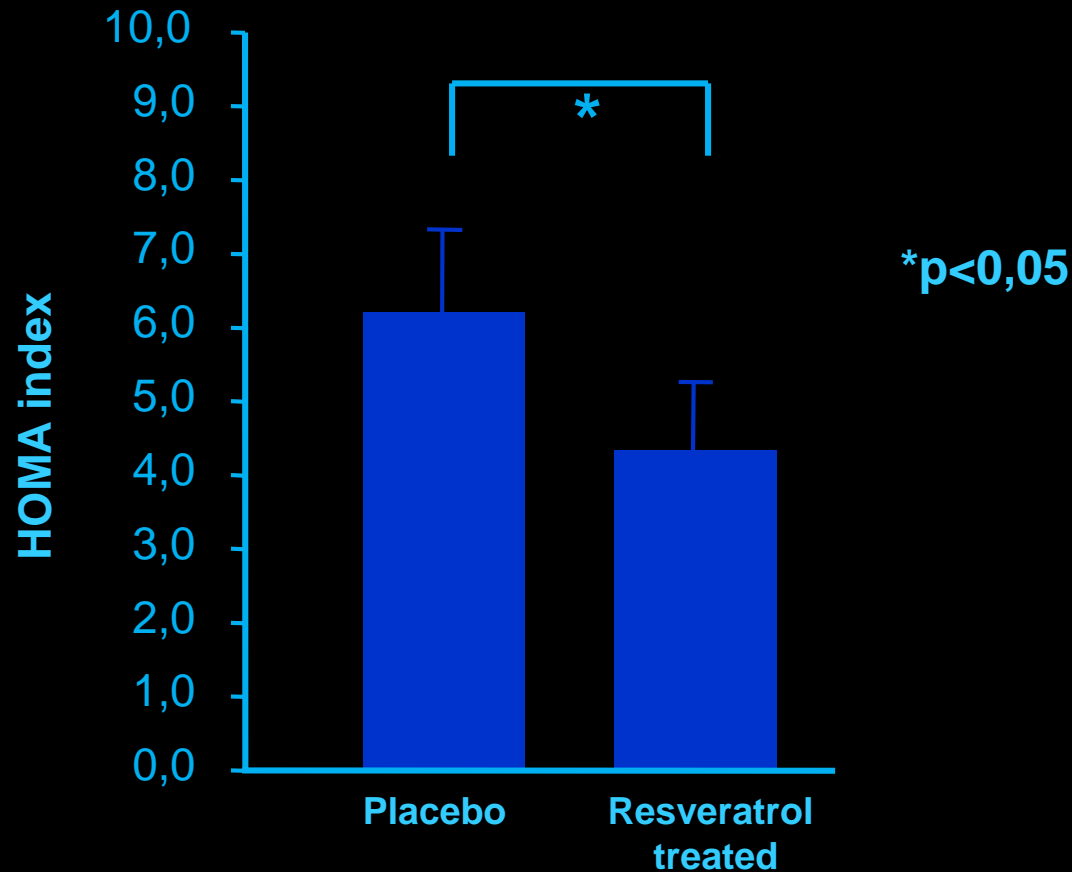


# Glucose monitoring after standard food consumption (n=8)

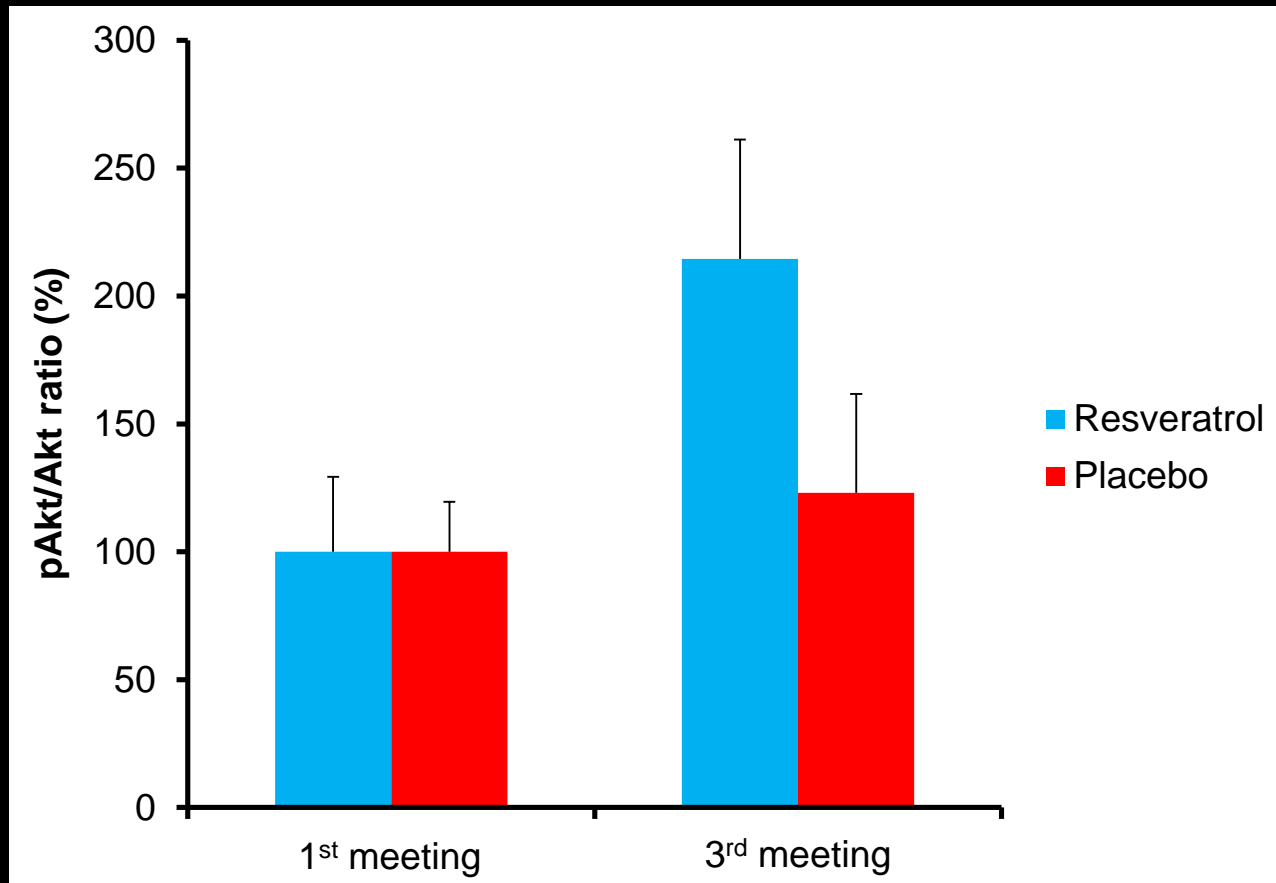
Blood glucose levels of Placebo and Resveratrol treated patients



