Modulation du Stress Oxydant
Nouveaux Concepts pour de Nouvelles Applications
Paris, 31 mai & 1 juin, 2016

Potential of polyphenol-rich food to improve vascular health and prevent endothelial senescence

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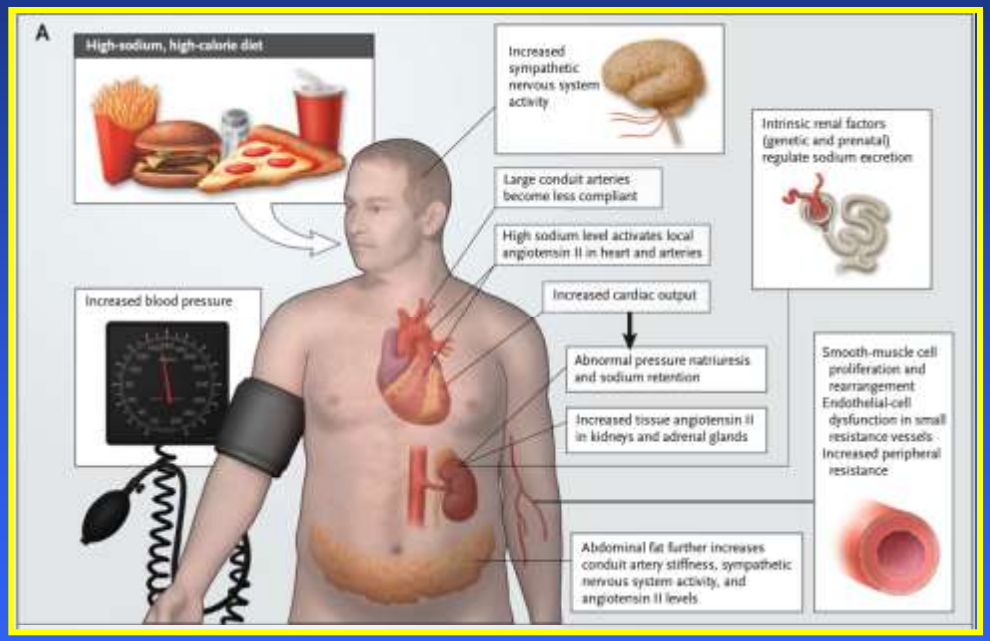
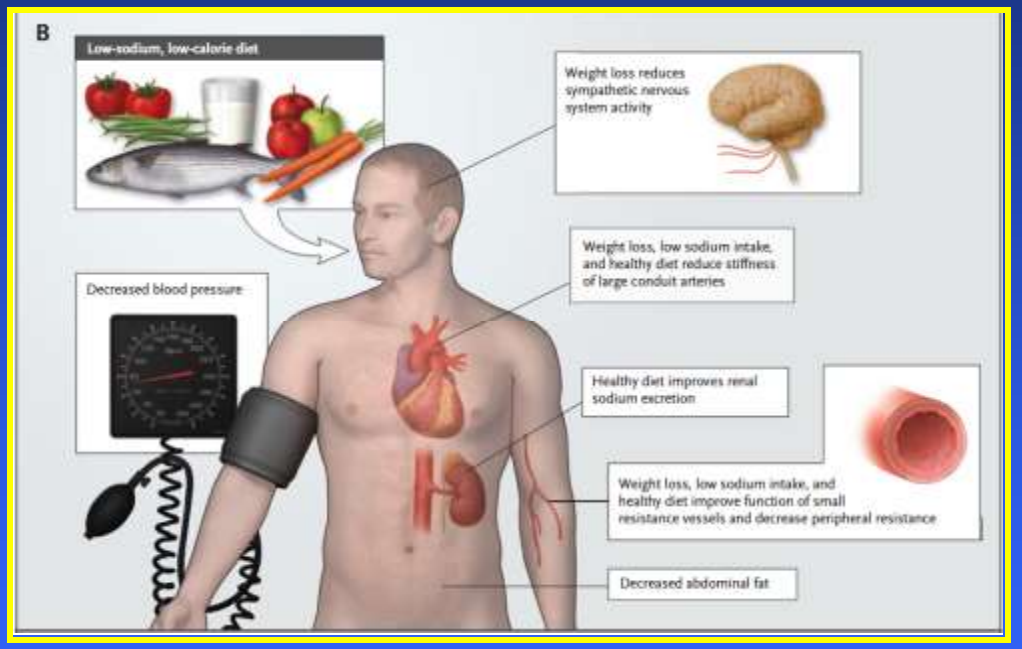
Diet and Cardiovascular Health

Unhealthy Diet



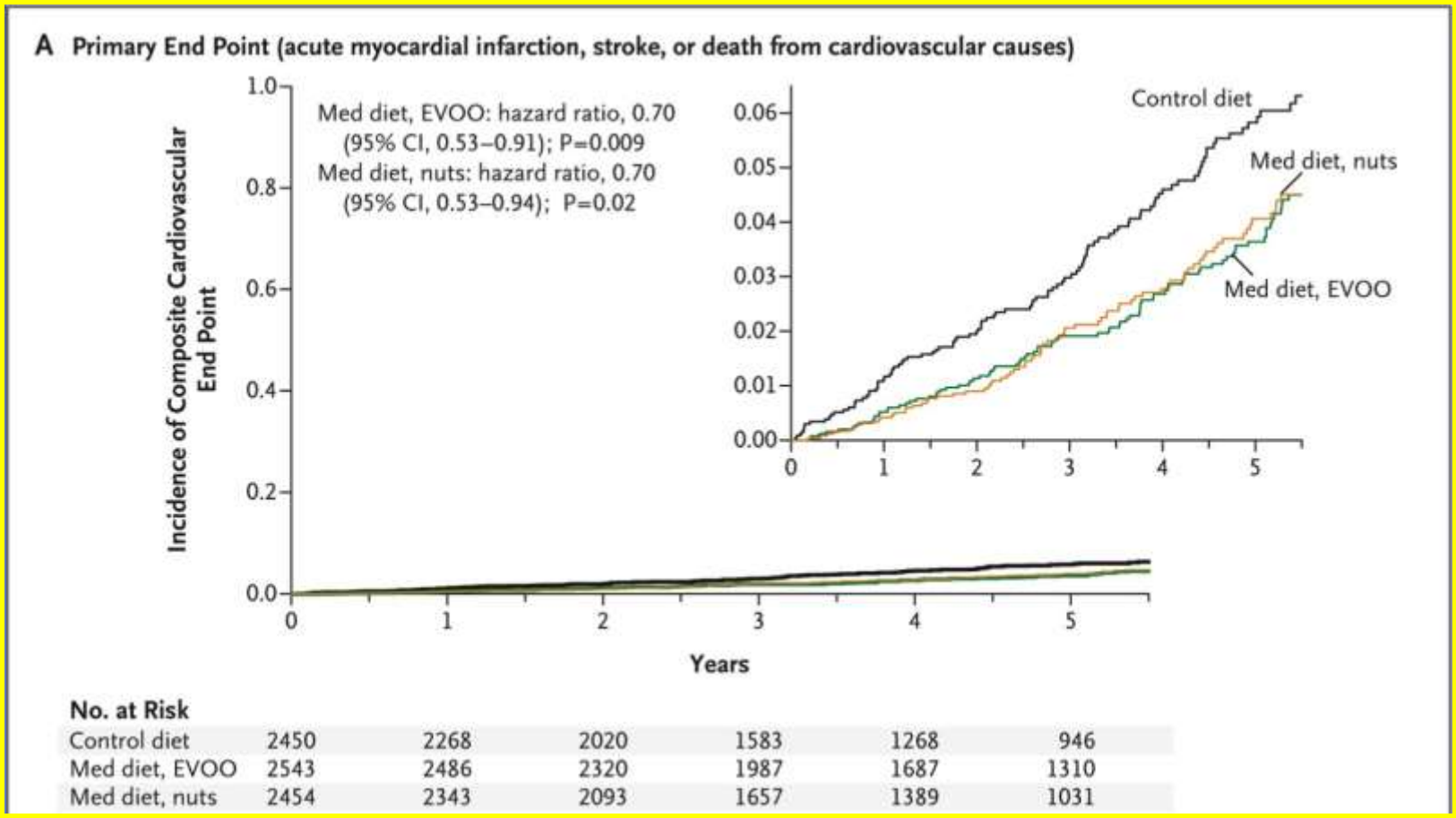
Healthy Diet
(DASH diet, Mediterranean diet)



Sacks and Campos
NEJM 2010;362:2102-12

Primary Prevention Study of Cardiovascular Disease and the Mediterranean Diet

- 7447 persons at high cardiovascular risk who were initially free of cardiovascular disease

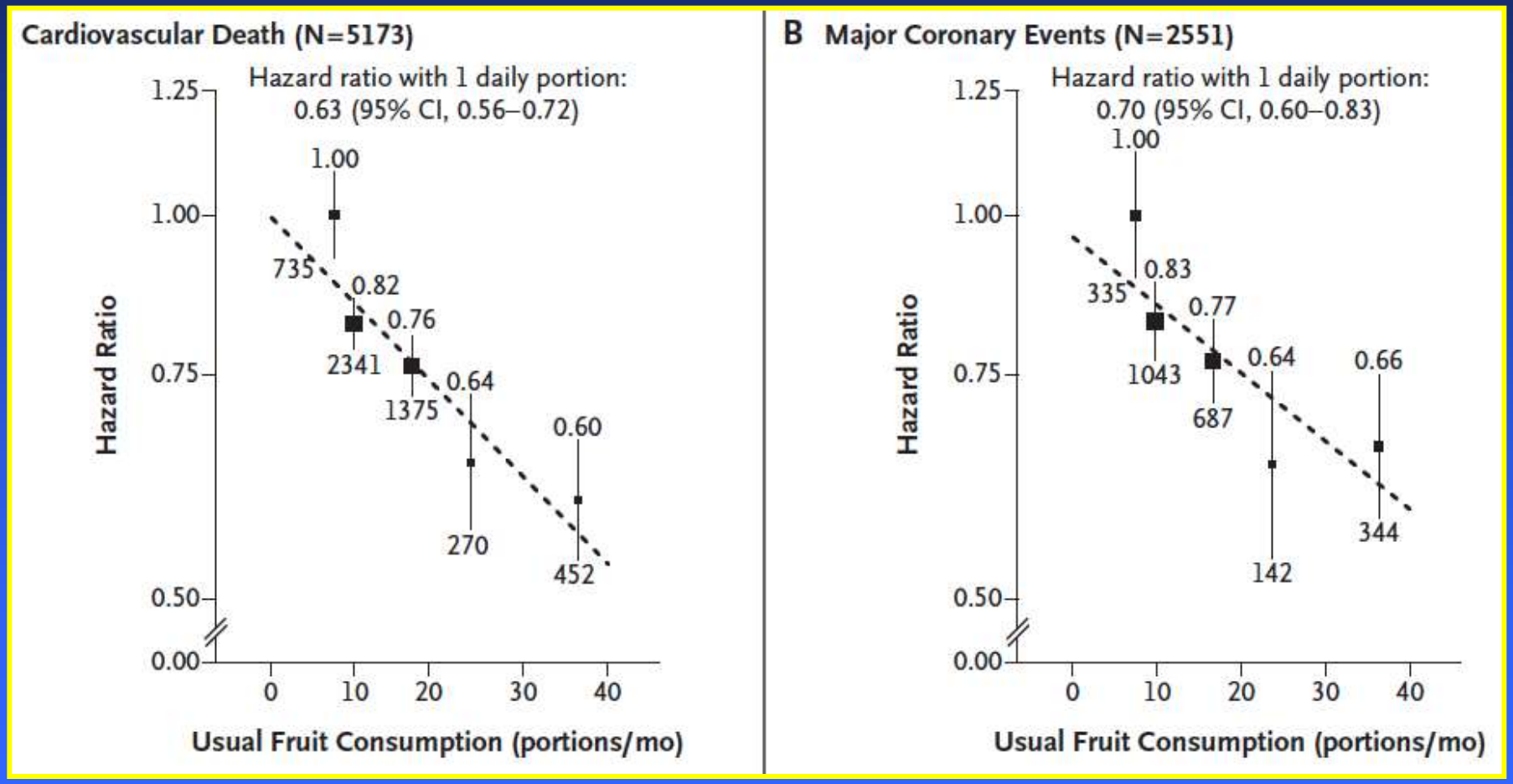


Relative risk reduction of approximately 30 %

Estruch et al., NEJM. 2013;368:1279-1290

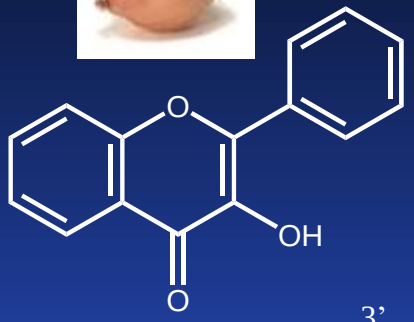
Fresh Fruit Consumption and Major Cardiovascular Disease in China

- 2004-2008: 512,891 adults, 30 to 79 years of age

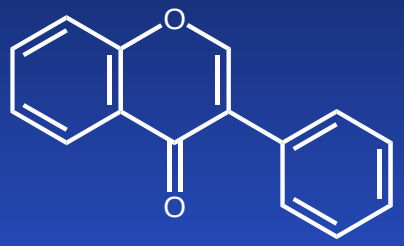


Du et al., NEJM. 2016;374:1332-1343

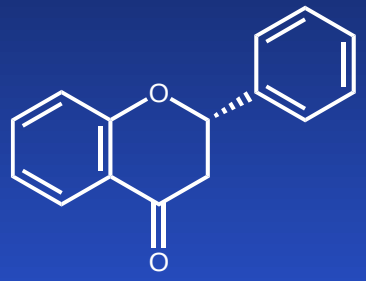
Structure and Sources of Flavonoids



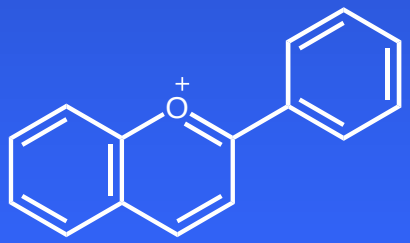
Flavonol
(quercetin, kaempferol)



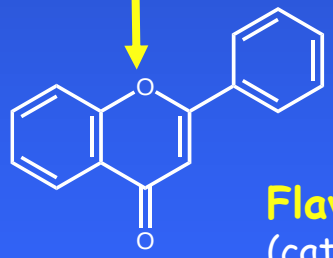
Isoflavones
(daidzein, genistein)



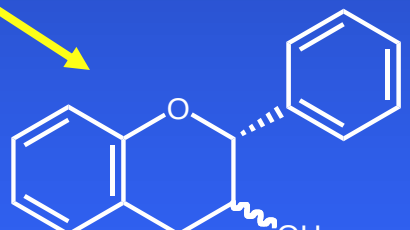
Flavonone
(naringenin, hesperitin)



Anthocyanins
(delphinidin, malvidin)



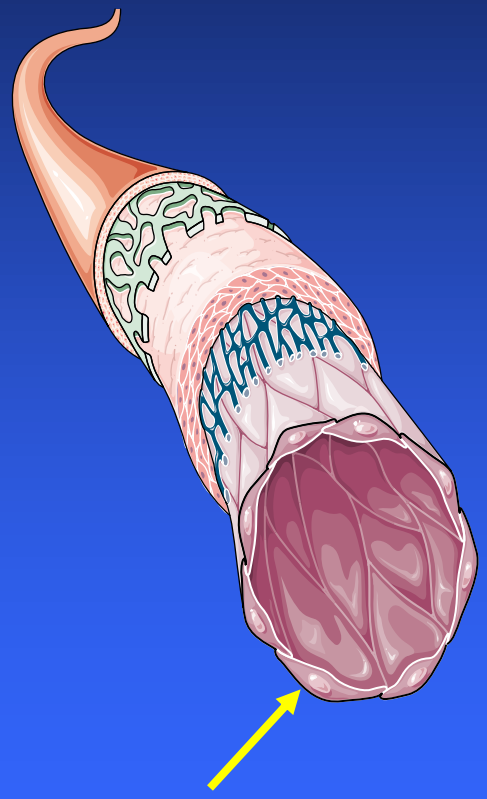
Flavone
(luteolin, apigenin)



Flavan-3-ol
(catechin, epicatechin)

Role of the Endothelium in Vascular Homeostasis

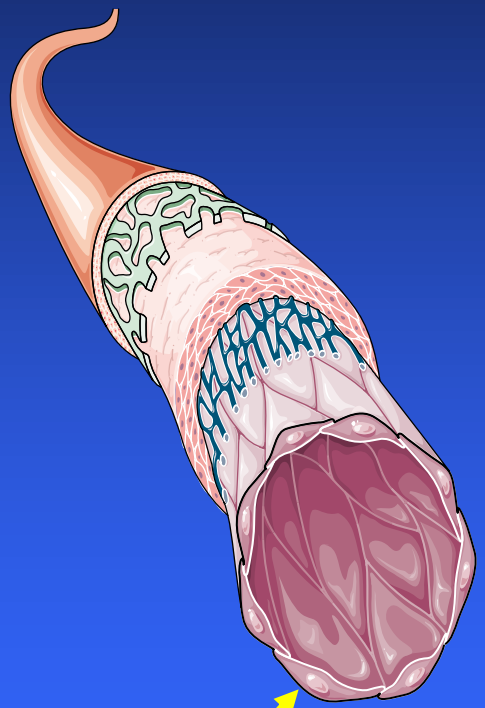
Healthy artery



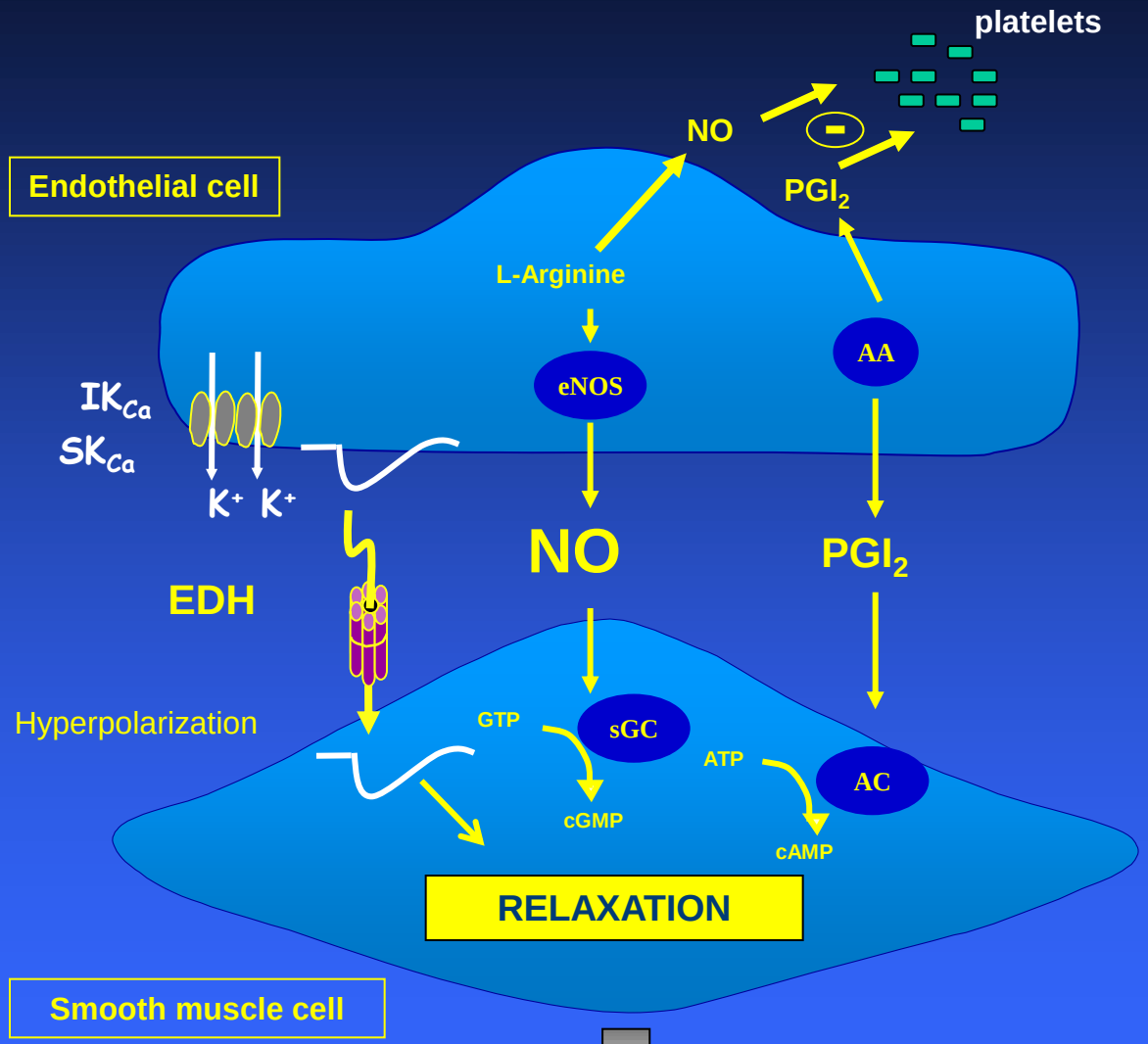
Endothelial cells

Role of the Endothelium in Vascular Homeostasis

Healthy artery

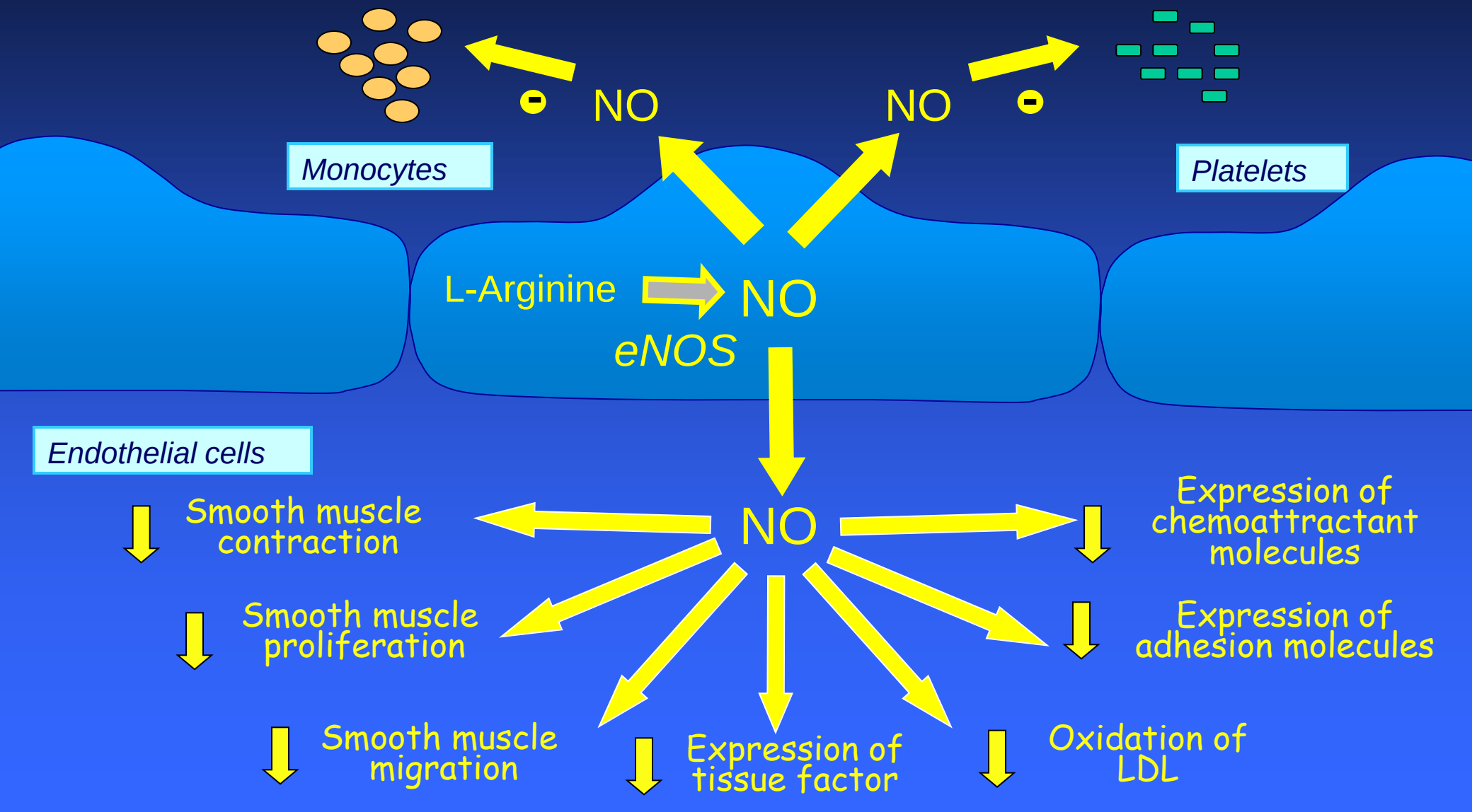


Endothelial cells

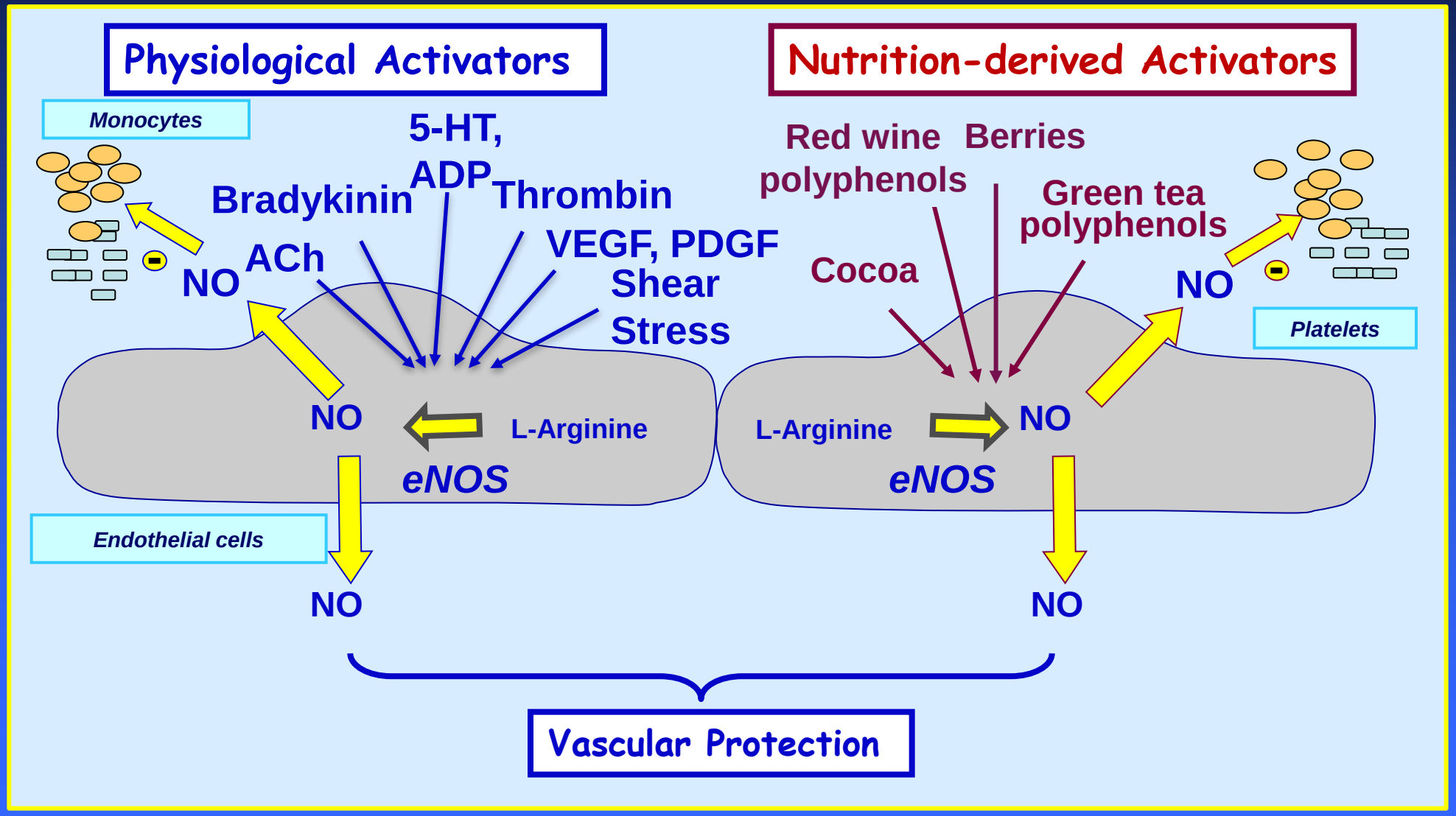


Vascular Protection

Endothelium-derived Nitric Oxide and Vascular Homeostasis

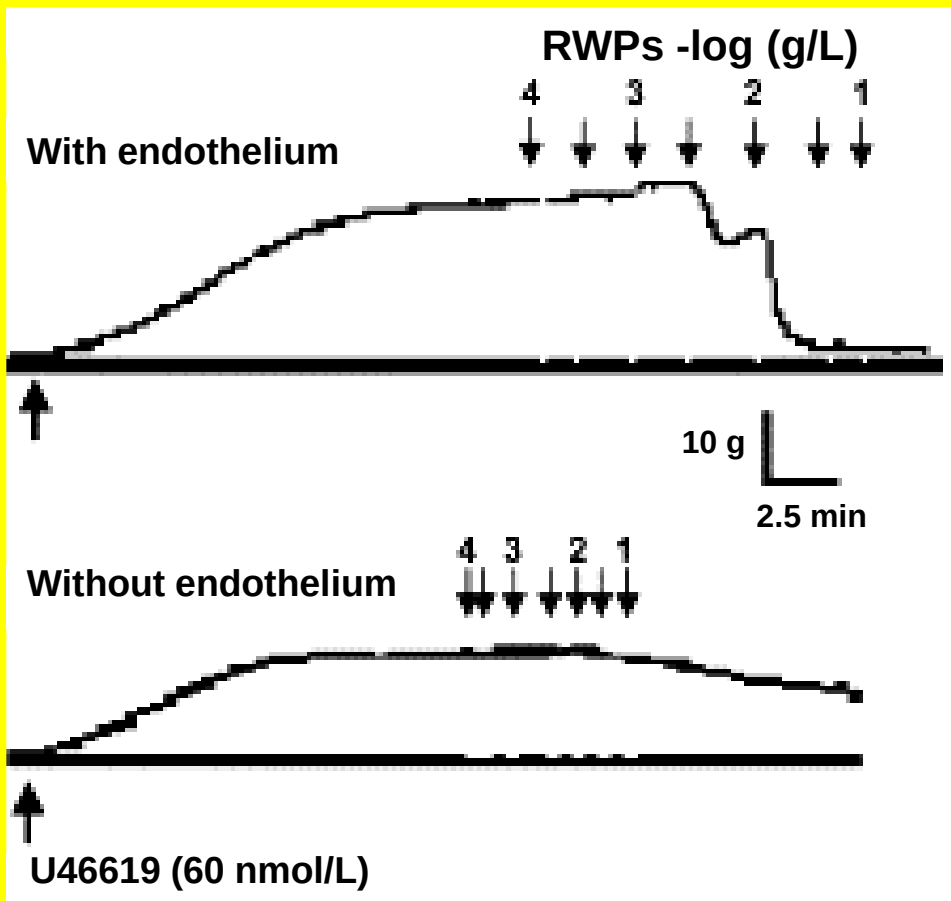


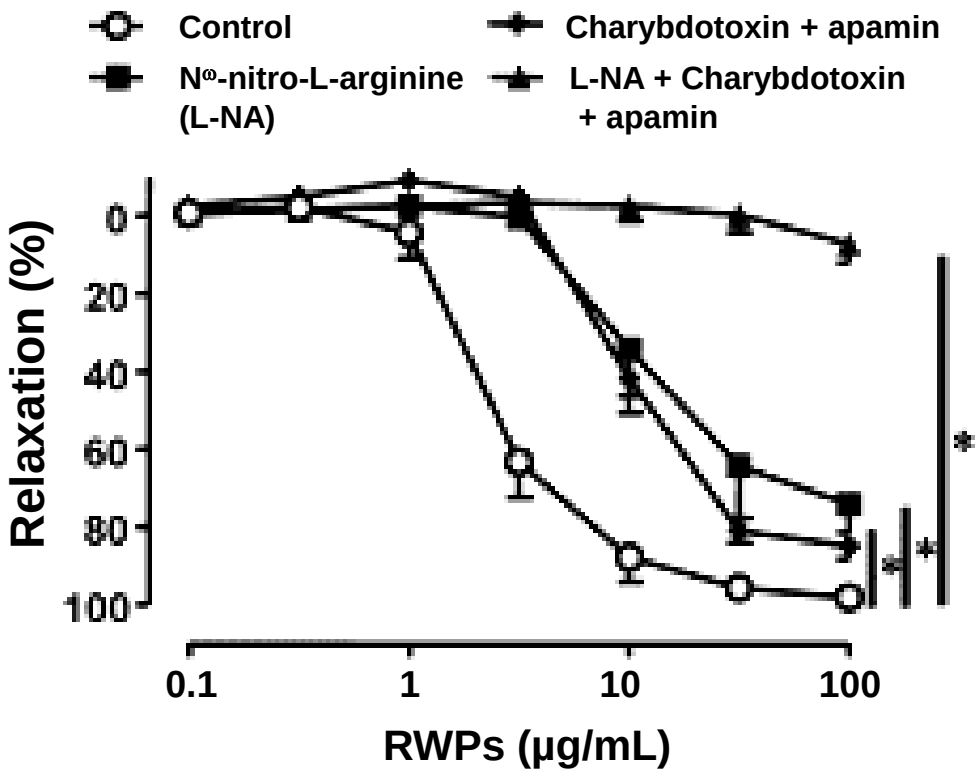
Physiological and Nutrition-derived Activators of the Endothelial Formation of NO



Red Wine Polyphenols cause Endothelium-Dependent Relaxations in the Porcine Coronary Artery

(in the presence of indomethacin)

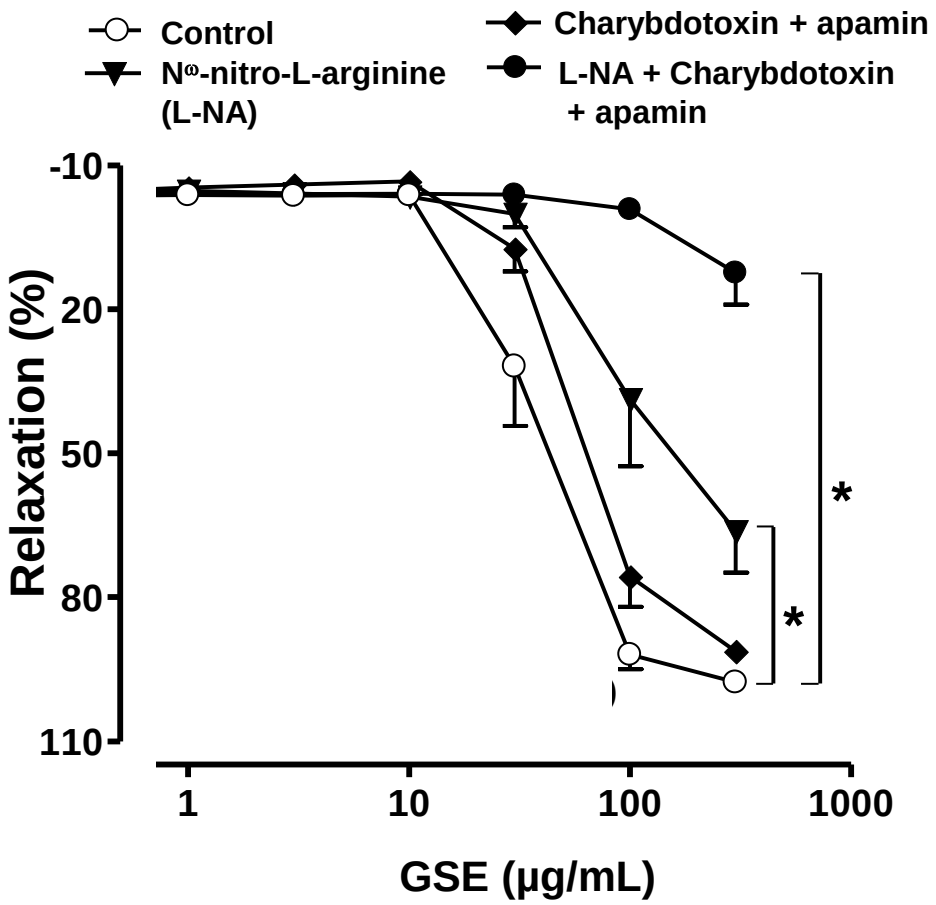


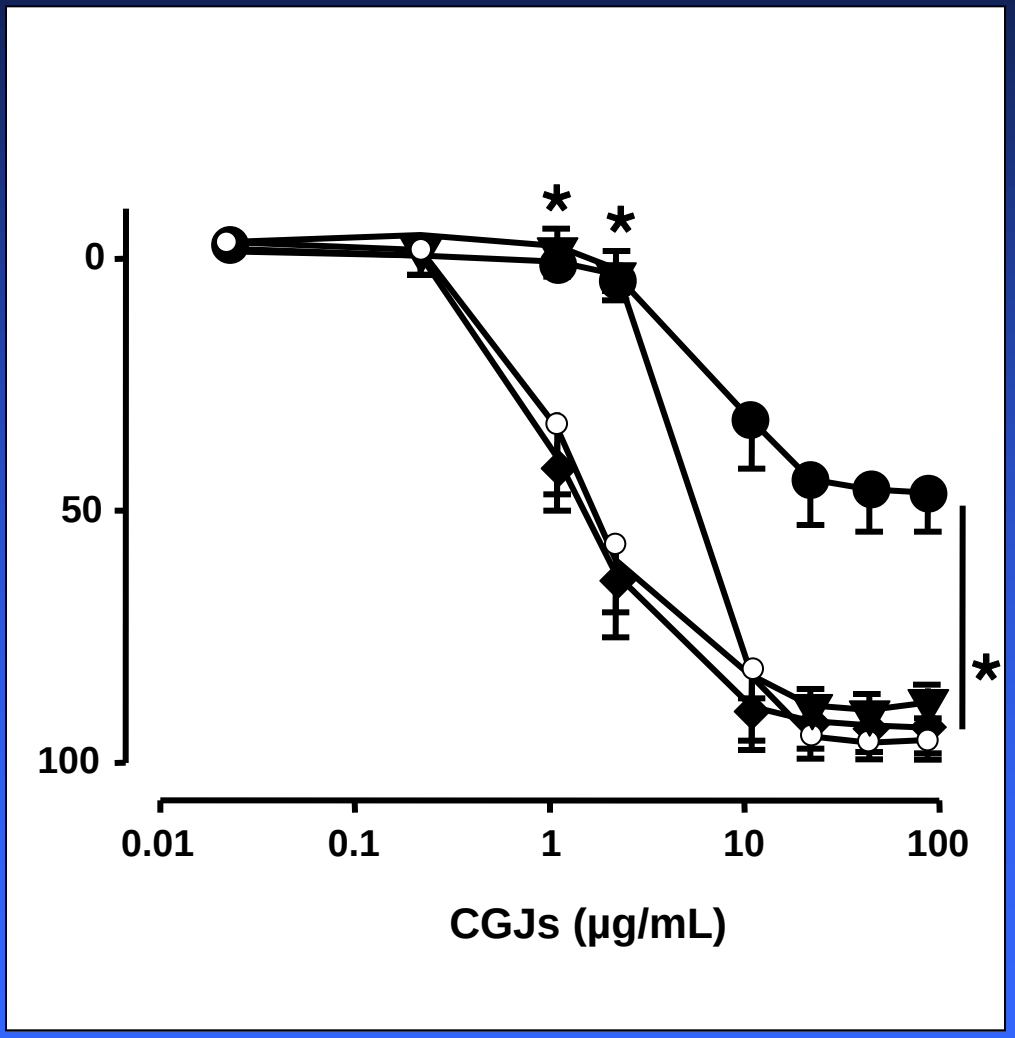


Ndiaye et al., BBRC 2003;310:371-377

Grape Skin Extract and Concord Grape Juice also cause Endothelium-Dependent Relaxations

(in the presence of indomethacin)

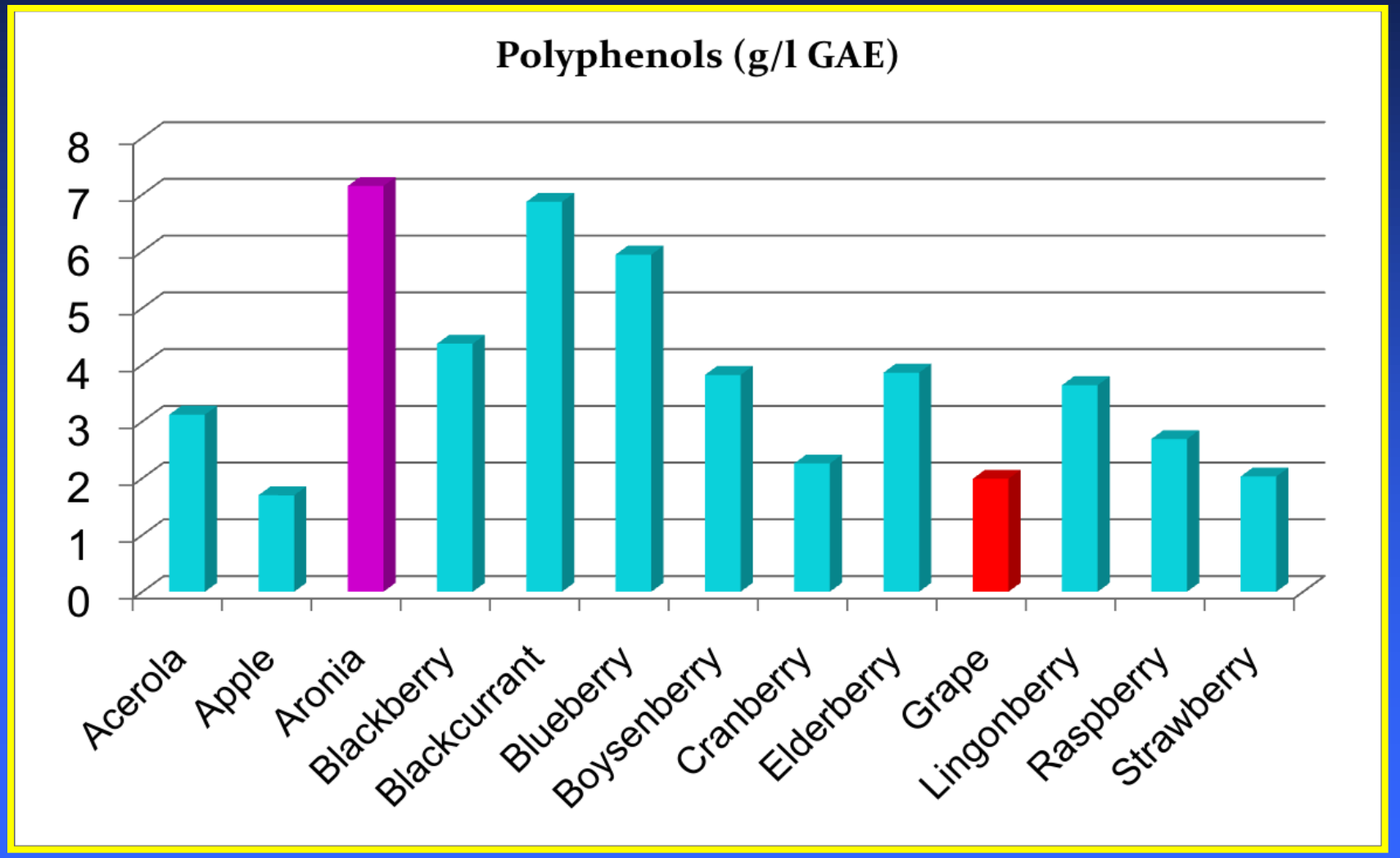




Madeira et al., J. Vasc. Res., 2009;46:406-416

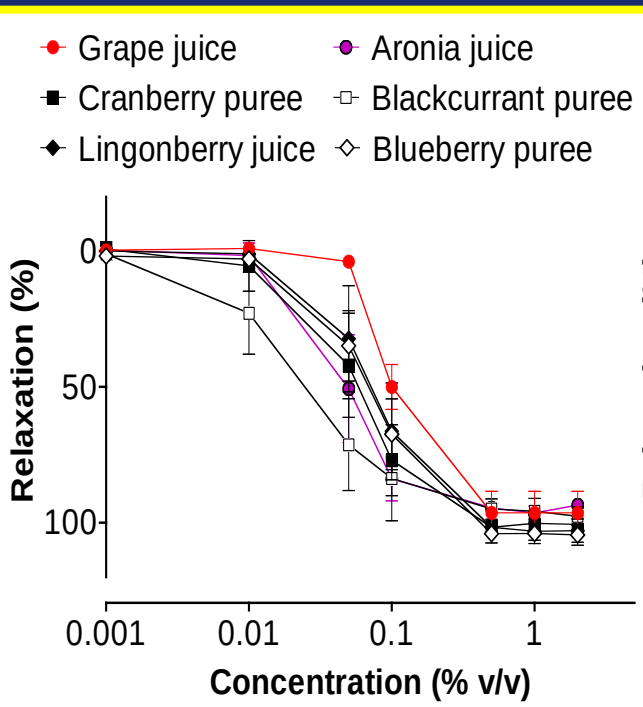
Anselm et al., Cardiovasc. Res. 2007;73:404-413

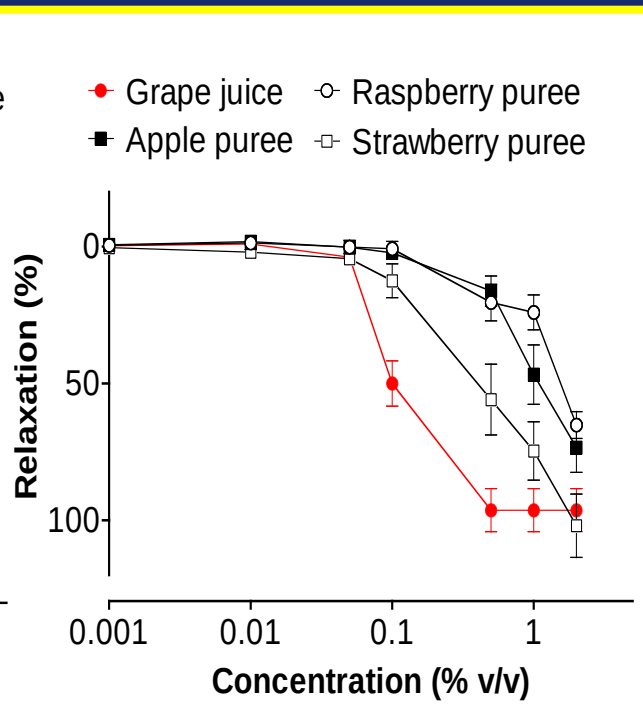
Polyphenol Content of Individual Fruit and Berry Juices and Purees

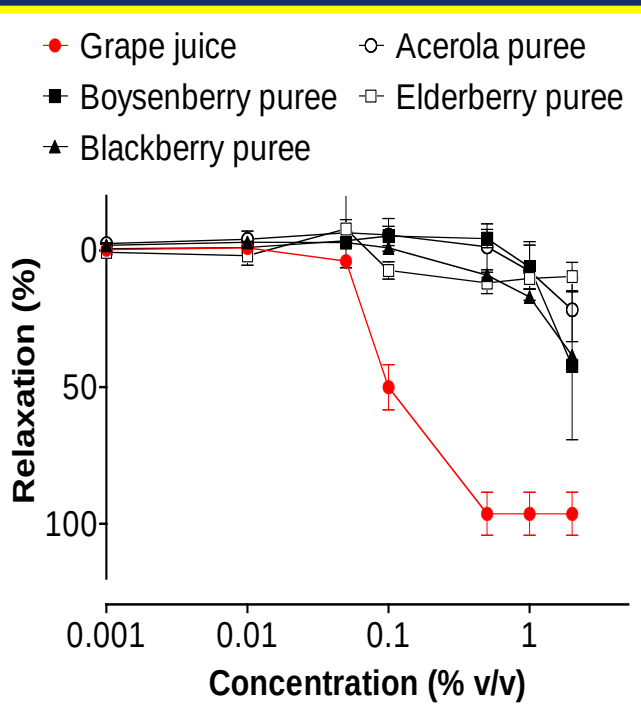


Auger et al., Food Funct. 2011;2:245-50

Selected Fruit and Berry Juices and Purees cause Endothelium-dependent Relaxations in the Porcine Coronary Artery