# Effect of Resveratrol treatment on HOMA index

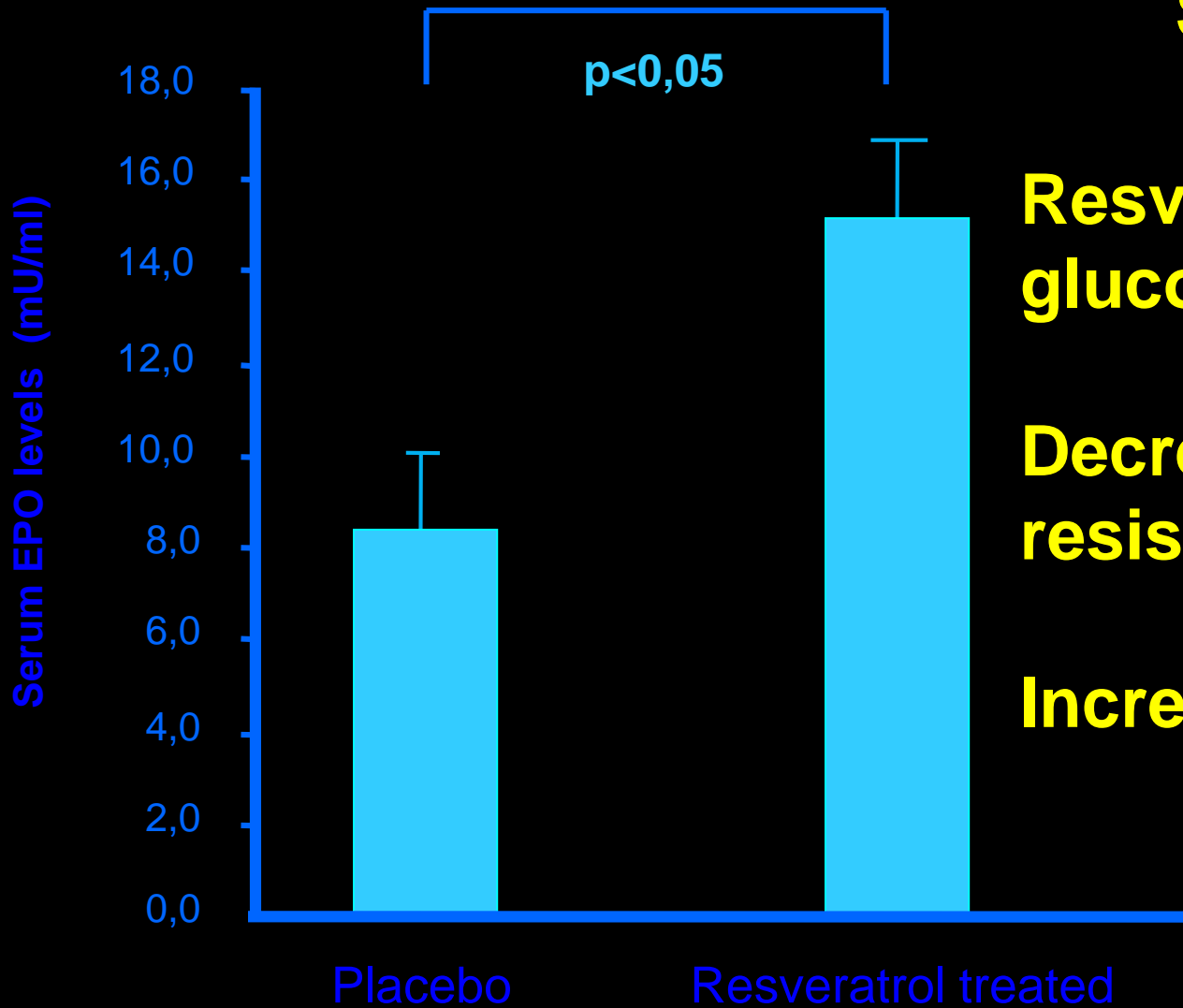


# Resveratrol activates Akt phosphorylation (Ser473) in thrombocytes



**p = 0,037**

# Effect of Resveratrol on serum erythropoietin (EPO)



## SUMMARY

**Resveratrol improves glucose utilization**

**Decreases insulin resistance in man**

**Increases EPO level**

# **Cardioprotection by resveratrol: A human clinical trial in patients with stable coronary artery disease**

Several beneficial effects of resveratrol (RES), a natural antioxidant present in red wine have