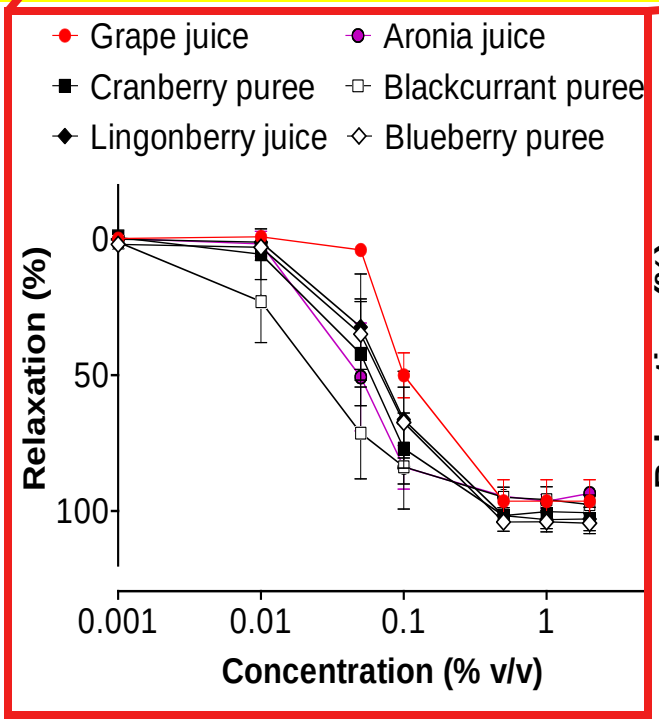
Auger et al., Food Funct. 2011;2:245-50

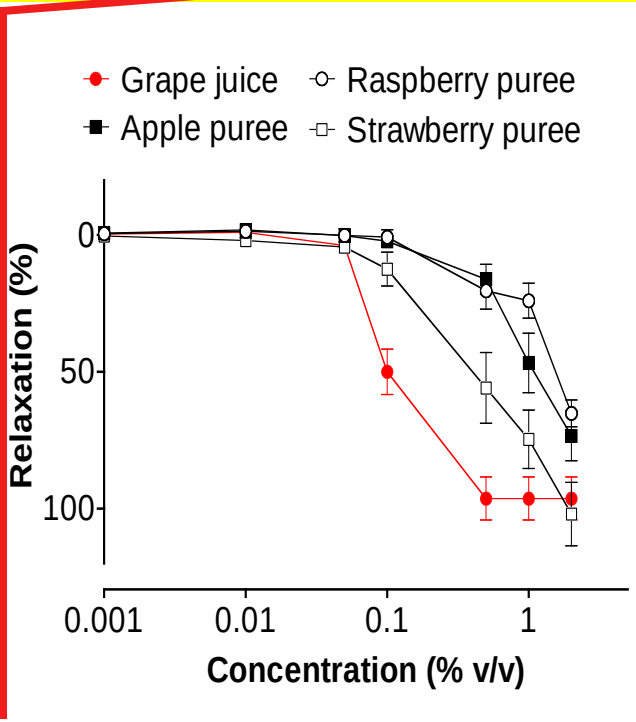
Selected Fruit and Berry Juices and Purees cause Endothelium-dependent Relaxations in the Porcine Coronary Artery

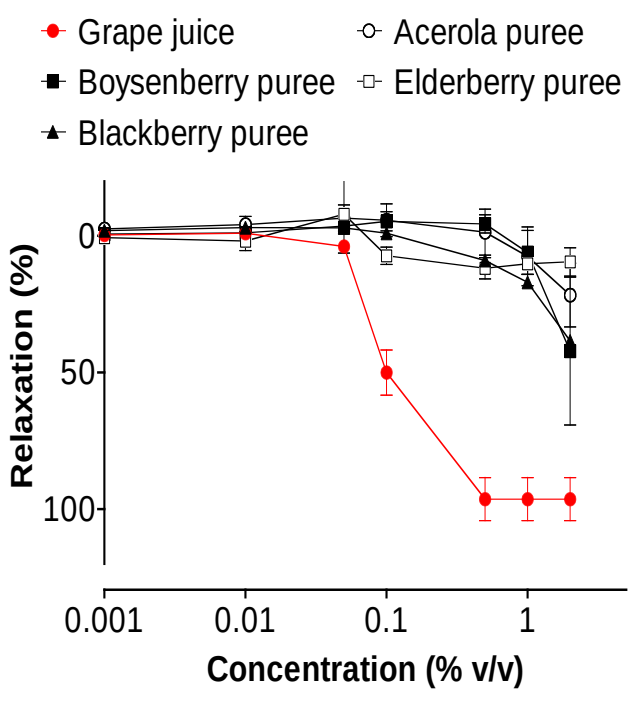
Aronia | Blackcurrant | Blueberry | Cranberry | Lingonberry







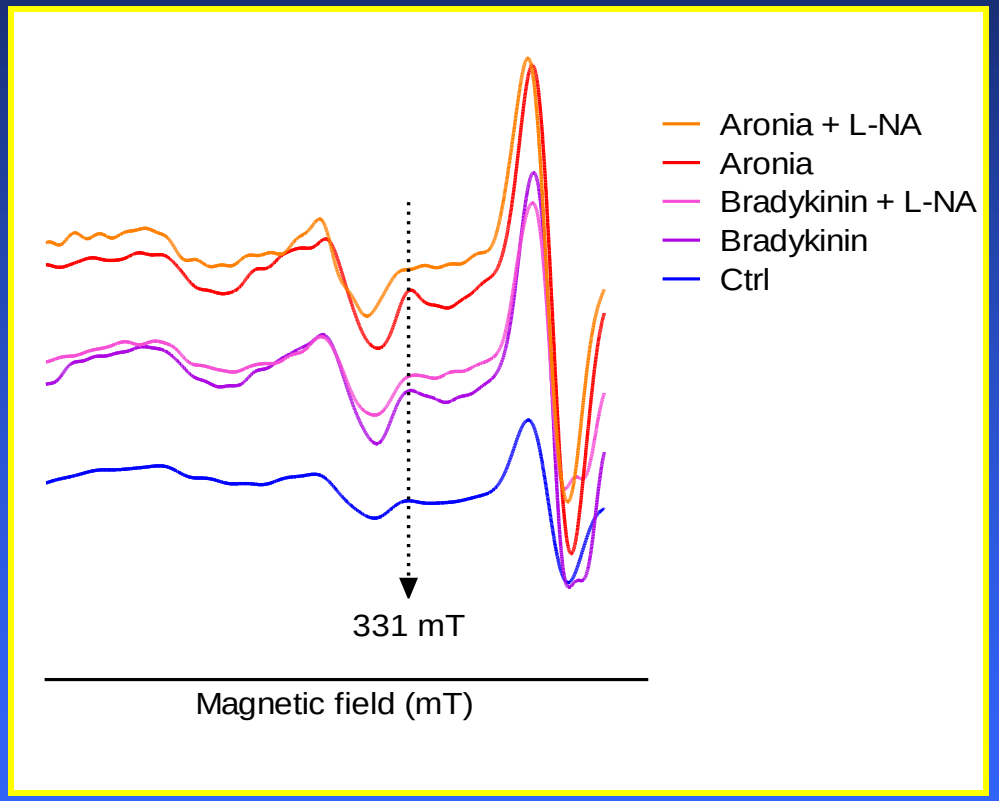


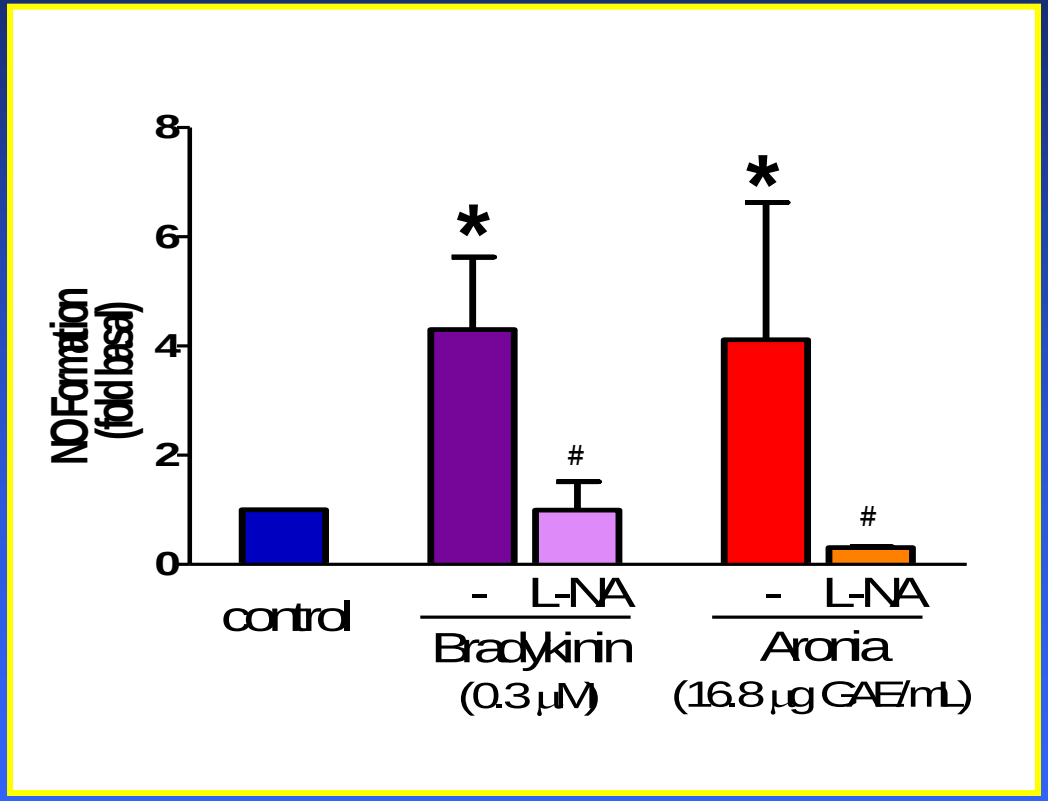


Auger et al., Food Funct. 2011;2:245-50

Aronia Juice Stimulates the Formation of NO in Coronary Artery Endothelial Cells

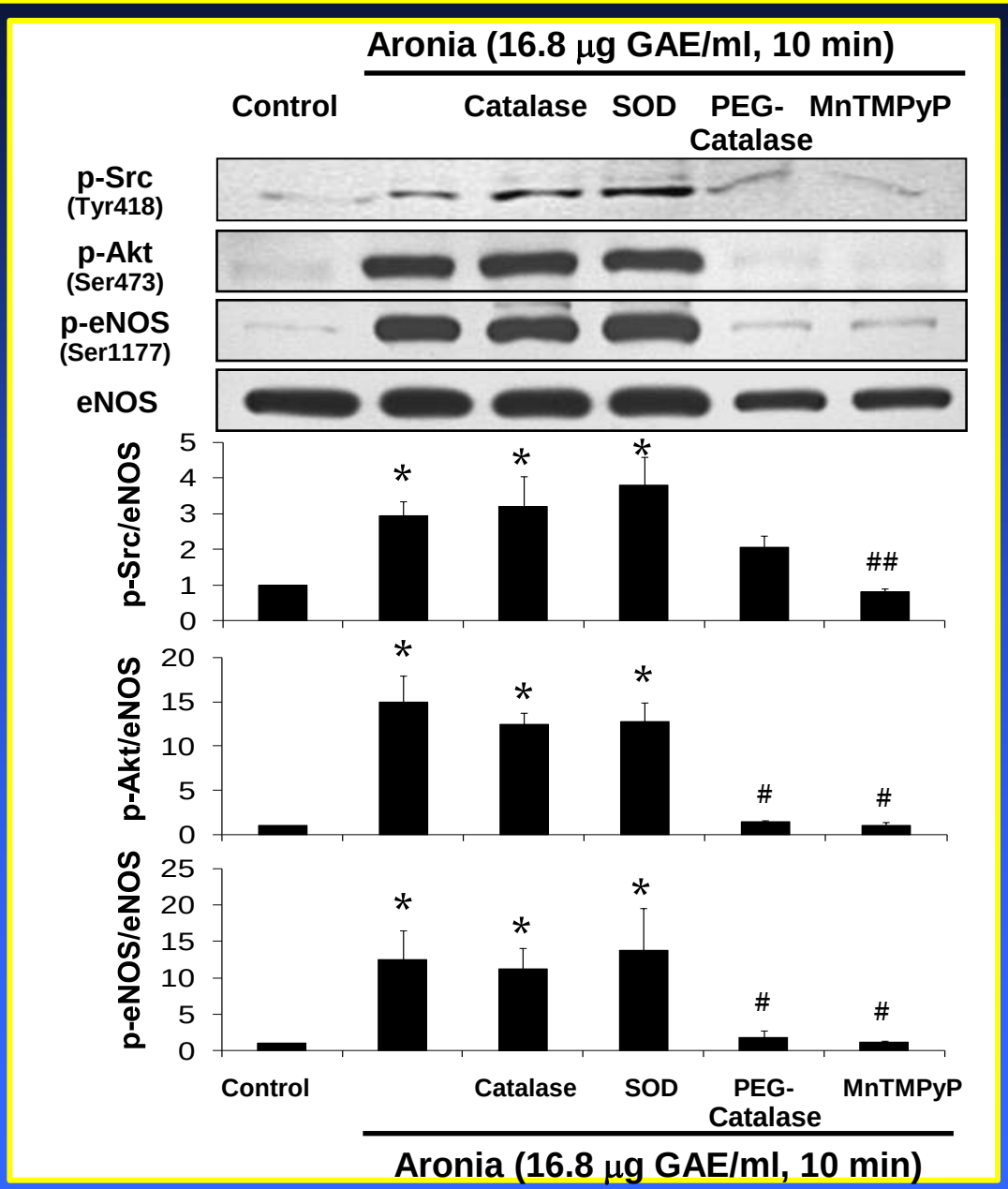
Electron Paramagnetic Resonance (EPR)





Kim et al., Nitric Oxide. 2013;35:54-64

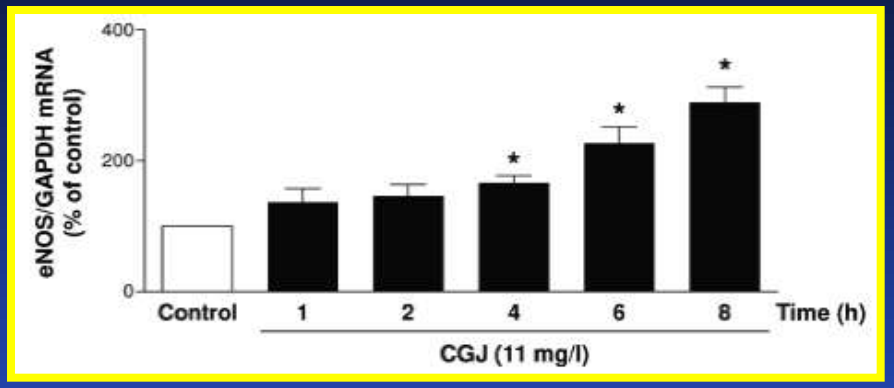
Aronia Juice Induces Phosphorylation of Src, Akt and eNOS through a Redox-sensitive Pathway in Endothelial Cells



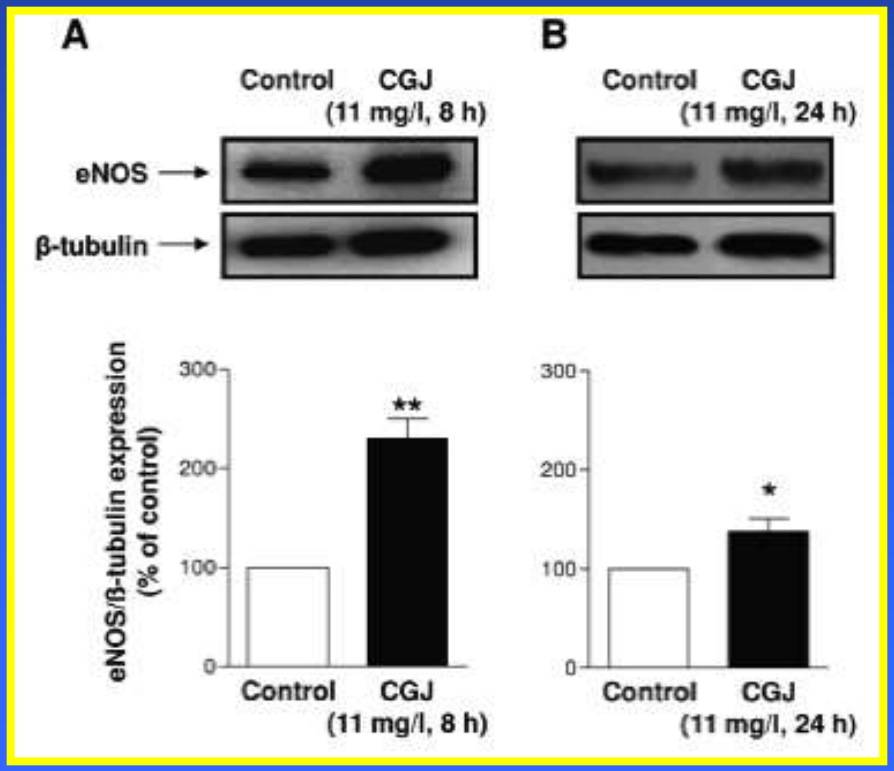
Kim et al., Nitric Oxide. 2013;35:54-64

Purple Grape Juice Upregulates eNOS Expression in Endothelial Cells

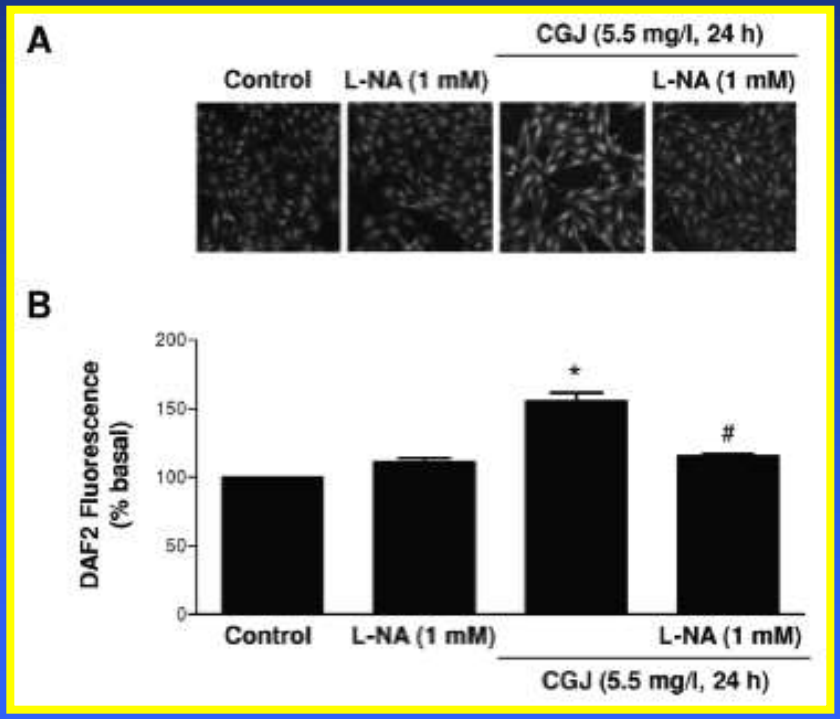
RT-PCR



Western blot



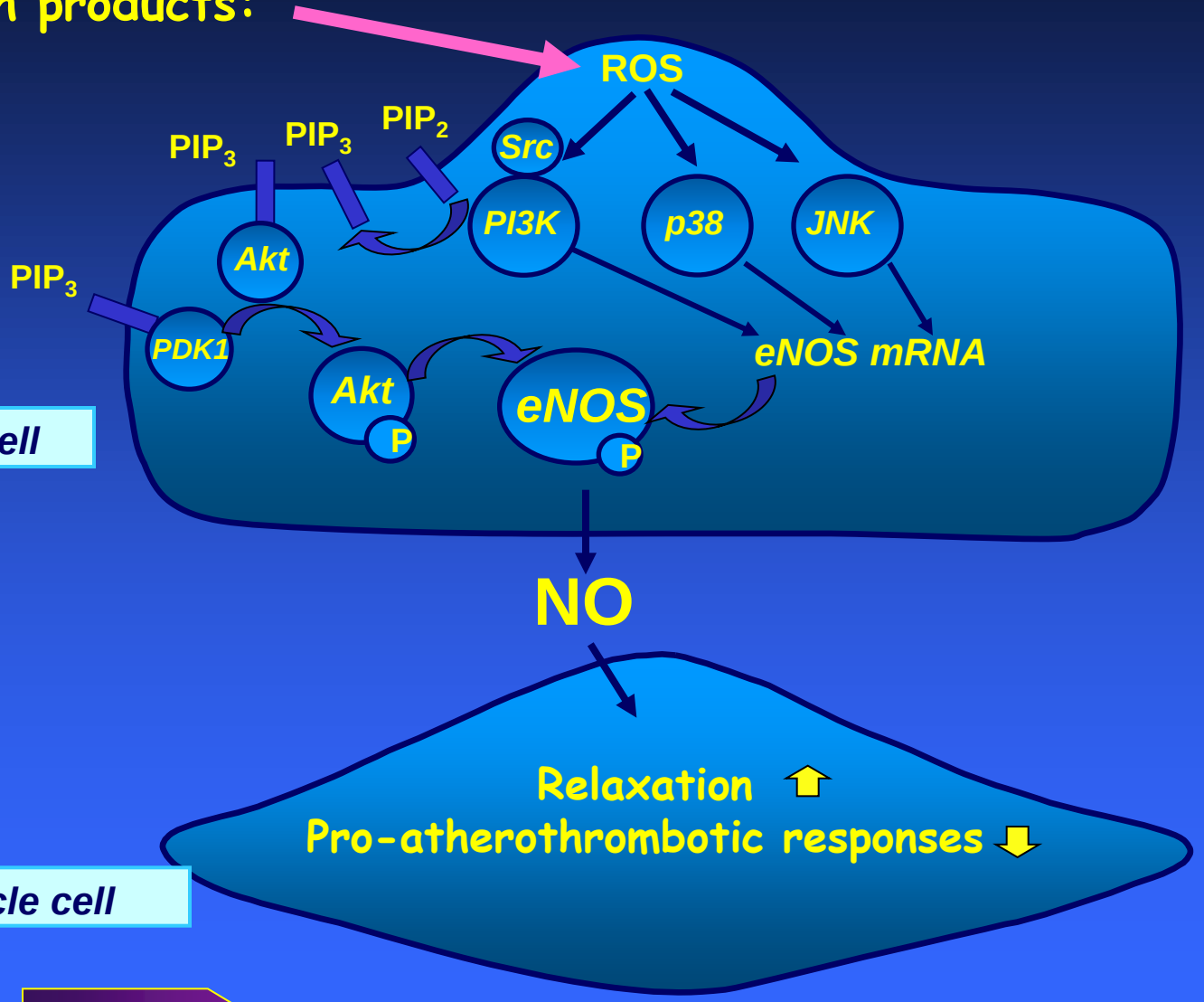
NO formation: DAF2 Fluorescence



Alhosin et al.,
PLoS ONE
2013;8:e57883

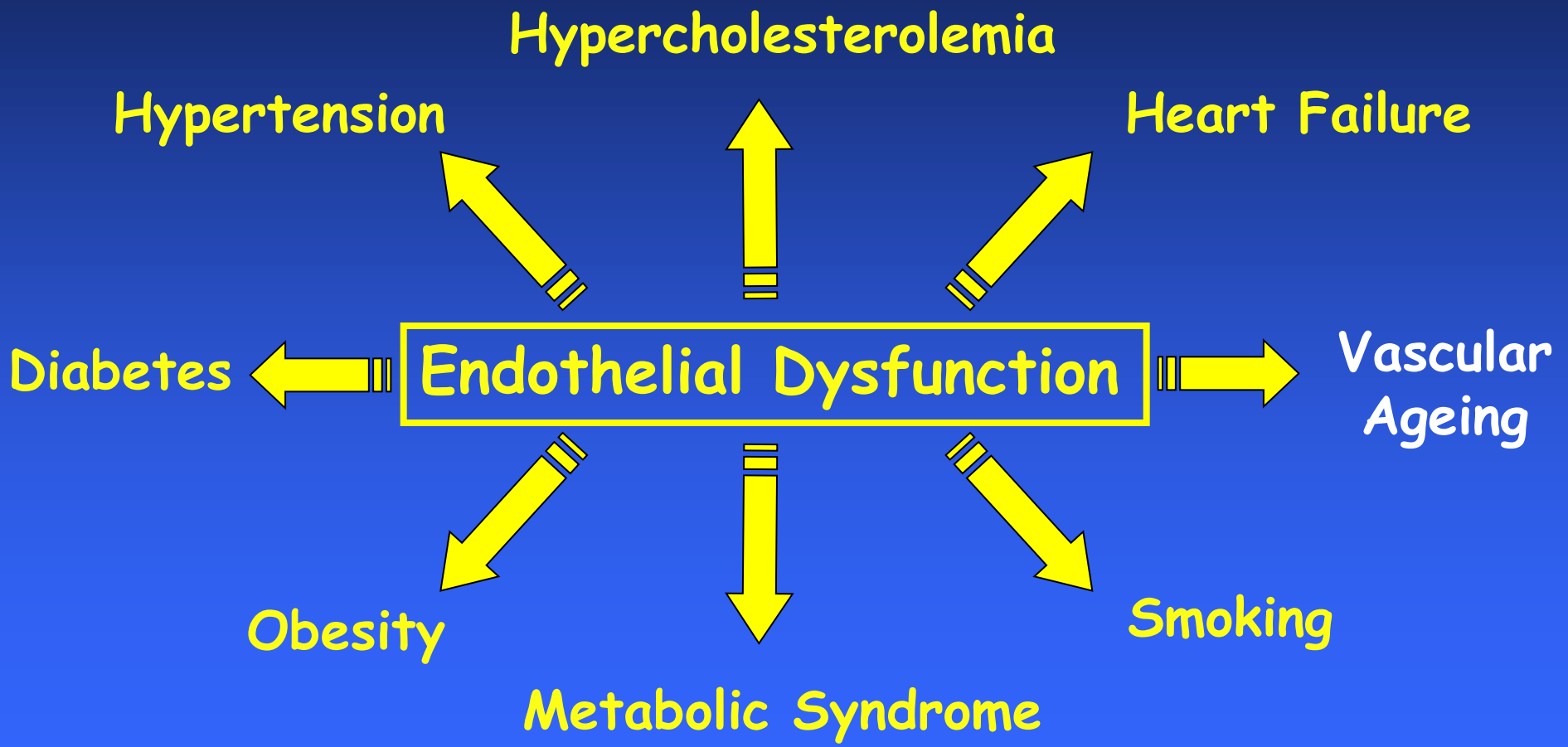
Natural Product-derived Polyphenols cause a Sustained Endothelial Formation of NO