already been described. The aim of our study was to investigate if RES had a clinically measurable cardioprotective effect in patients after myocardial infarction.

In this double-blind, placebo controlled trial 40 post-infarction Caucasian patients were randomized into two groups. One group received 10 mg RES capsule daily for 3 months.

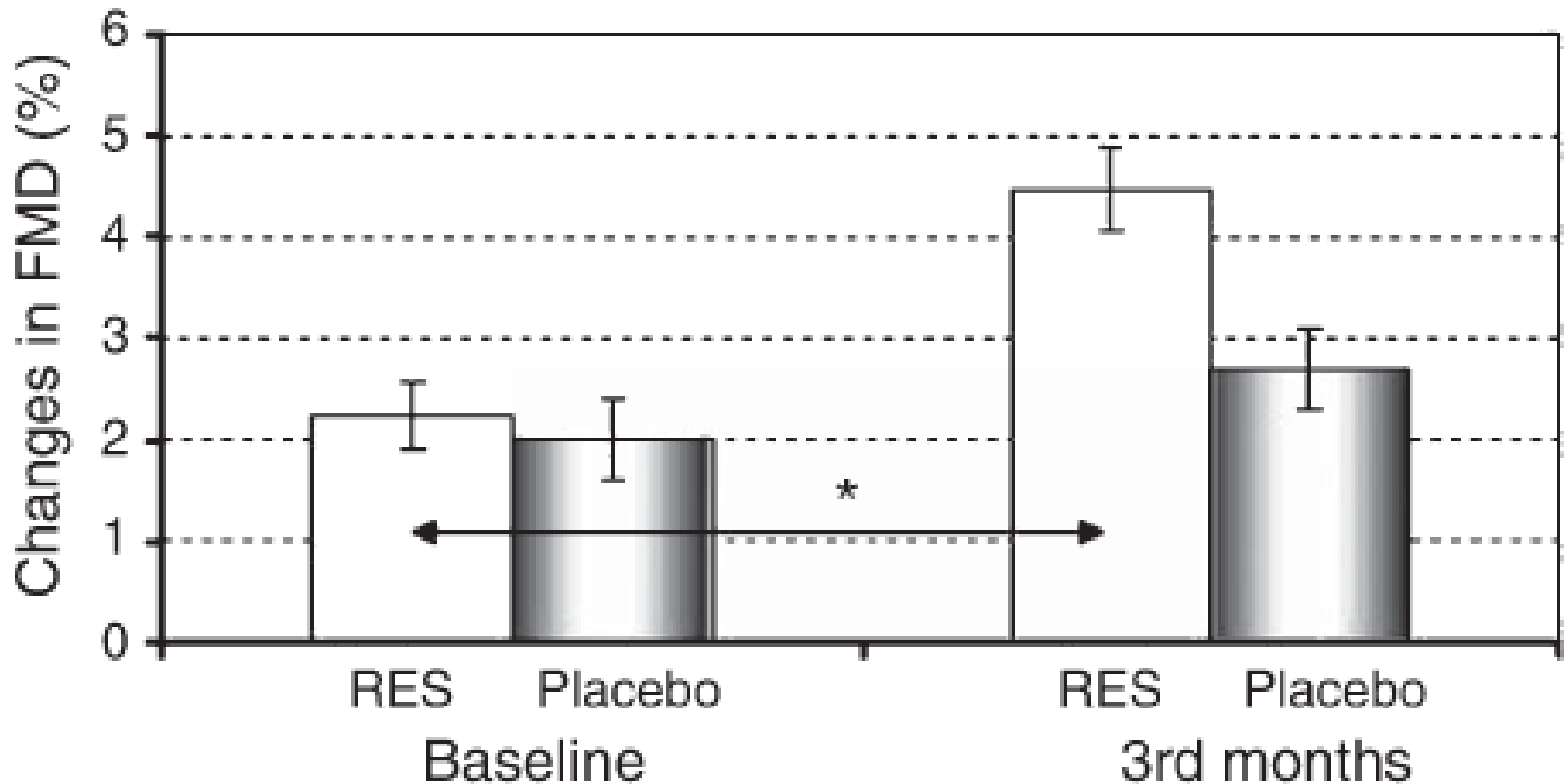
Systolic and diastolic left ventricular function, flow-mediated vasodilation (FMD), several laboratory and hemorheological parameters were measured before and after the treatment.