Polyphenol-rich products:
Aronia
Blueberry
Cranberry
Lingonberry
Grape



Improved Vascular Health

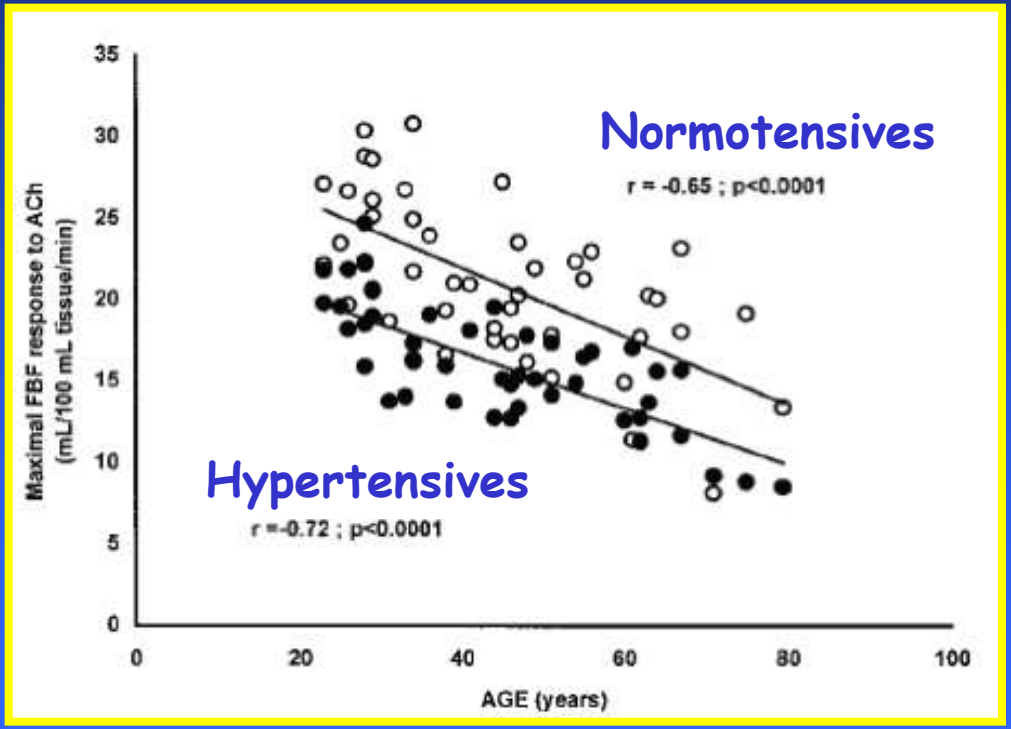
Cardiovascular Diseases are Characterizded by Oxidative Stress-related Endothelial Dysfunction



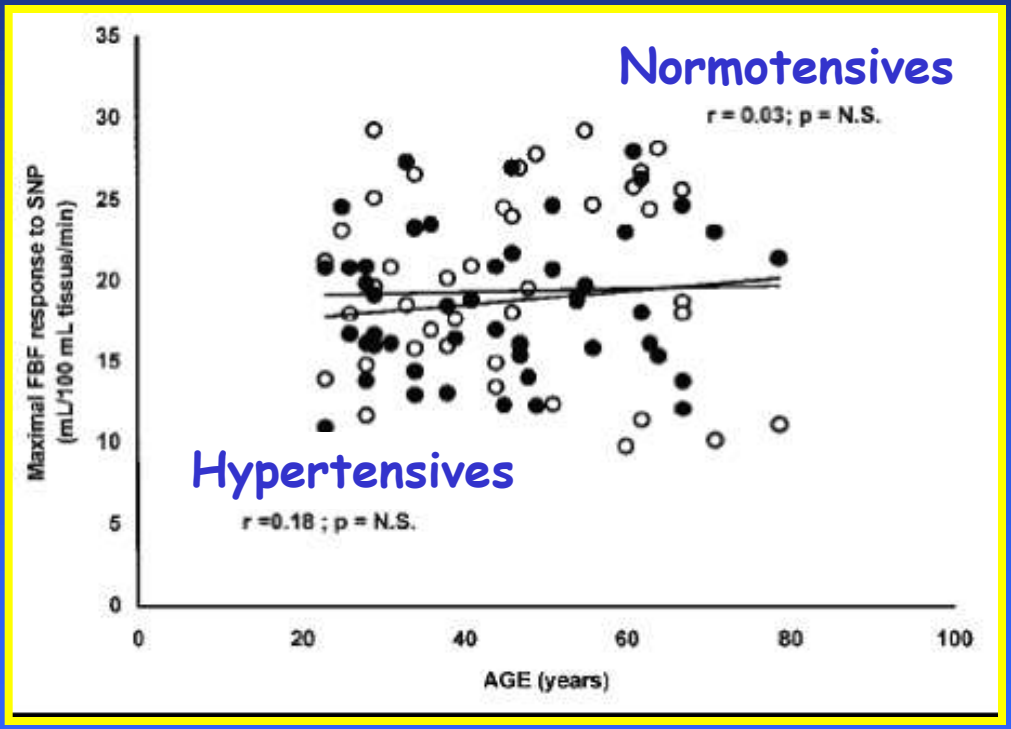
Age-related Endothelial Dysfunction in Normotensive and Hypertensive Humans

Forearm blood flow plethysmography

Endothelium-dependent vasodilator Acetylcholine



Endothelium-independent vasodilator Sodium nitroprusside

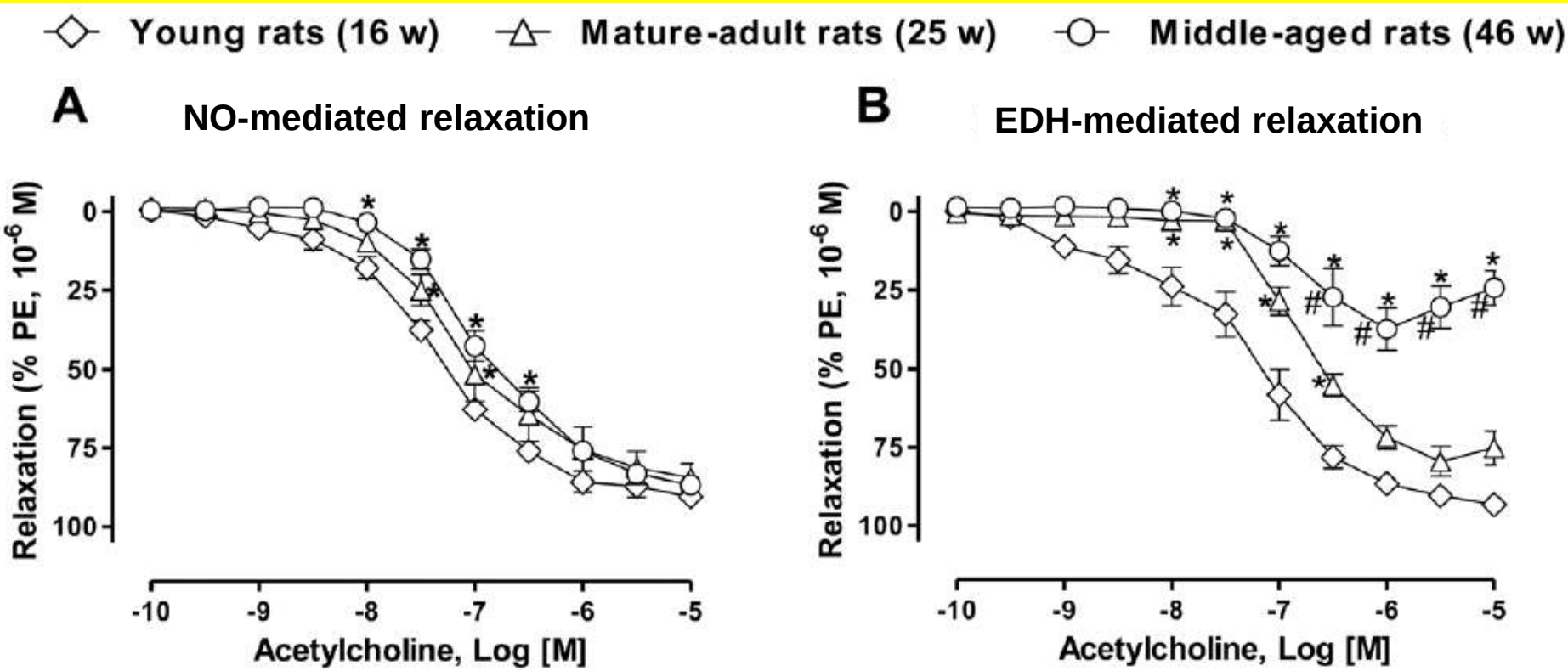


Taddei et al., Hypertension 2001;38:274-279

Ageing-related Endothelial Dysfunction

Male Wistar rats

Mesenteric artery



Idris Khodja et al., PLoS ONE 2012;7(2):e32039

RWPs and Endothelial Dysfunction in Ageing

Curative study

Vascular reactivity

Immunohistochemistry

46 47 48 49 50 week

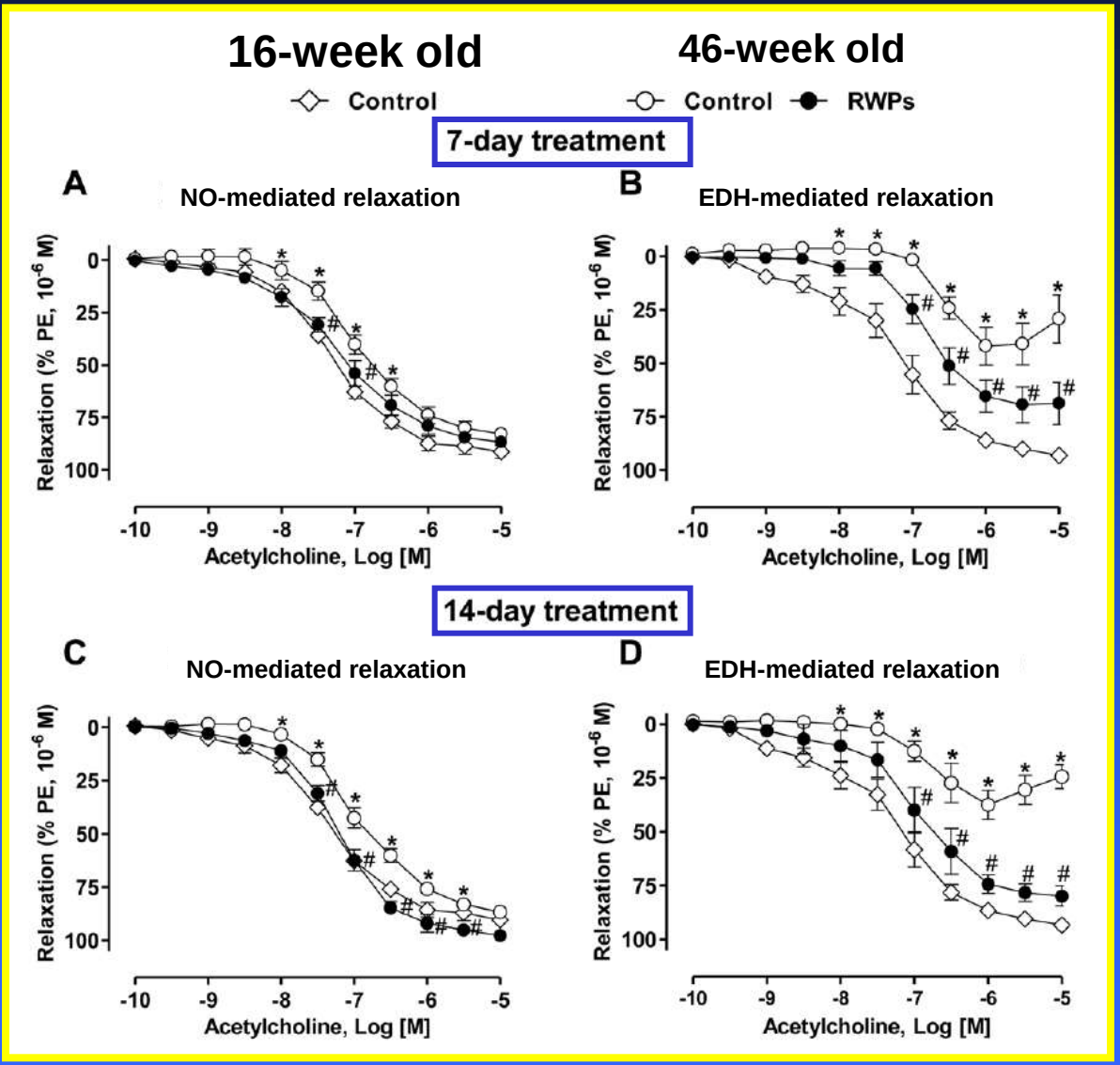
RWPs
(100 mg/kg/day)

Solvent

RWPs
Corbières wine
2.9 g/L polyphenols
(Onivins
Ministry of Agriculture)

RWPs improve Ageing-related Endothelial Dysfunction

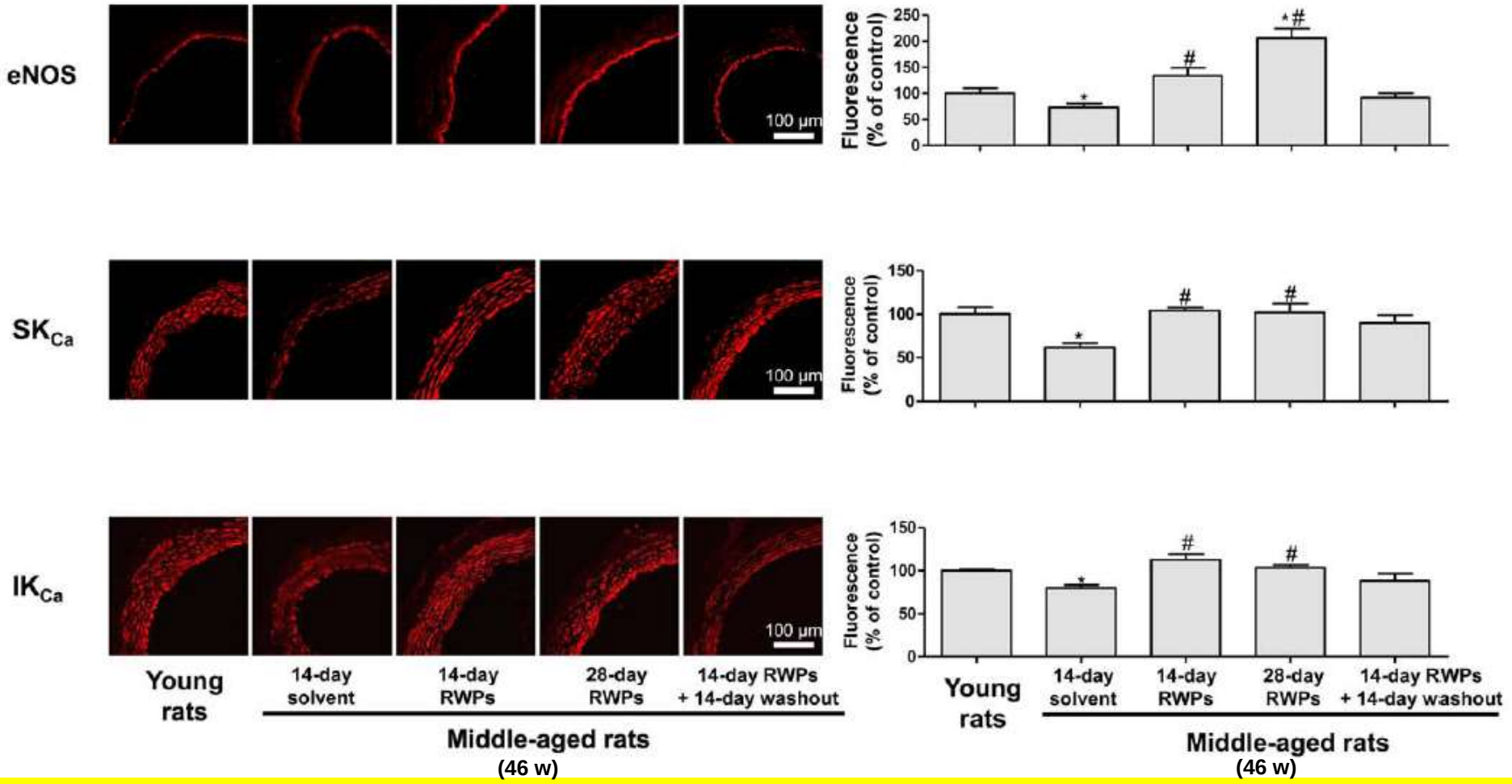
Mesenteric artery



Idris Khodja et al., PLoS ONE 2012;7(2):e32039

Ageing-related Endothelial Dysfunction

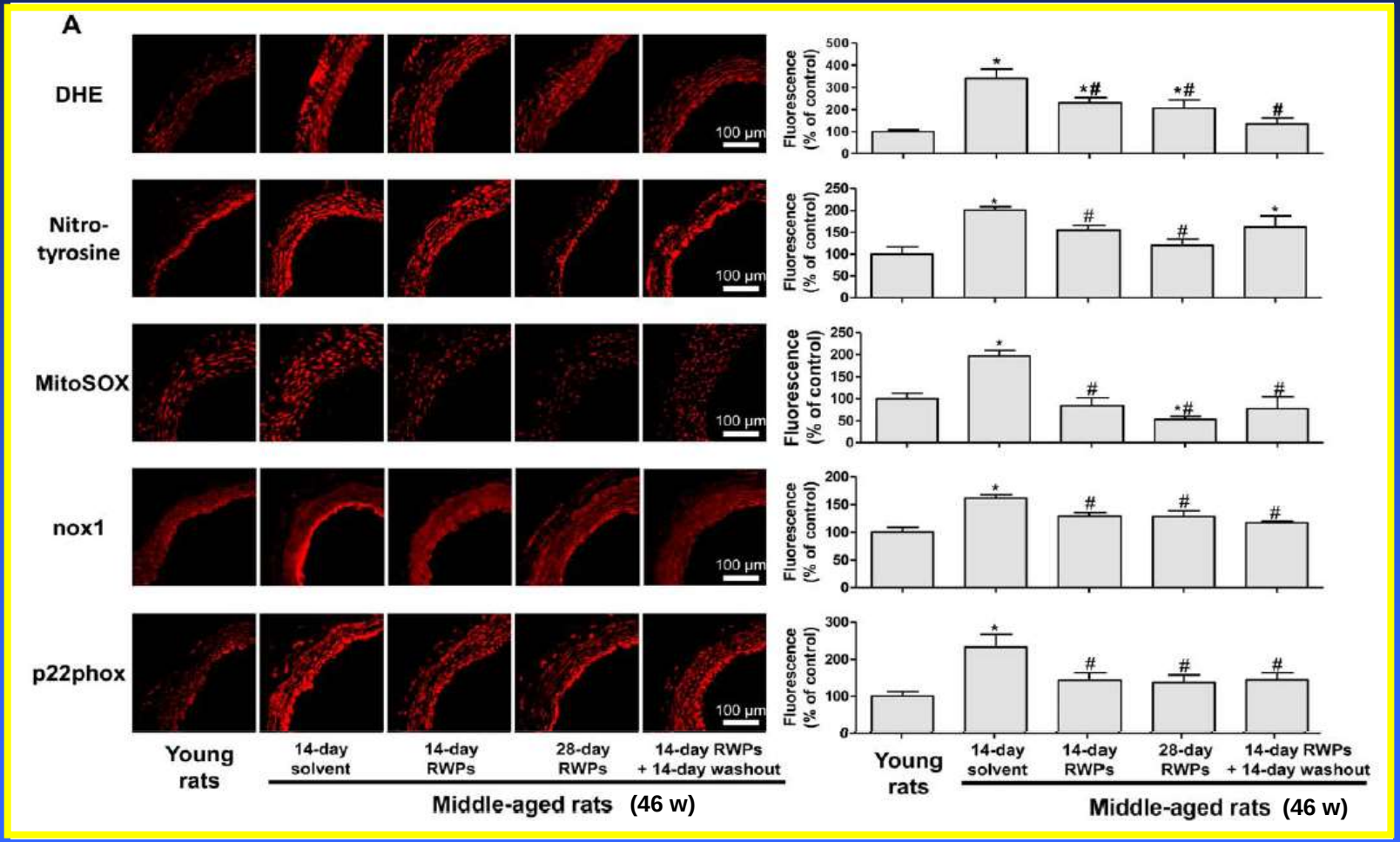
Mesenteric artery



Idris Khodja et al., PLoS ONE 2012;7(2):e32039

Vascular oxidative stress in Ageing

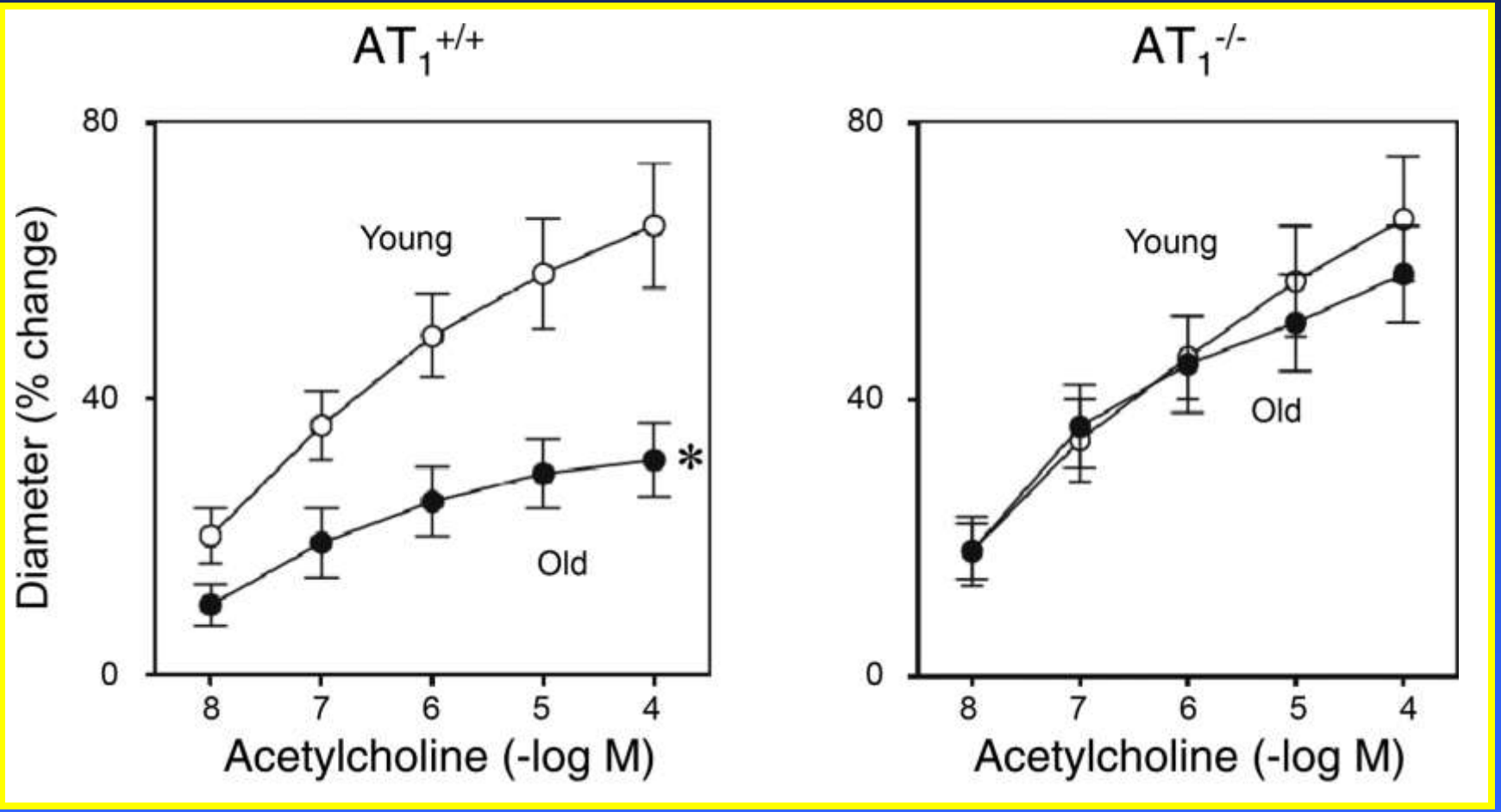
Mesenteric artery



Idris Khodja et al., PLoS ONE 2012;7(2):e32039

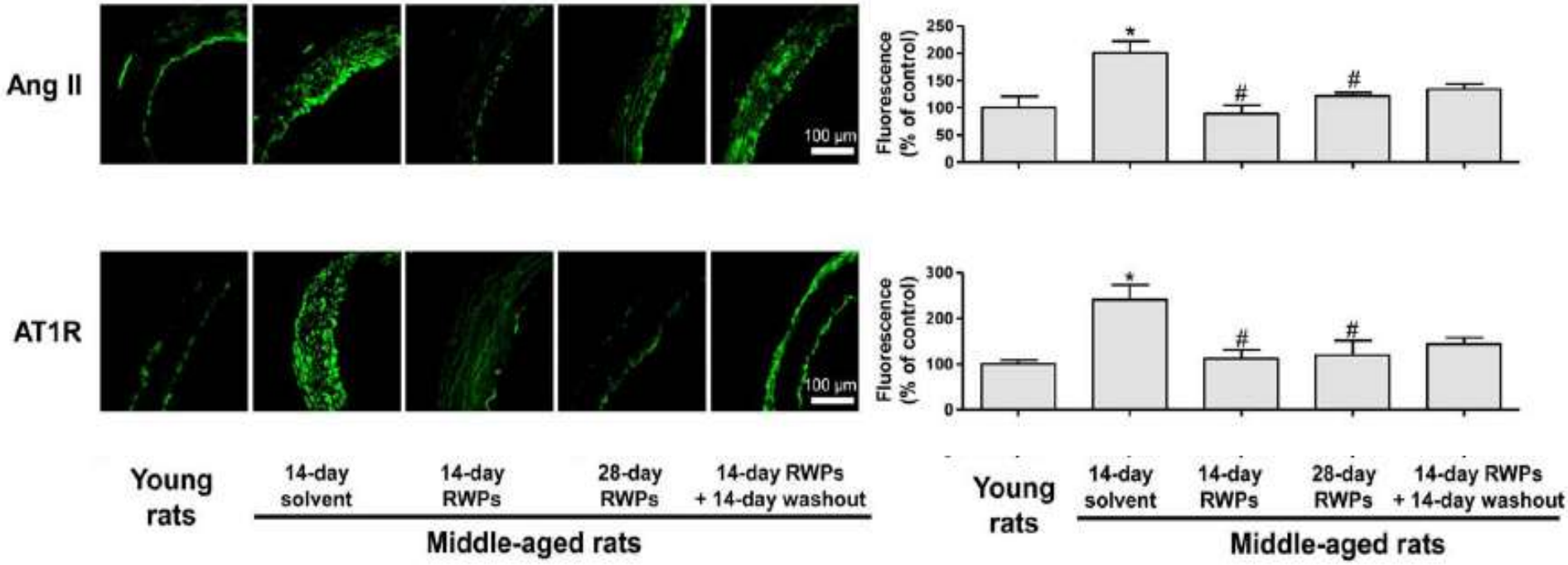
Ageing-related Endothelial Dysfunction: Role of the Angiotensin System

Mice basilar artery rings



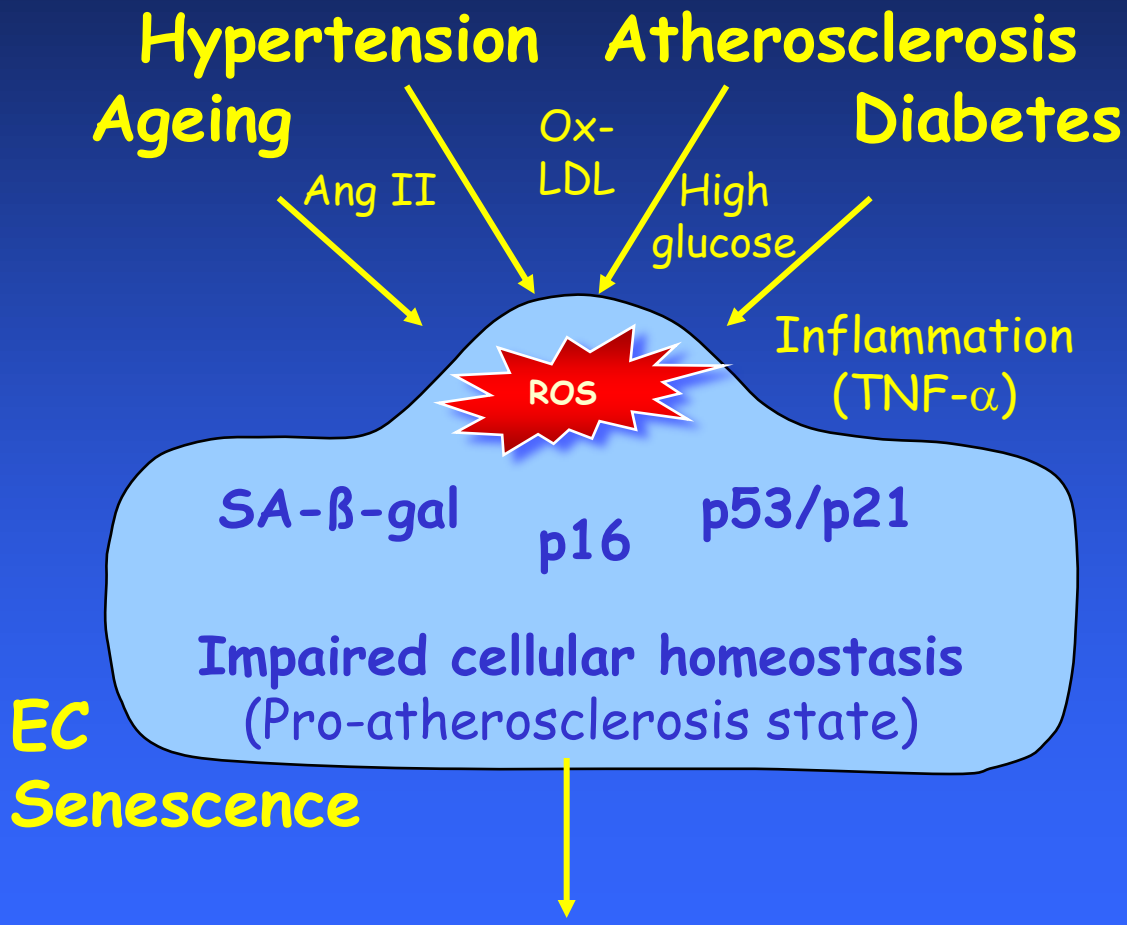
Modrick et al., Am J Physiol 2009;296:H1914-1919

Ageing-related Endothelial Dysfunction and the Angiotensin System

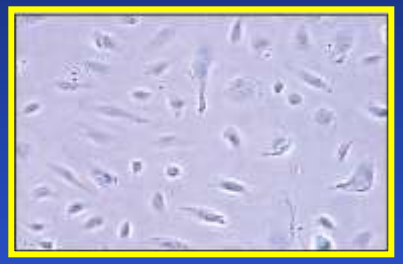


Idris Khodja et al., PLoS ONE 2012;7(2):e32039

Endothelial Cell Senescence Promotes Endothelial Dysfunction



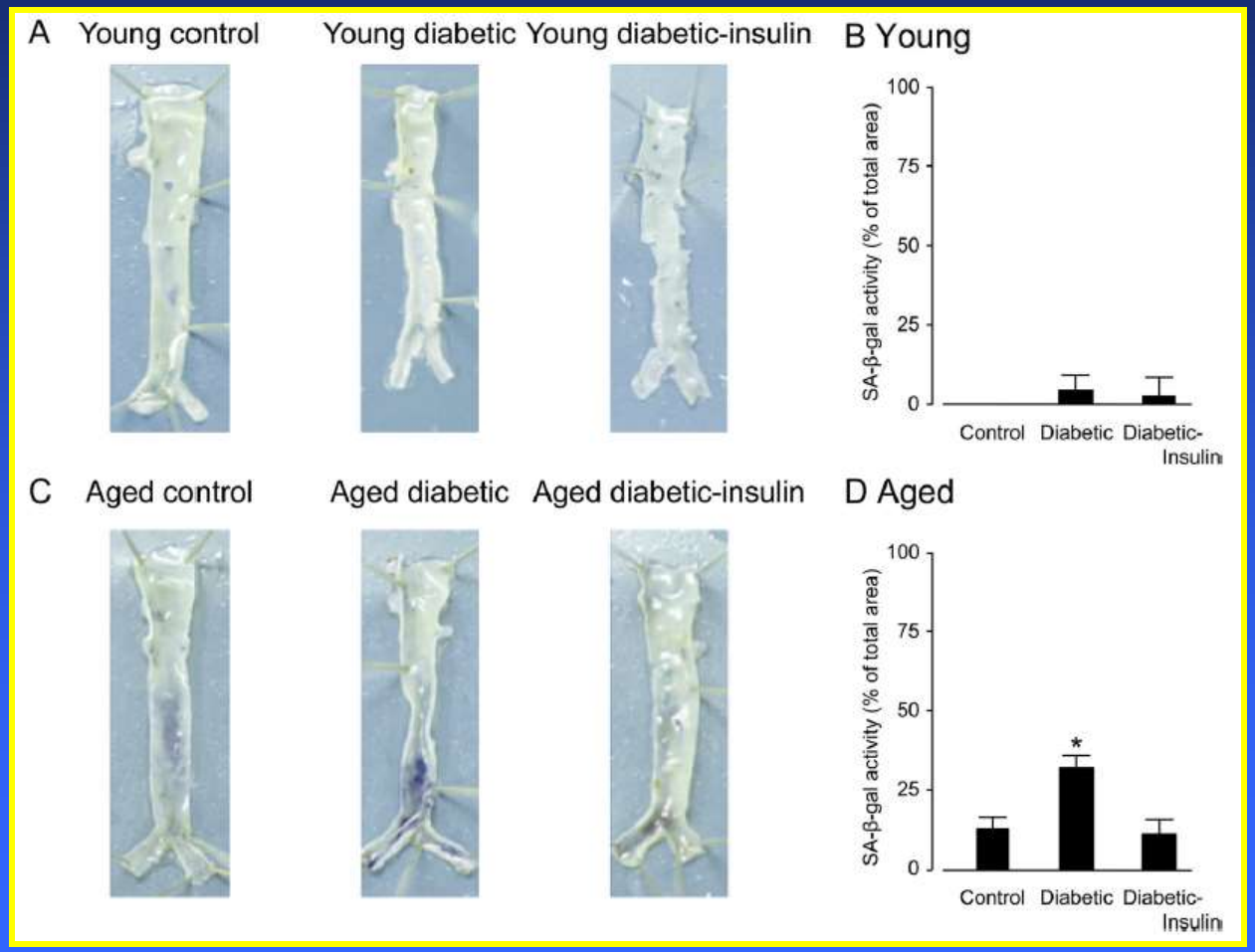
Control endothelial cells



Senescent endothelial cells

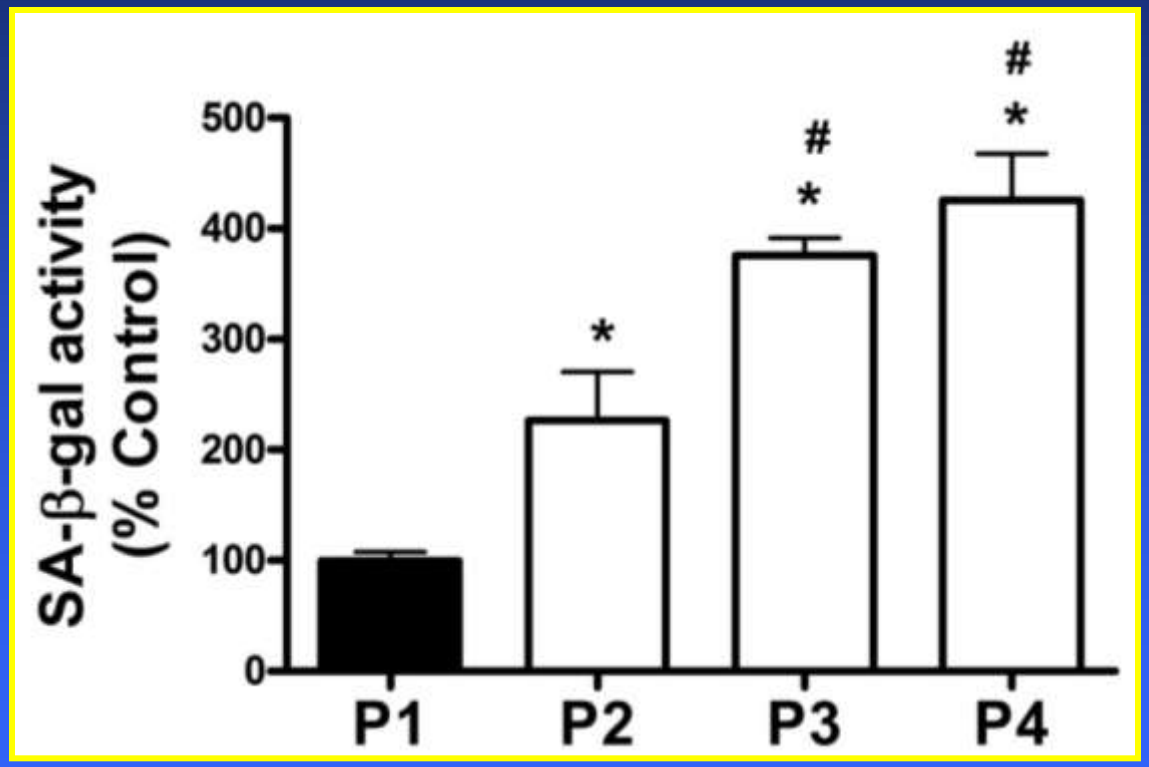
SA-ß-gal Activity in the Aortic Endothelium of Young and Aged Control and STZ-induced diabetic rats

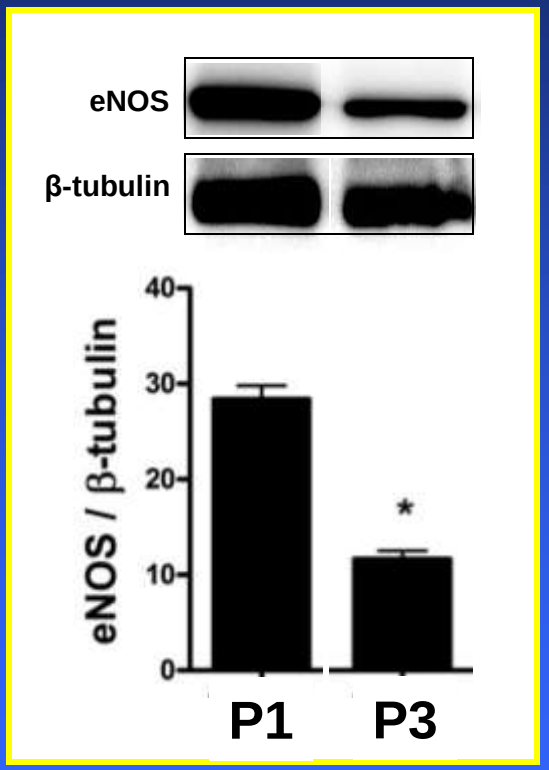
Senescence-associated beta-galactosidase staining



Matsui-Hirai et al., JPET 2011;337:591-599

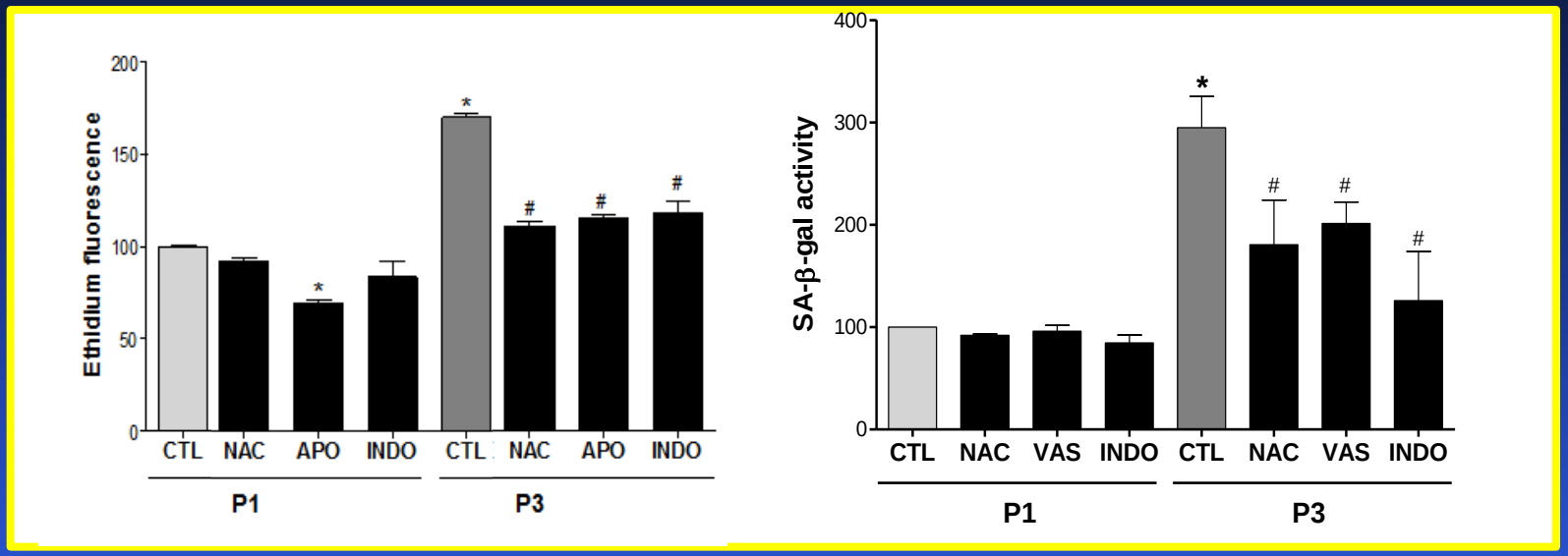
Replicative Senescence in Cultured Coronary Artery Endothelial Cells

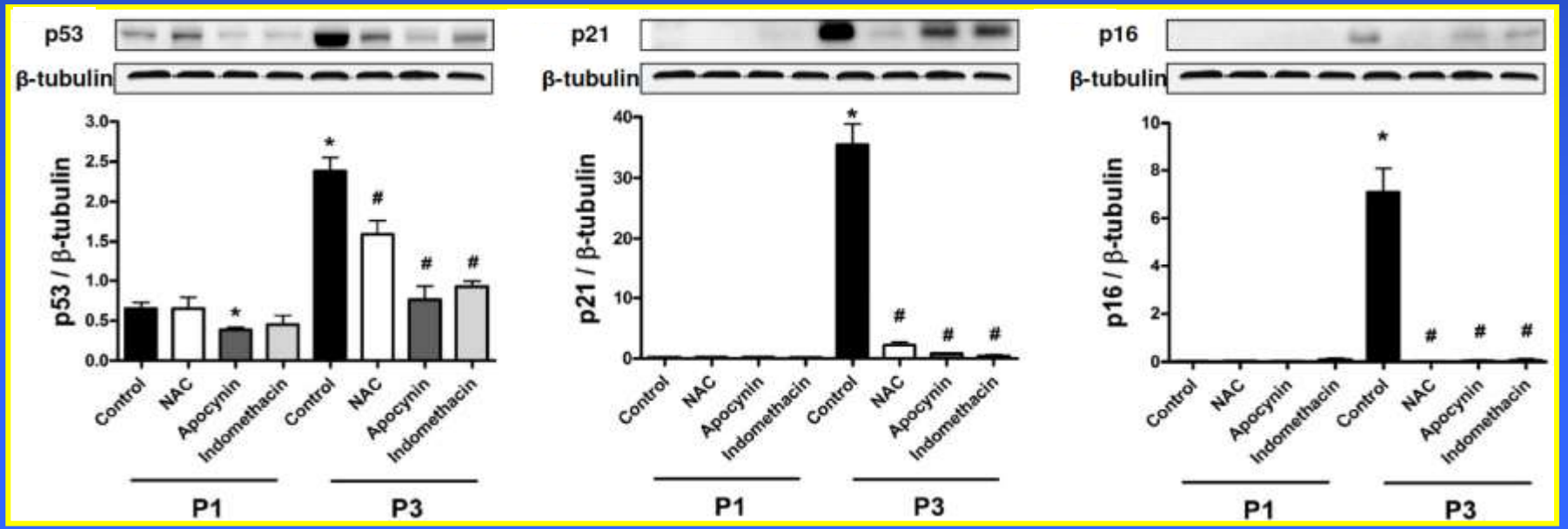




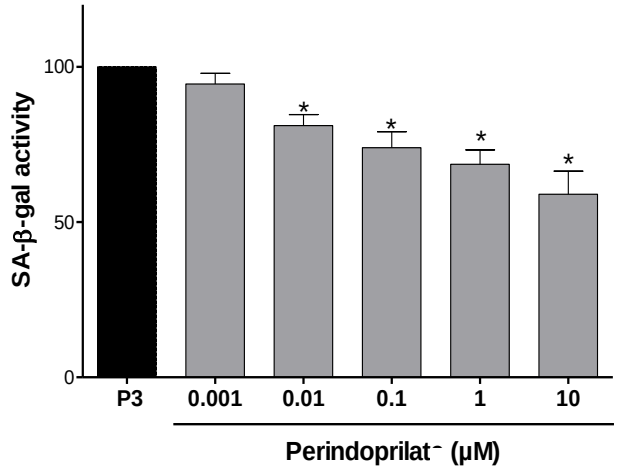
Khemais-Benkhiat et al.,J. Gerontol. 2015, Dec 15. pii: glv213

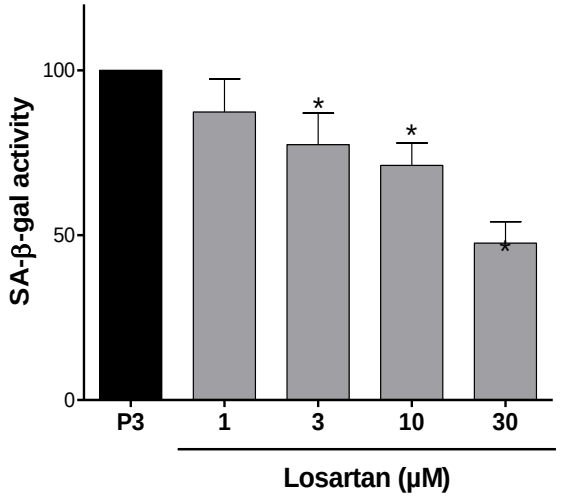
NADPH oxidase- and COX-dependent ROS Promote Replicative Endothelial Cell Senescence