*Magyar et al. Clin Hemorheol Microcirc. 2012;50(3):179-87.*

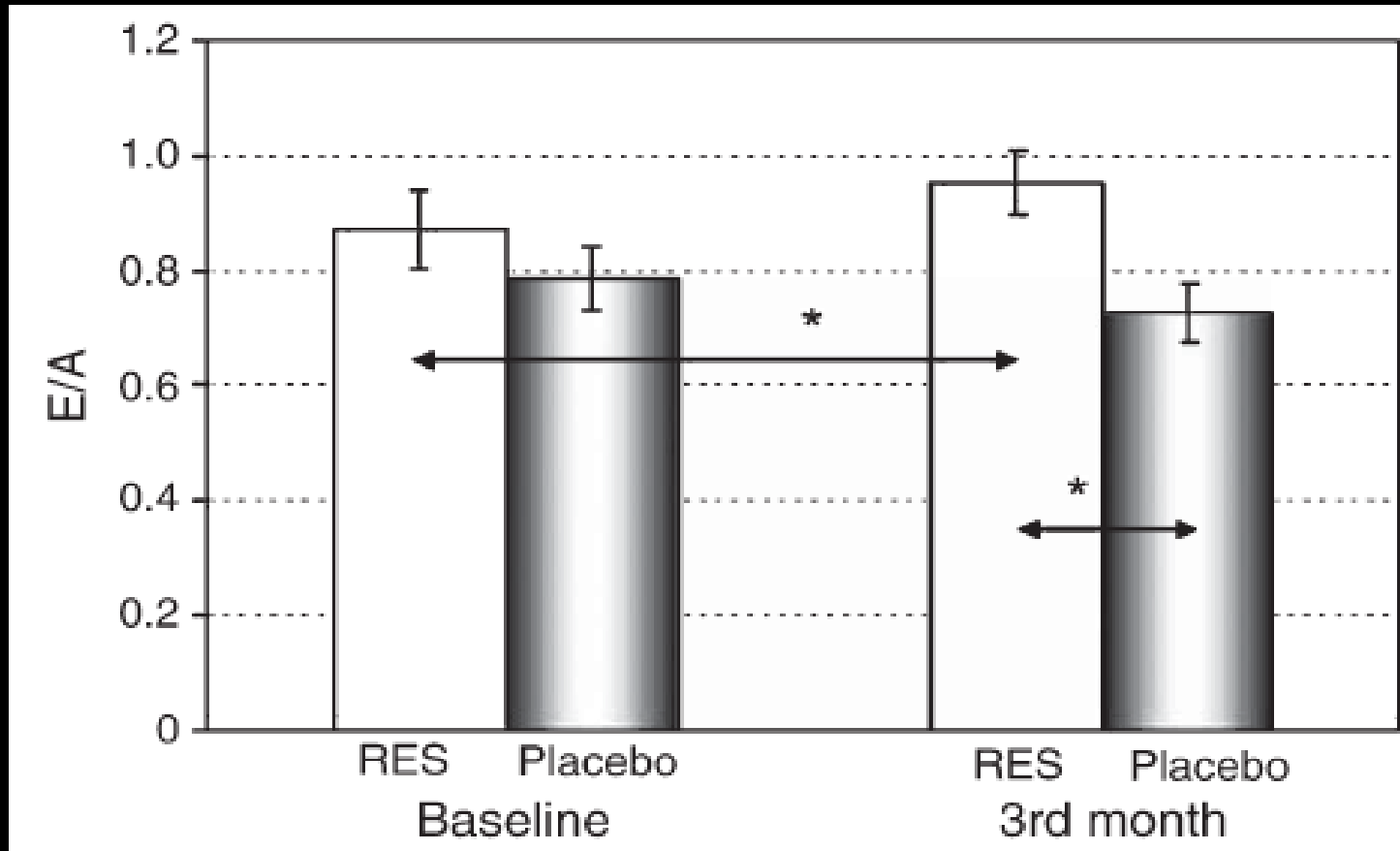
# Cardioprotection by resveratrol: A human clinical trial in patients with stable coronary artery disease