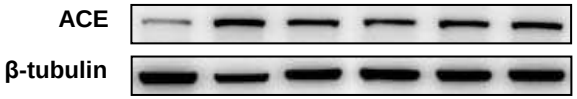


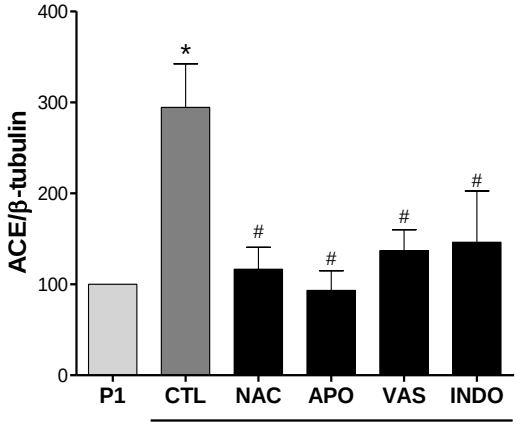


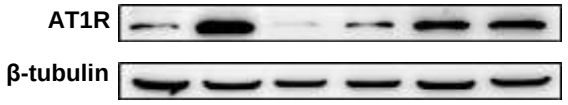
Role of the Angiotensin System in the Induction of Replicative Endothelial Cell Senescence

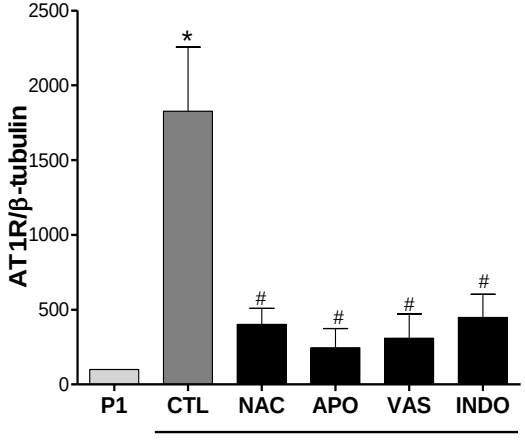




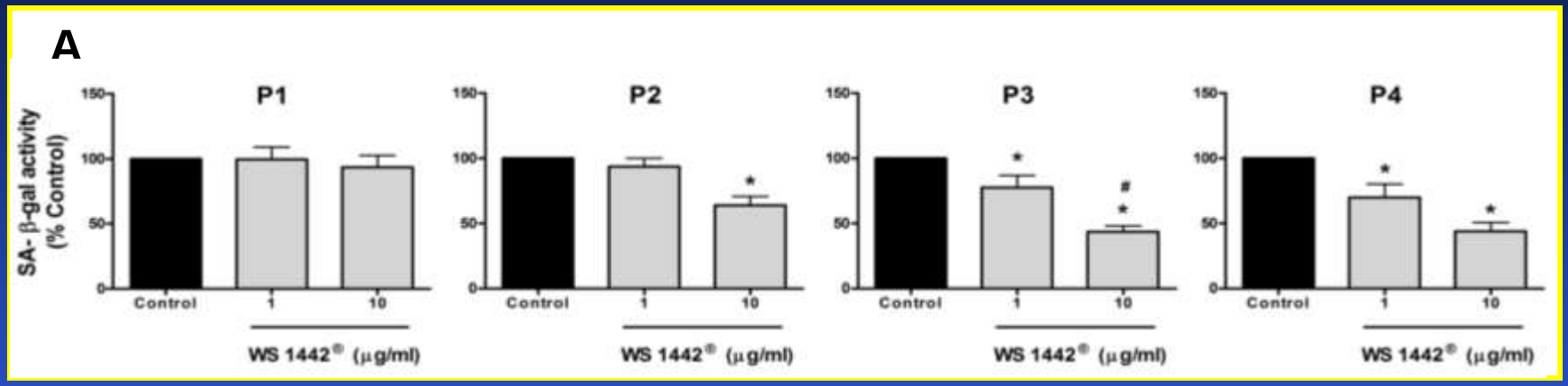


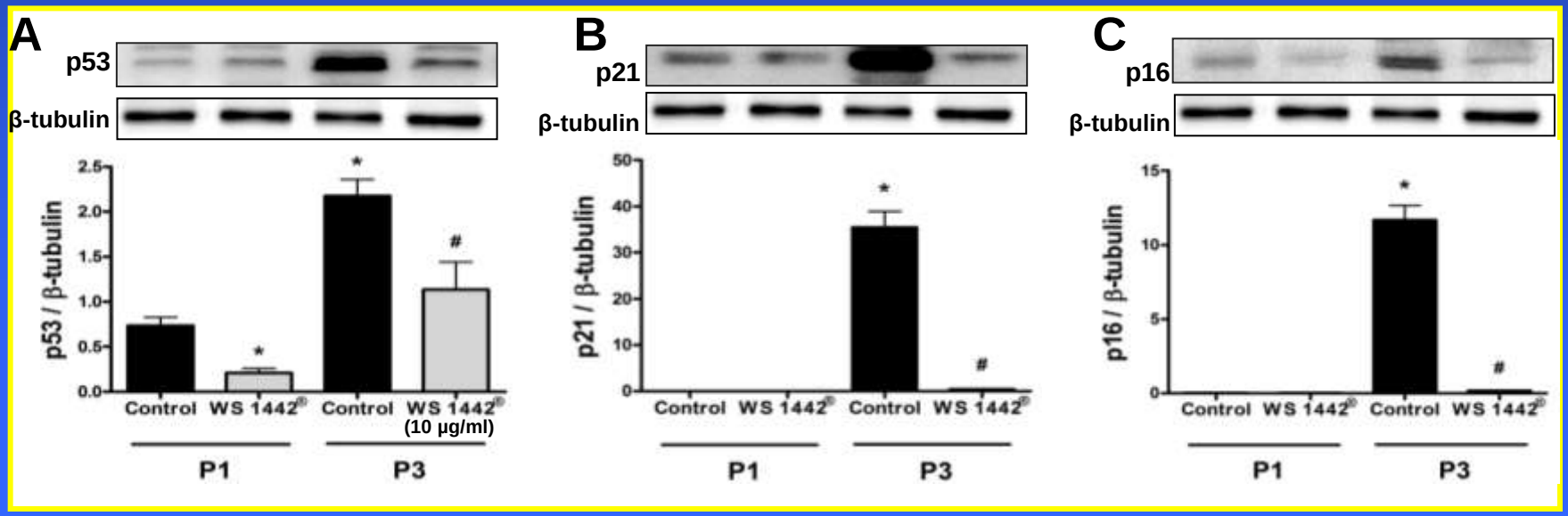






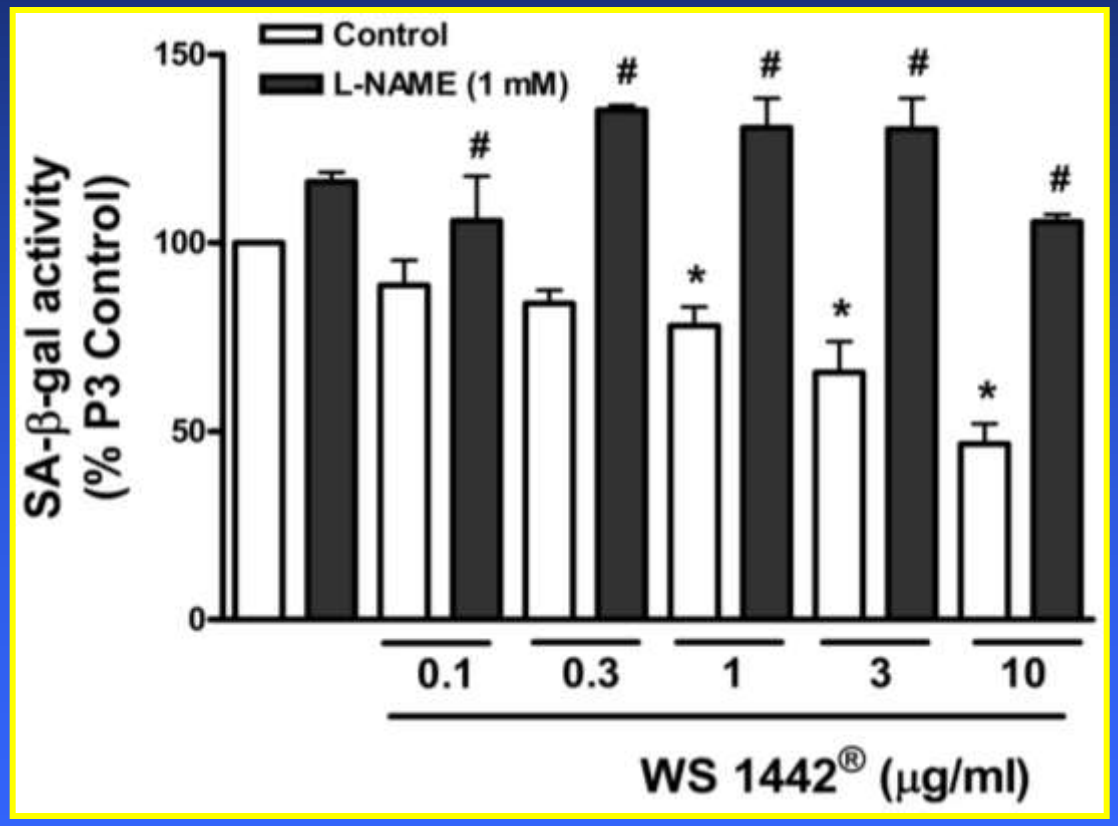
Polyphenol-rich Crataegus Extract Prevents Replicative Endothelial Cell Senescence

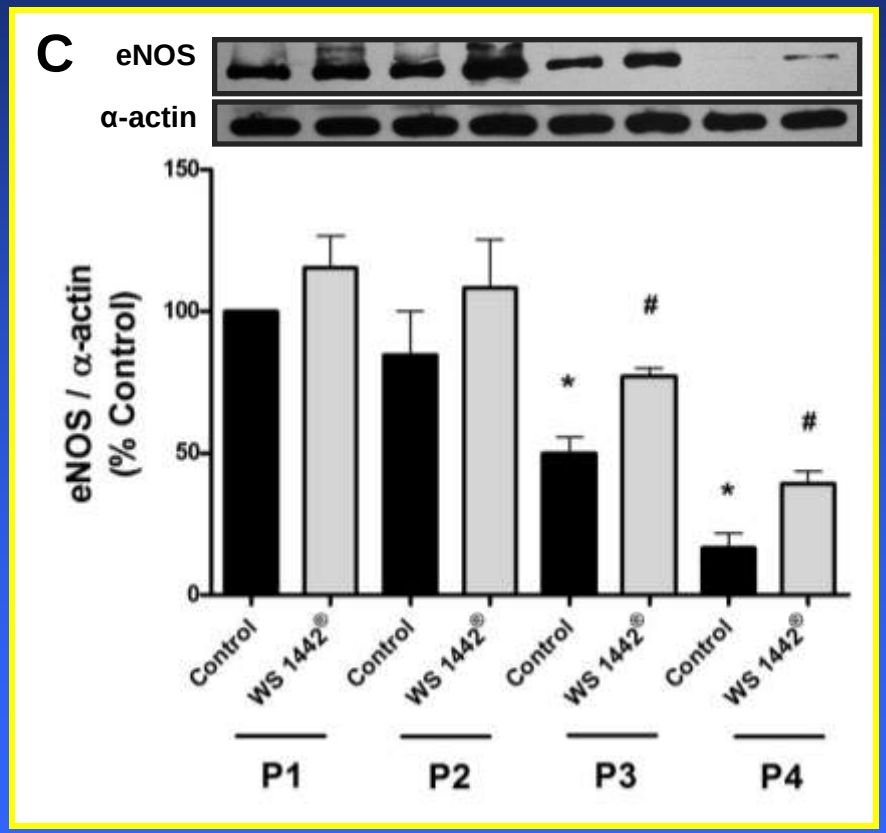




Khemais-Benkhiat et al.,J. Gerontol. 2015, Dec 15. pii: glv213

Role of eNOS-derived NO in the preventive effect of Crataegus Polyphenols on Endothelial Senescence

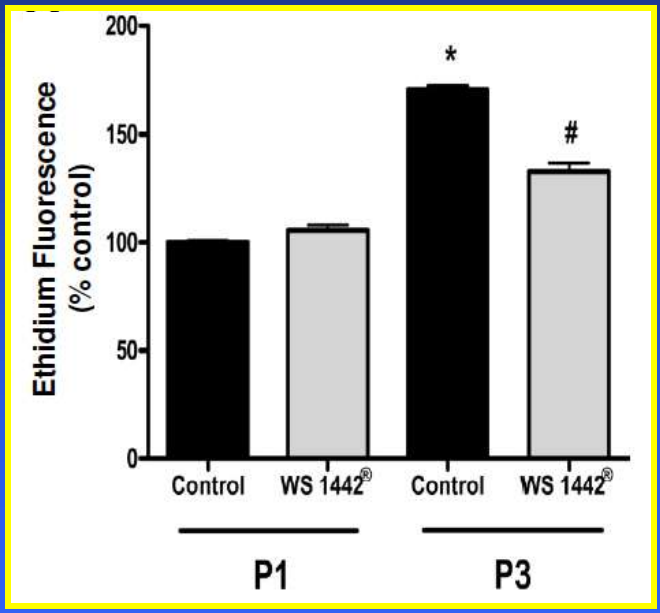




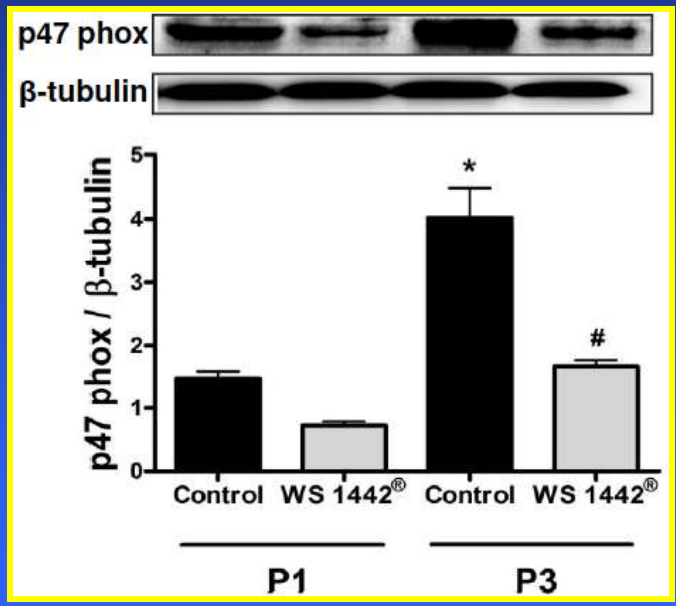
Khemais-Benkhiat et al.,J. Gerontol. 2015, Dec 15. pii: glv213

Crataegus Polyphenols Prevent NADPH oxidase- and COX-mediated Oxidative Stress in Senescent Endothelial Cells

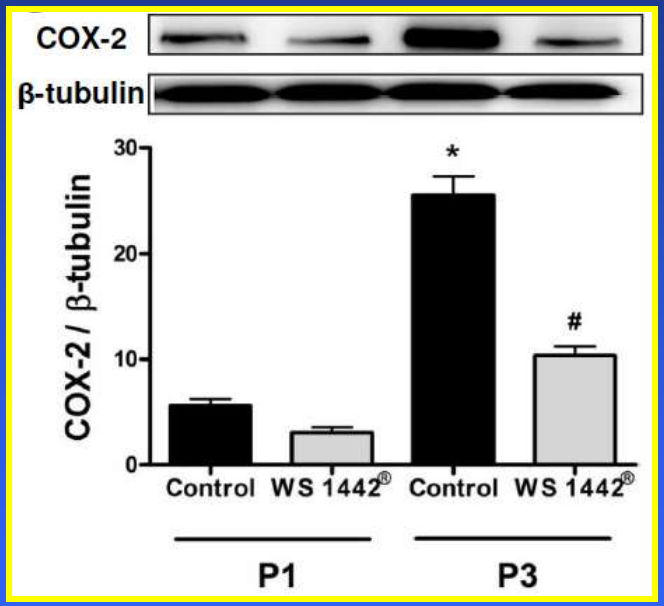
ROS formation



NADPH oxidase



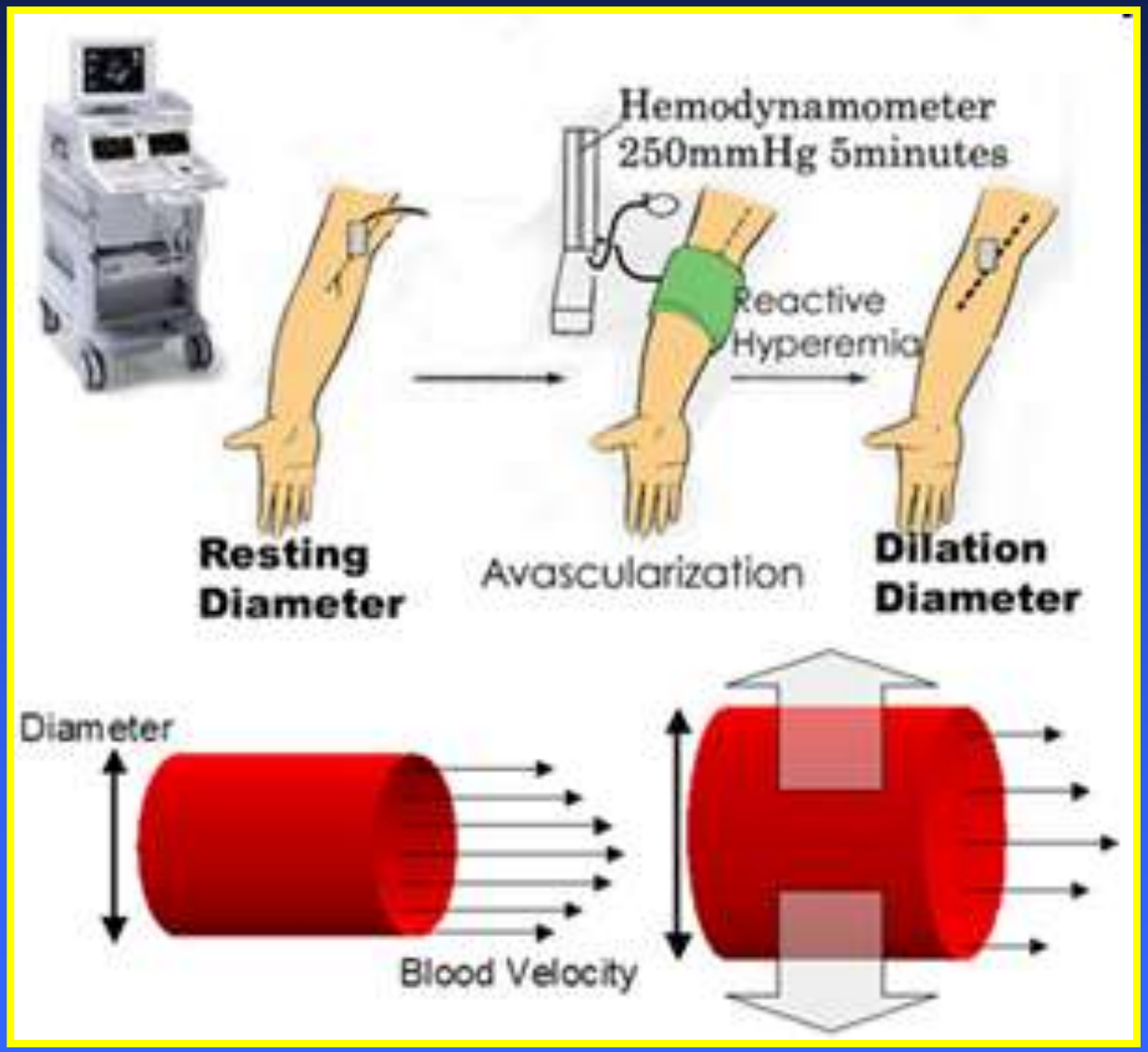
COX-2



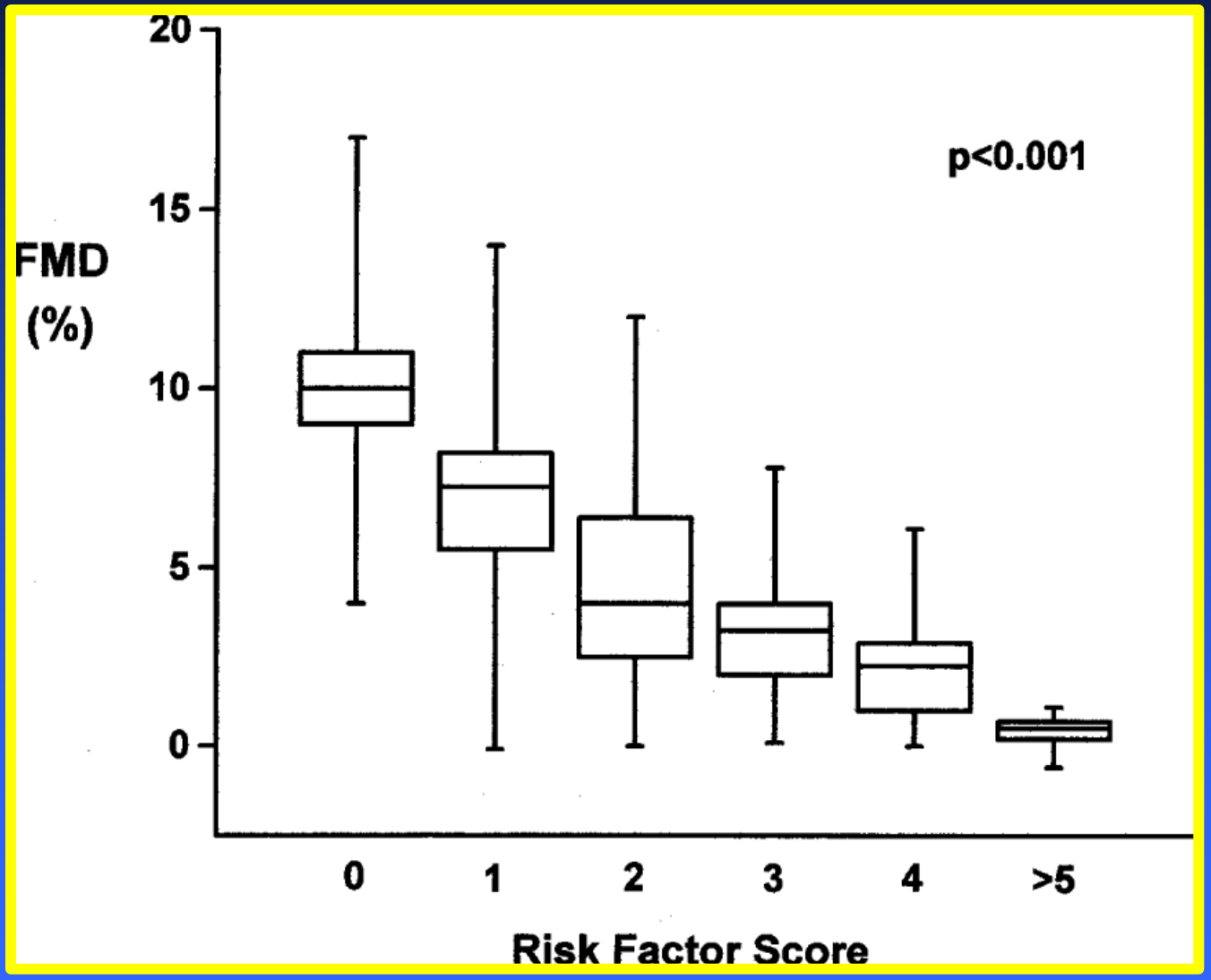
Khemais-Benkhiat et al.,J. Gerontol. 2015, Dec 15. pii: glv213

Endothelial Function in Humans

Flow-mediated vasodilatation



Relationship between Vascular Risk Factors and Flow-mediated Dilatation (FMD)



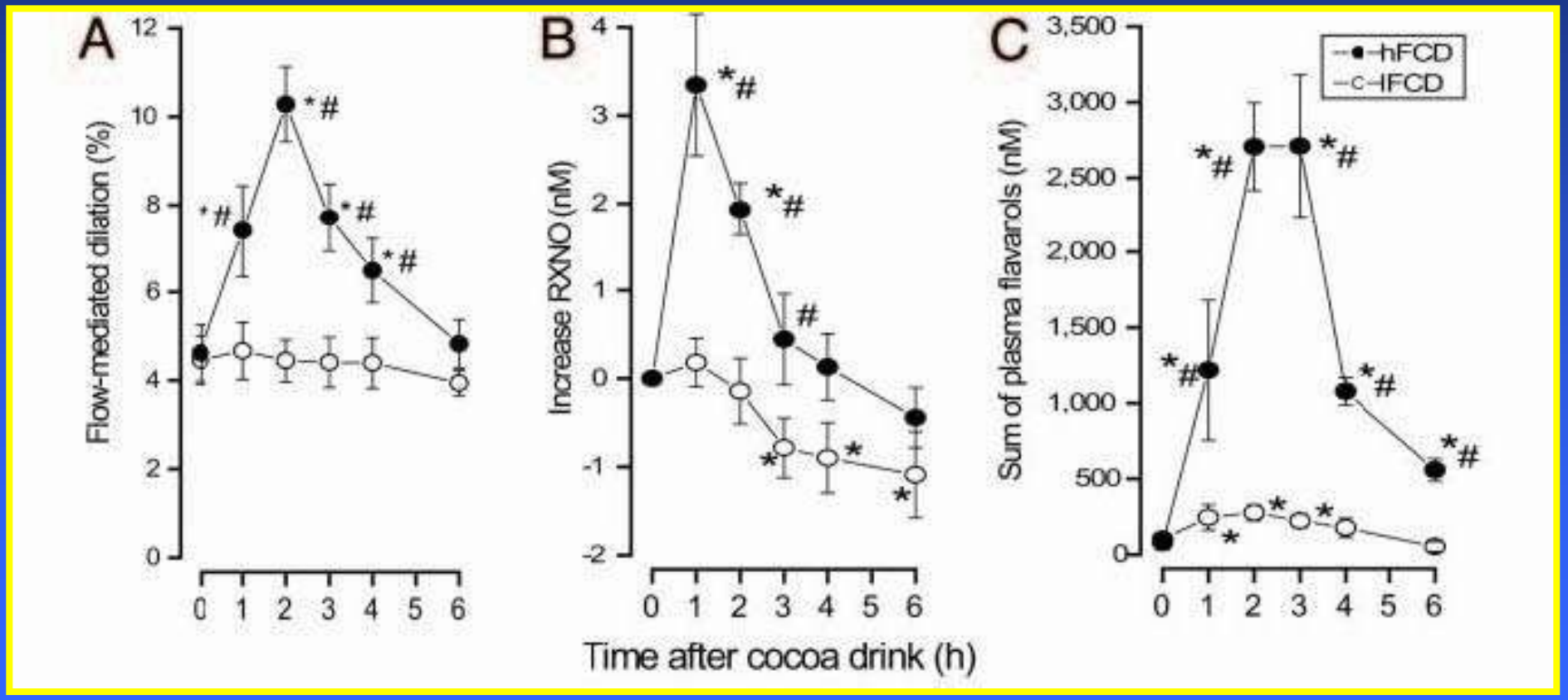
Risk factors:

- Smoking history
- Cholesterol level
- Diabetes
- Hypertension
- Age
- Male gender
- Family history

Celermajer et al., Am Coll Cardiol 1994;24:1468-1474

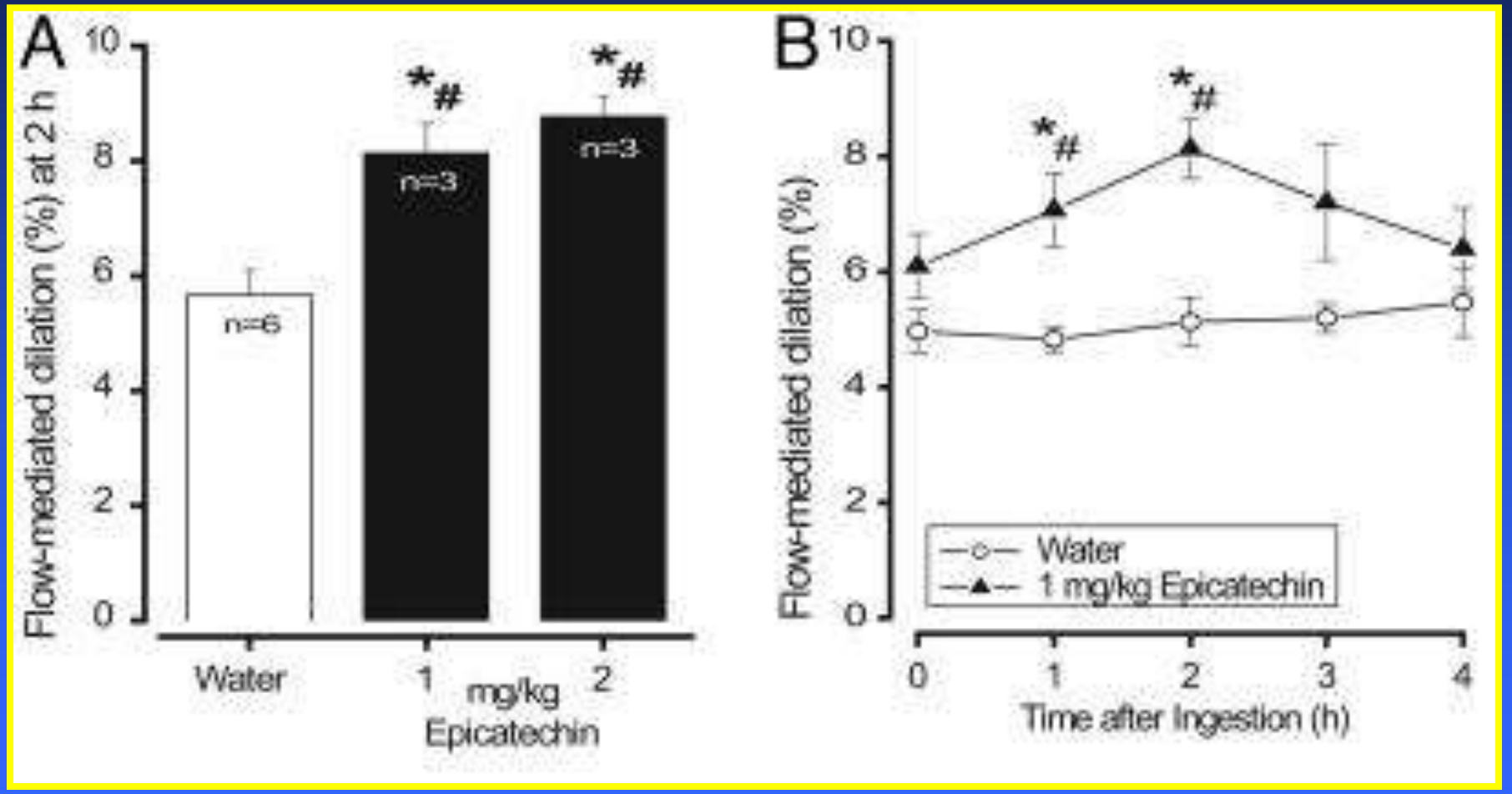
Ingestion of Flavanol-rich Cocoa Enhanced Flow-mediated Vasodilatation in Healthy Adults

- High-flavanol cocoa drink (hFCD) 917 mg
- Low-flavanol cocoa drink (lFCD) 37 mg of total flavanols



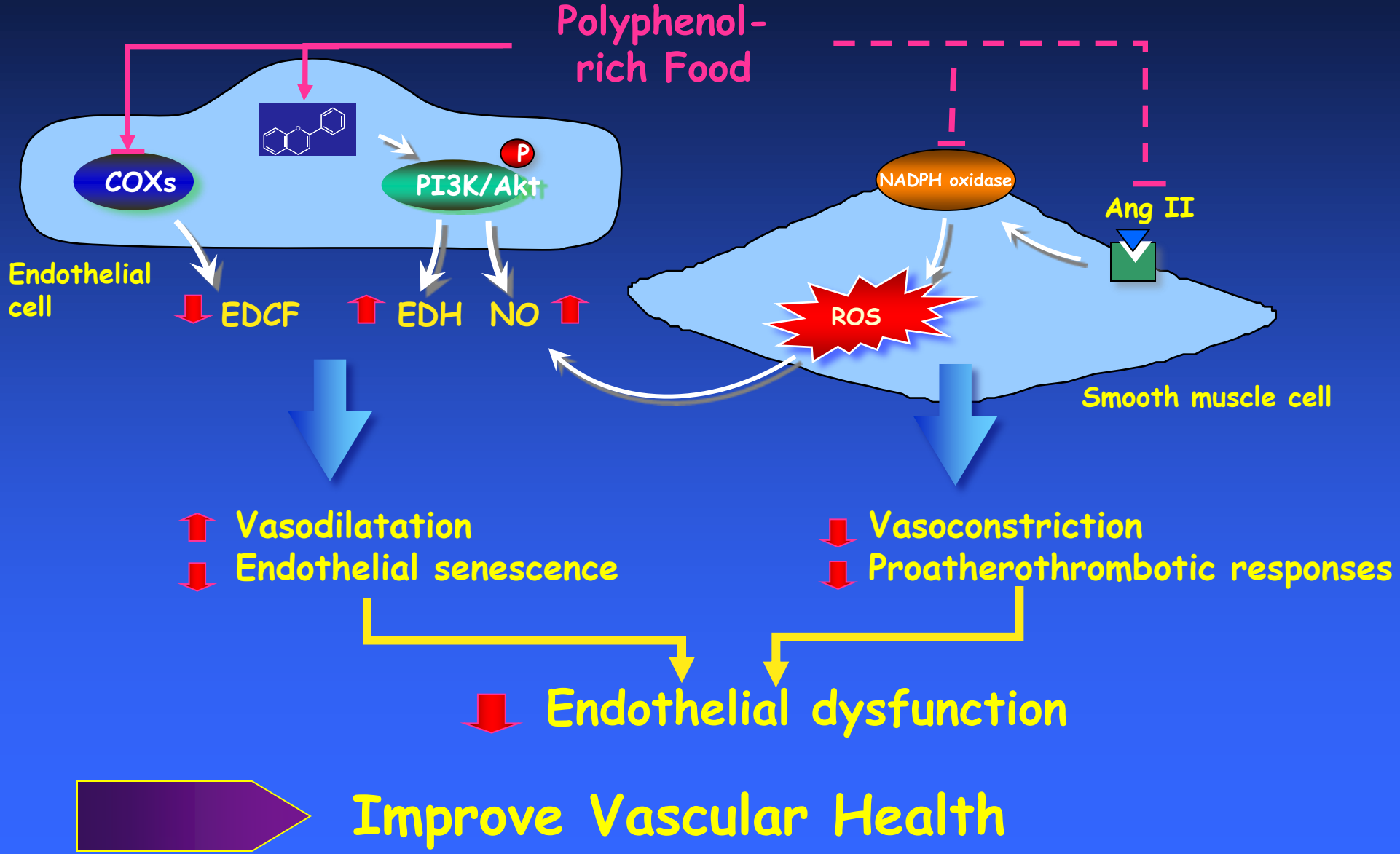
Schroeter *et al.* PNAS 2006; 103: 1024-1029

Ingestion of (-)-Epicatechin Enhanced Flow-mediated Vasodilatation in Healthy Adults



Schroeter *et al.*
PNAS 2006; 103: 1024-1029

Protective Effects of Polyphenols on Ageing-related Endothelial Dysfunction



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I. Dandache
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S. Khemais
J.H. Kim
P.N. Nguyen
J.O. Lee
J. Qaiser
S. Rachid
T.P. Ribeiro
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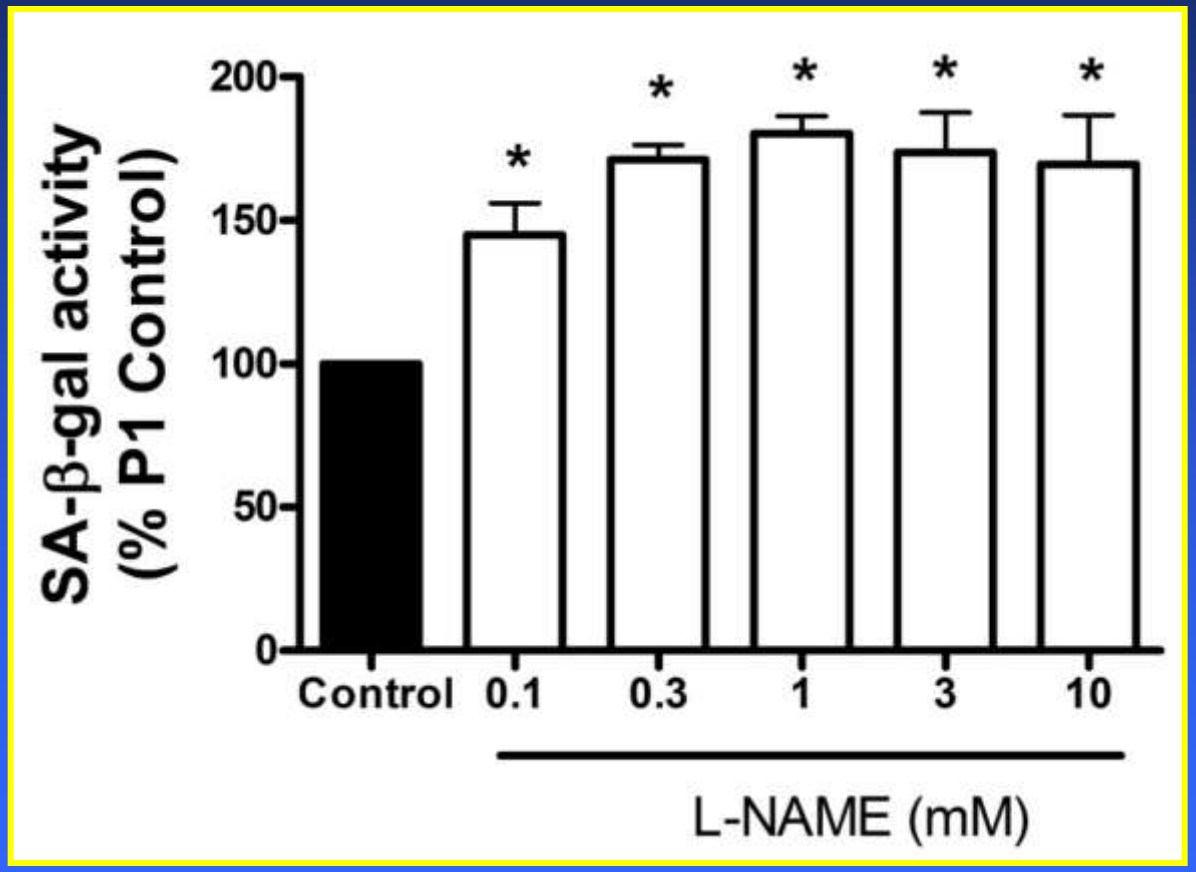
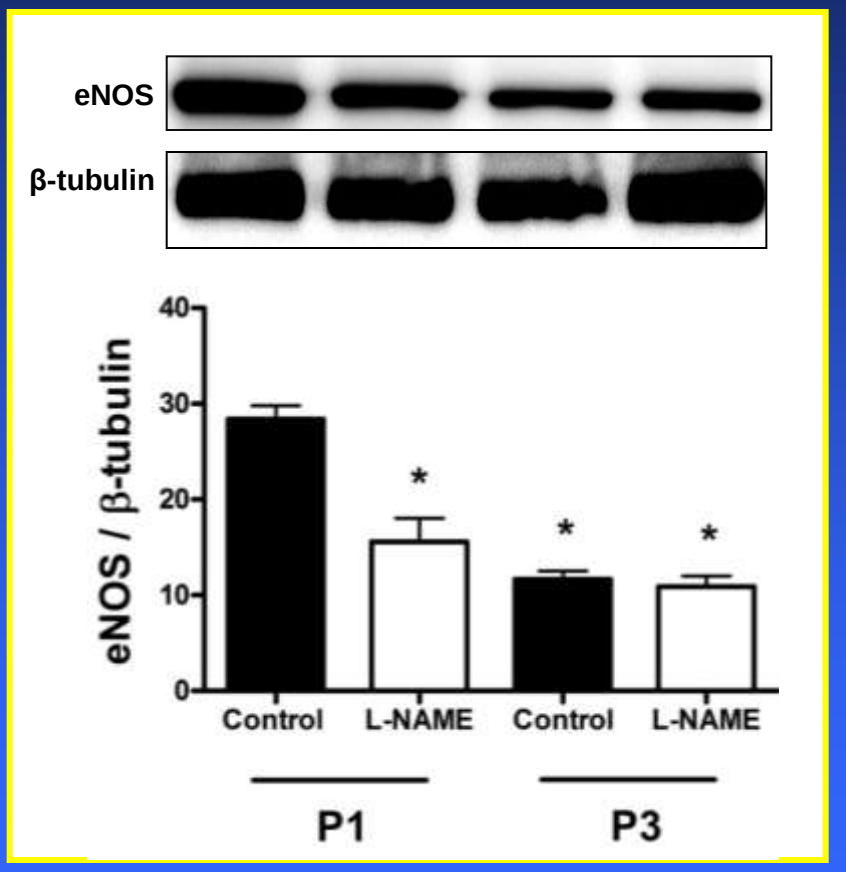
F. Zgheel

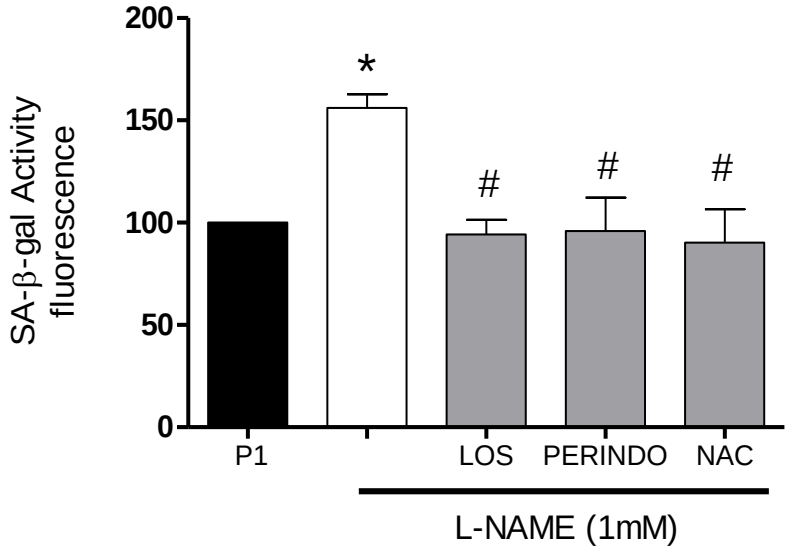
Premature Endothelial Cell Senescence Induced by eNOS inhibition

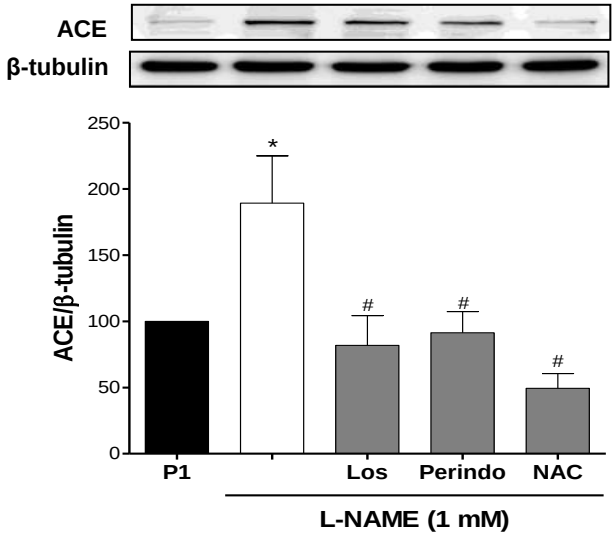


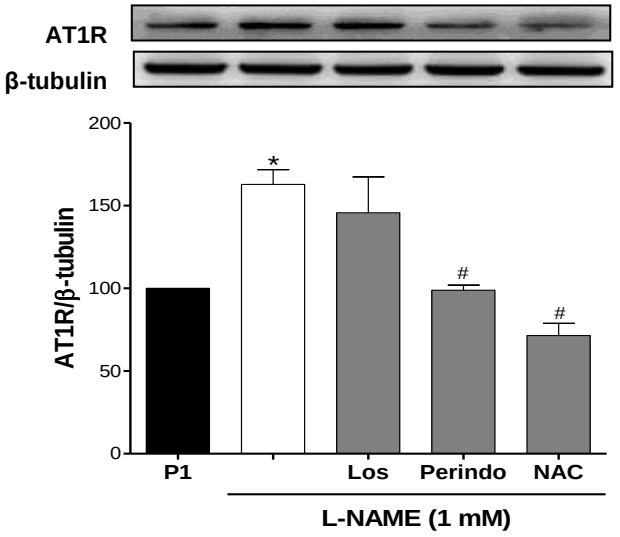


Khemais-Benkhiat et al.,J. Gerontol. 2015, Dec 15. pii: glv213

The local Angiotensin System Promotes Premature Endothelial Cell Senescence

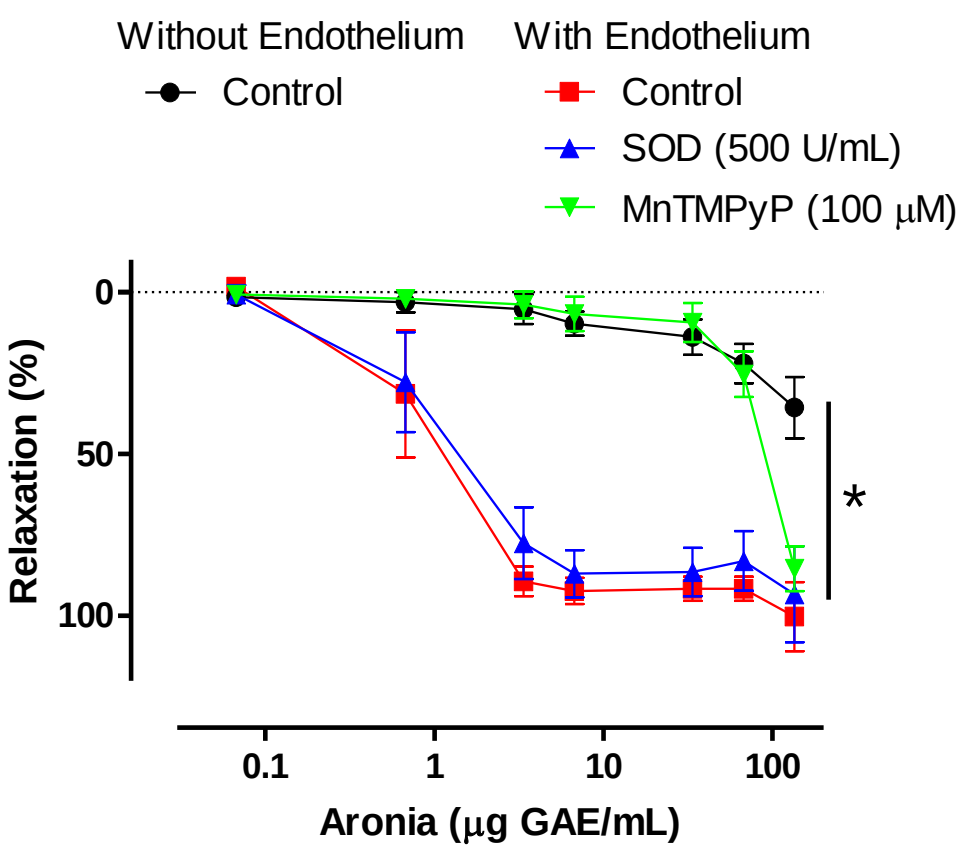


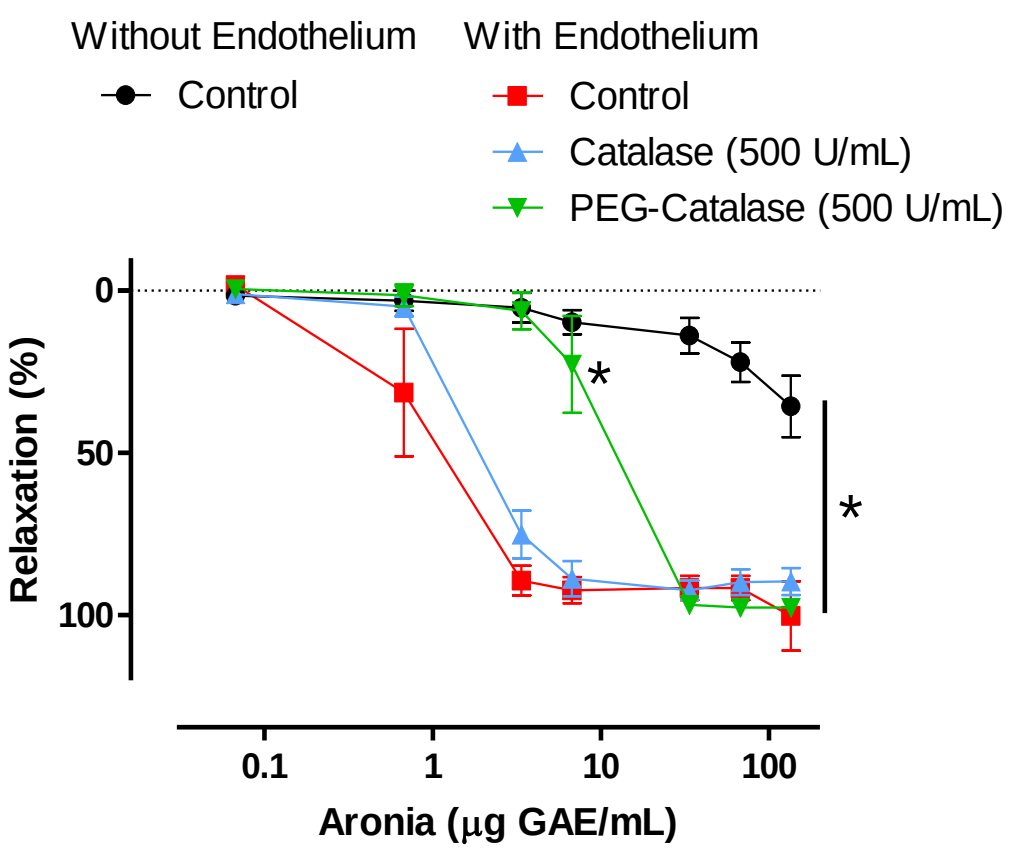




Aronia Juice induces Redox-sensitive Endothelium-dependent Relaxations in the Porcine Coronary Artery

in the presence of indomethacin (10^{-5} M), charybdotoxin (10^{-7} M), and apamin (10^{-7} M)