| Characteristics of patients         | Resveratrol-treated group ( <i>n</i> = 20) | Placebo-treated group ( <i>n</i> = 20) | <i>P</i> -value |
|-------------------------------------|--|--|-----------------|
| Male gender                         | 13   | 13                                     |                 |
| Age, year (mean ± SEM)              | 65.3 ± 9.7                                 | 67.4 ± 7.7                             | ns              |
| Major CV risk factors               |  |  |                 |
| Diabetes                            | 7 (35%)                                    | 8 (40%)                                | ns              |
| Hypertension                        | 20 (100%)                                  | 19 (95%)                               | ns              |
| Dyslipidemia                        | 13 (65%)                                   | 14 (70%)                               | ns              |
| Smoking                             | 3 (15%)                                    | 4 (20%)                                | ns              |
| Obesity (BMI > 30)                  | 8 (40%)                                    | 7 (35%)                                | ns              |
| BMI (kg/m <sup>2</sup> )            | 29.3 ± 2.1                                 | 28.1 ± 3.2                             | ns              |
| Secondary prevention drug treatment |  |  |                 |
| Antiplatelet drugs                  | 17 (85%)                                   | 18 (90%)                               | ns              |
| Salicylate                          | 15 (75%)                                   | 17 (85%)                               | ns              |
| Thienopyridine                      | 5 (25%)                                    | 7 (35%)                                | ns              |
| ACEI/ARB                            | 18 (90%)                                   | 18 (90%)                               | ns              |
| Beta-blockers                       | 18 (90%)                                   | 17 (85%)                               | ns              |
| Statins                             | 15 (75%)                                   | 16 (80%)                               | ns              |

**Effect of resveratrol on FMD (*Flow-mediated vasodilatation*)**  
**3 month after heart attack. Mean $\pm$ SEM, \* $p < 0.05$ %.**



# Effect of resveratrol on the left ventricular diastolic function in E/A value (ratio of early [E] to late [A] ventricular filling velocities). Mean $\pm$ SEM, . \* $p < 0.05$ .



These data show that resveratrol improved left ventricle diastolic function, endothelial function, lowered LDL-cholesterol level and protected against unfavourable hemorheological changes measured in 40 post-infarction patients with coronary artery disease (CAD).



# General conclusion

***In vitro* and in animal disease models resveratrol is protective, but has limited effects in normal cells and animals.**

**In clinical studies, Resveratrol generally has protective effects in several diseases, but it has mild effects in healthy people!**

# Participants

A close-up photograph of a bunch of dark purple grapes hanging from a vine with green leaves. The grapes are the central focus, showing their individual round shapes and the way they cluster together. The background is slightly blurred, showing more of the vine and leaves, which are bathed in natural light.

Hocsak E, Jakus PB, Kalman N, Antus C, Radnai B, Tucsek Z, Gallyas F Jr, Veres B, Mark L, Brasnyo P, Molnár GA, Mohás M, Markó L, Laczy B, Cseh J, Mikolás E, Szijarto IA, Merei A, Halmai R, Meszaros LG, Wittmann I, Magyar K, Halmosi R, Palfi A, Feher G, Czopf L, Fulop A, Battyany I, Szabados E and Toth K.