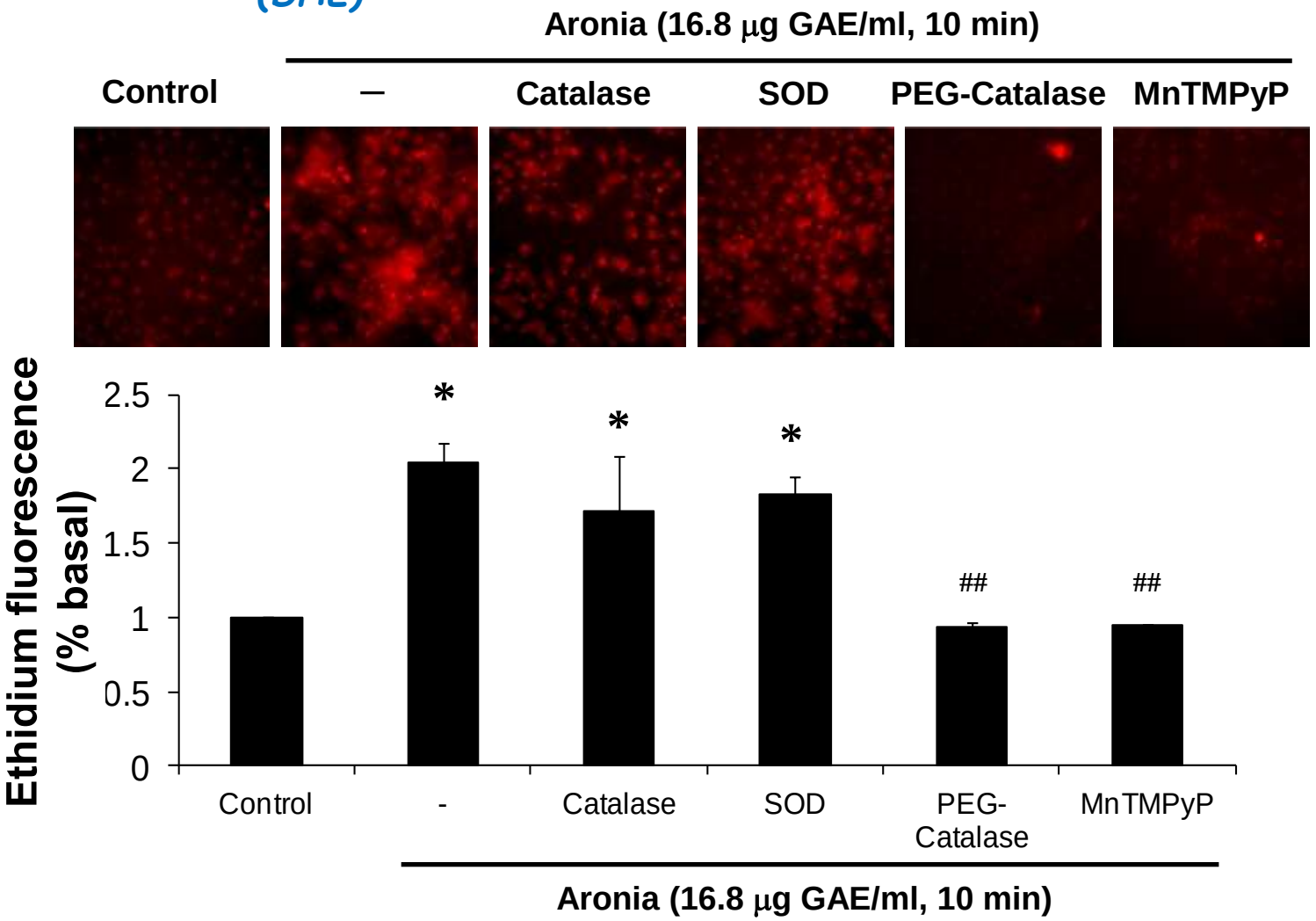




Kim et al., Nitric Oxide. 2013;35:54-64

Aronia Juice Induces the Intracellular Formation of ROS in Endothelial Cells

Fluorescent probe: Dihydroethidine (DHE) *in the presence of L-NA (10^{-4} M)*

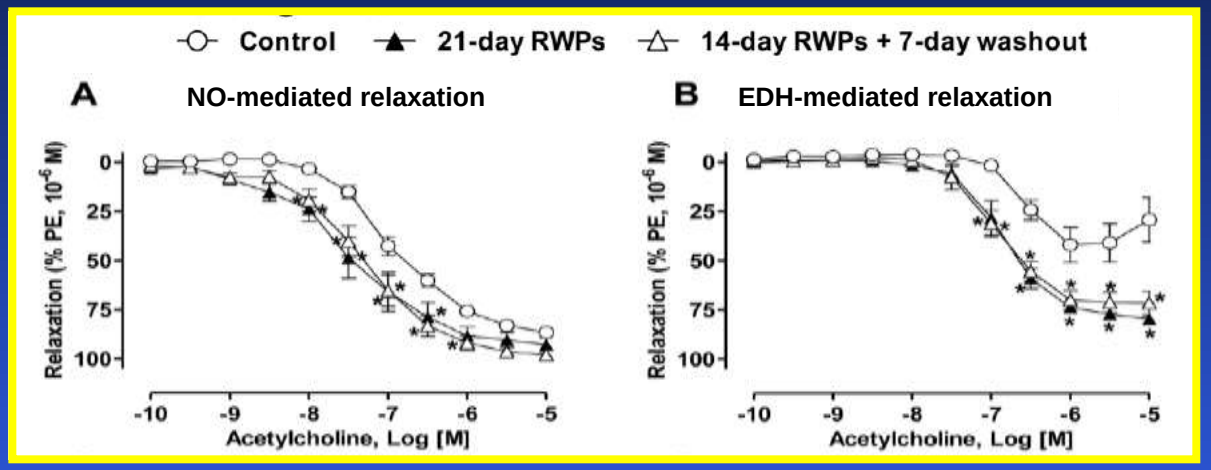


Kim et al., Nitric Oxide. 2013

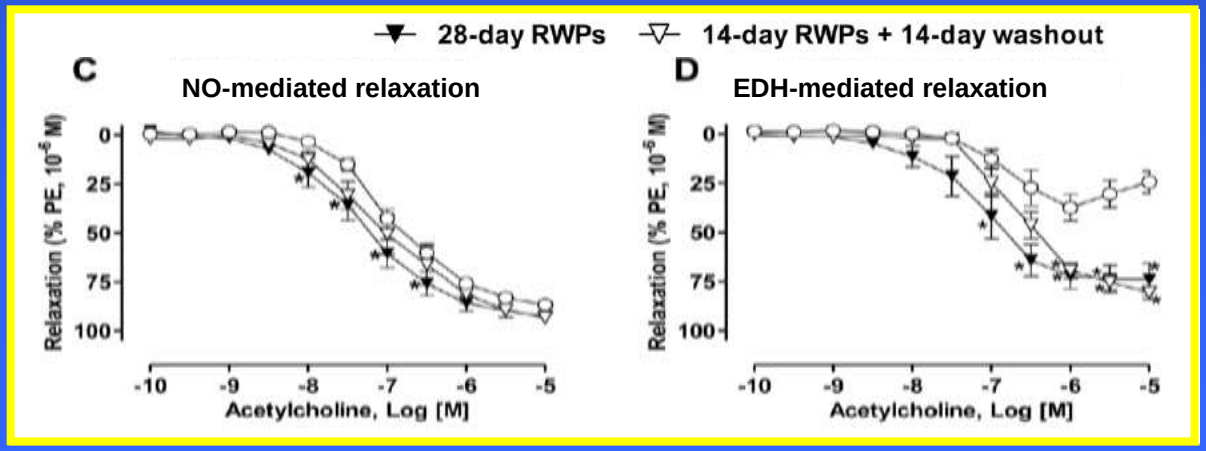
Ageing-related Endothelial Dysfunction

Mesenteric artery (46 w)

14-day RWPs treatment + 7-day washout

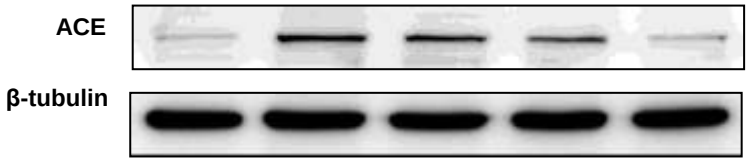


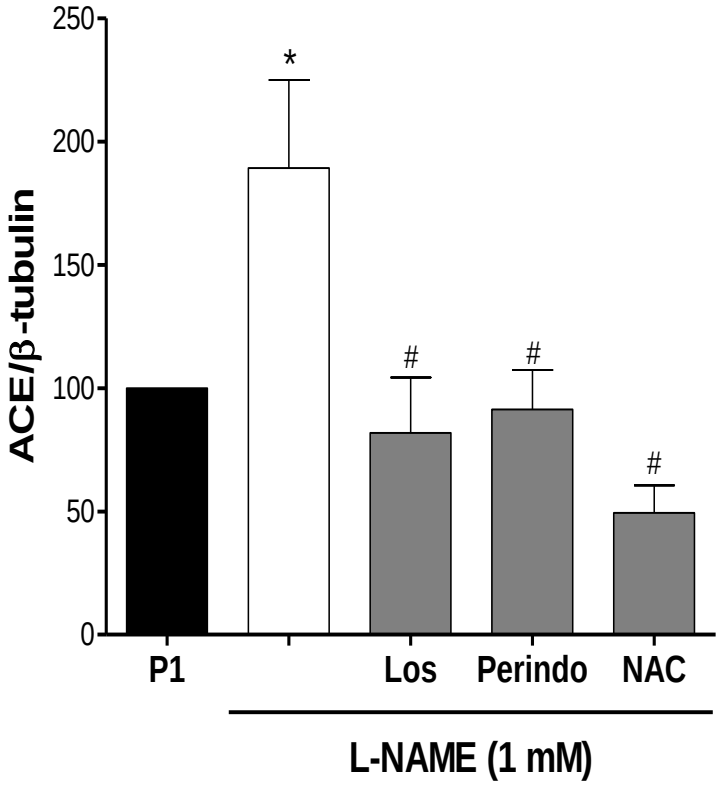
14-day RWPs treatment + 14-day washout

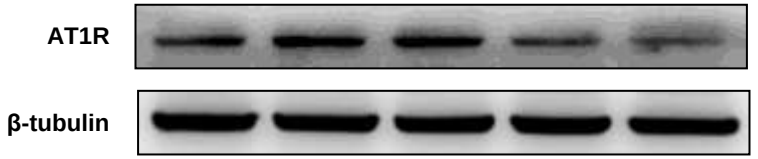


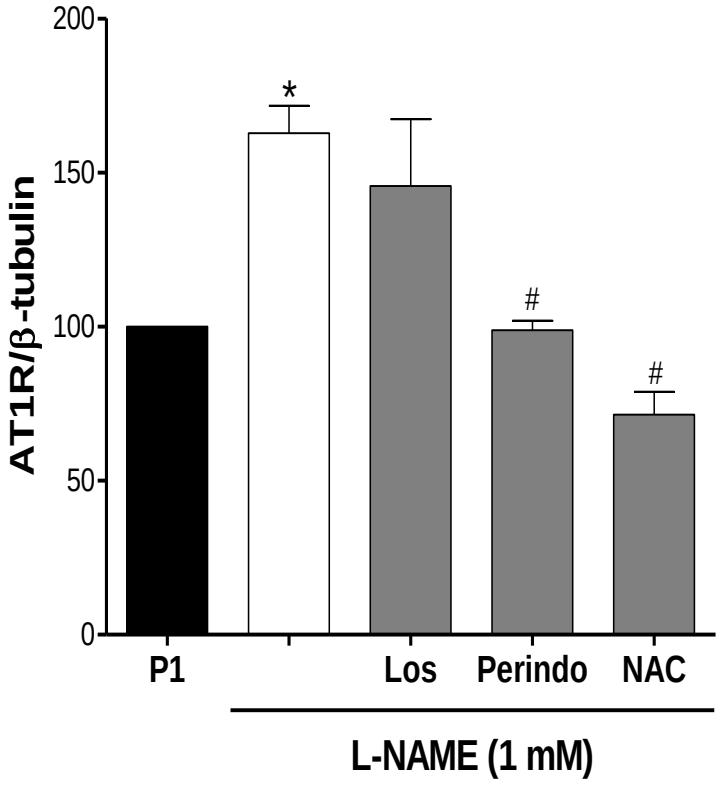
Idris Khodja et al., PLoS ONE 2012;7(2):e32039

Redox-sensitive upregulation of the local Angiotensin System in Premature Endothelial Cell Senescence

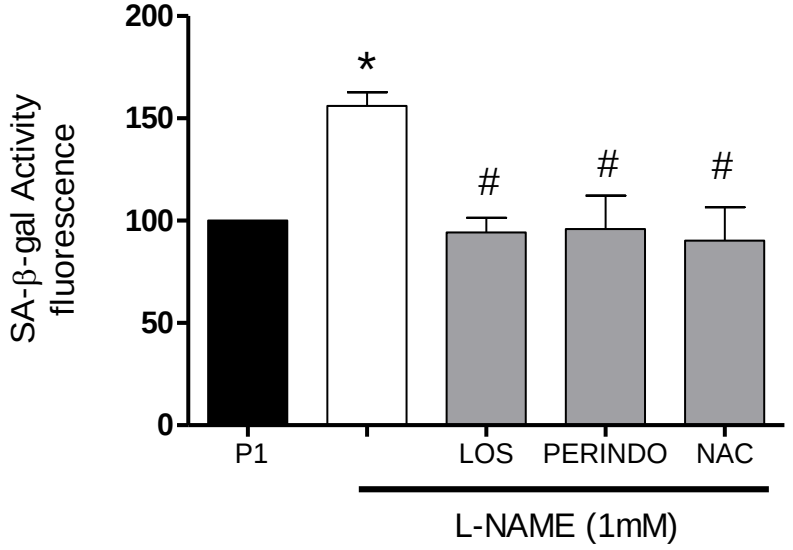


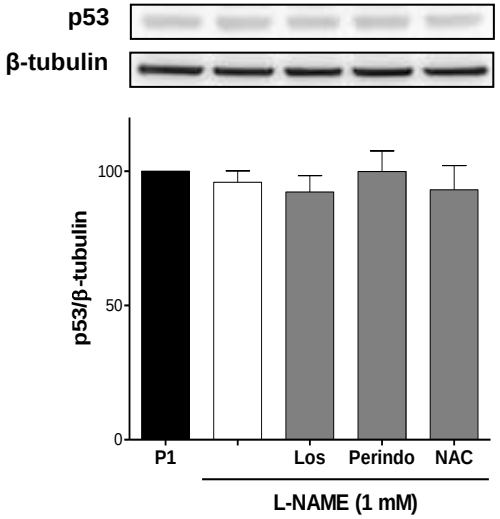


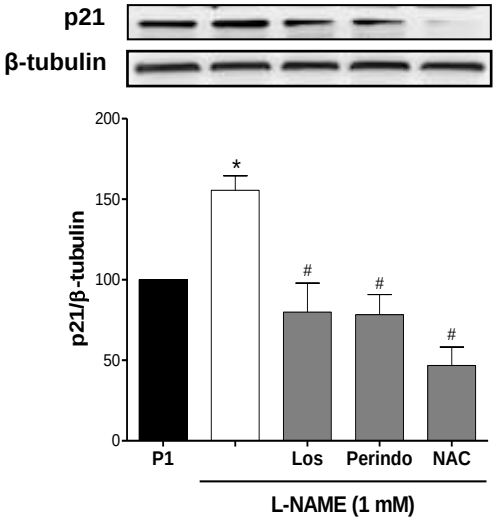


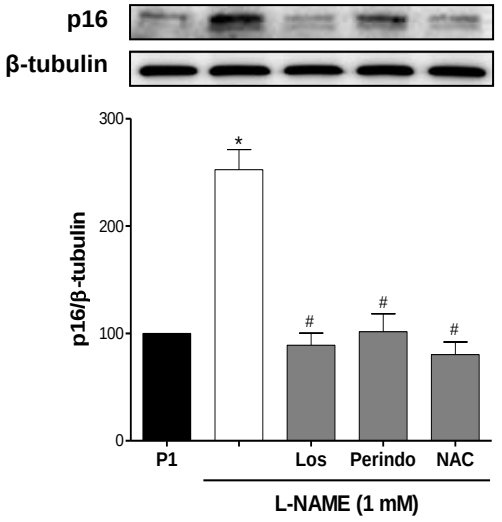


The local Angiotensin System Promotes Premature Endothelial Cell Senescence



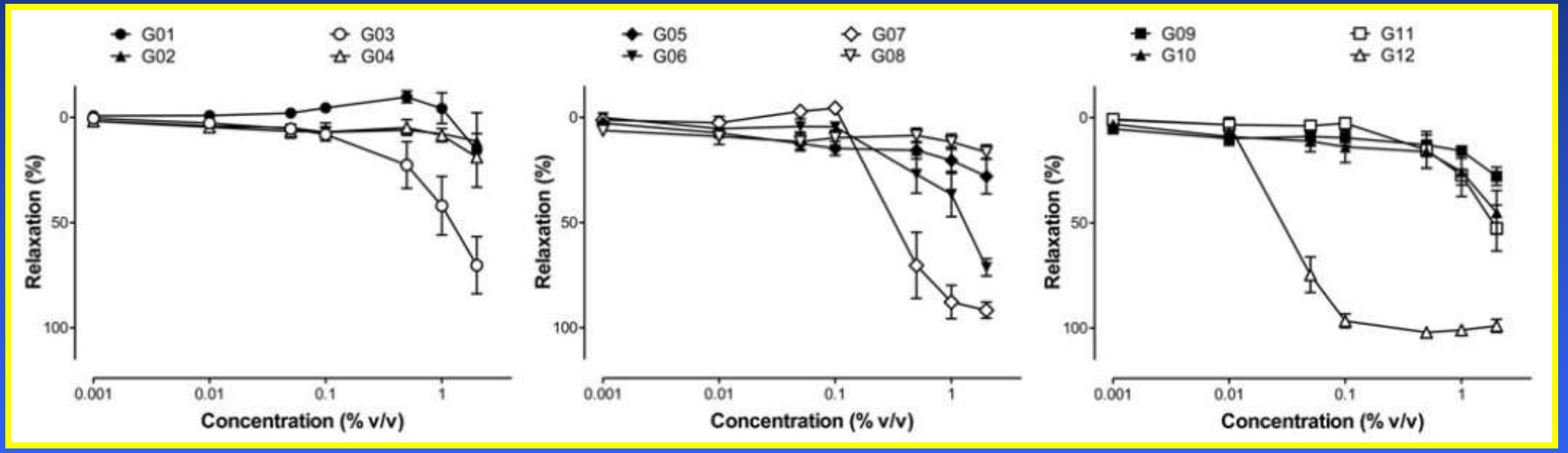






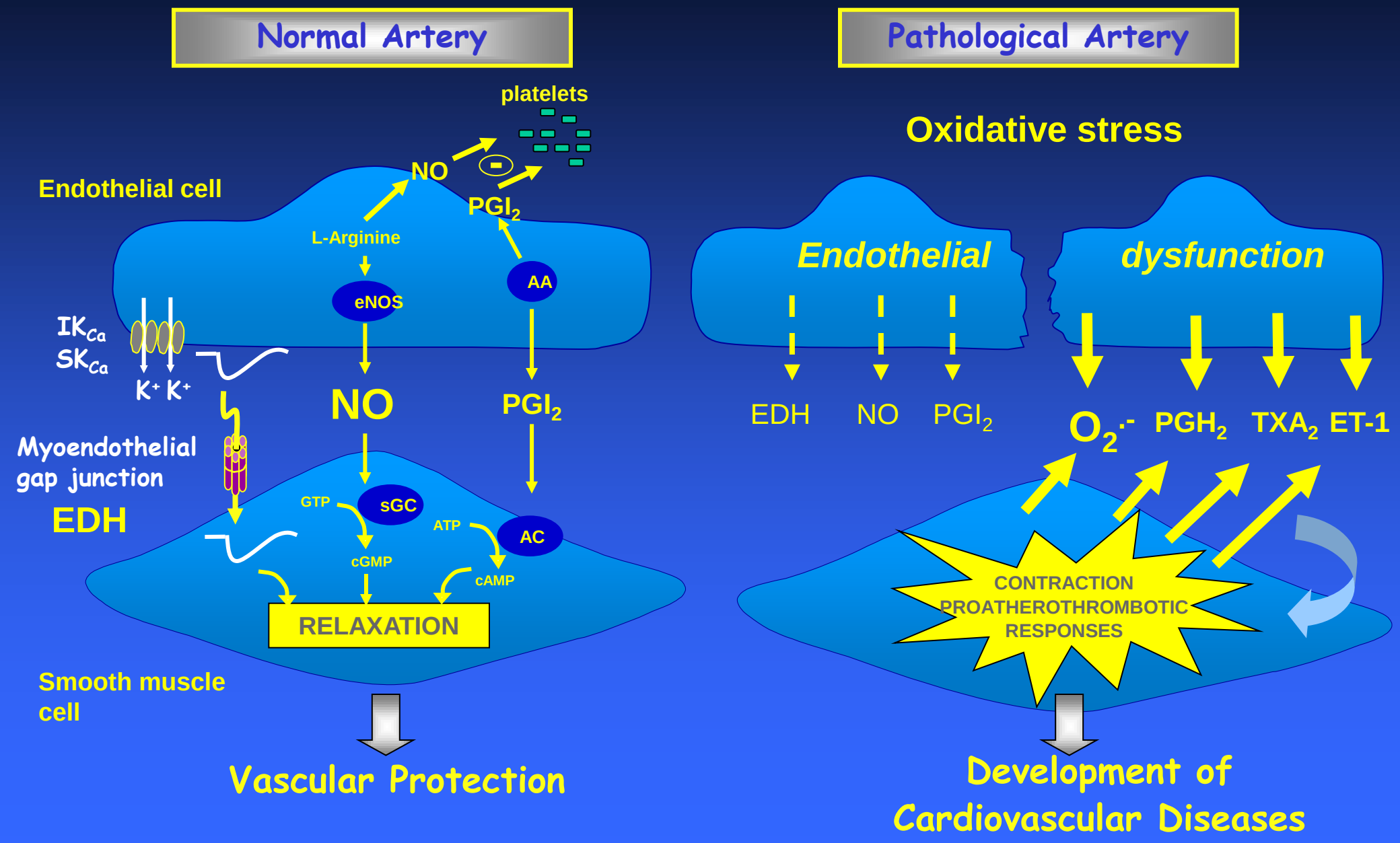
Commercial Grape Juices-induced Endothelium-dependent Relaxations in Coronary Artery rings

12 different commercial grape juices

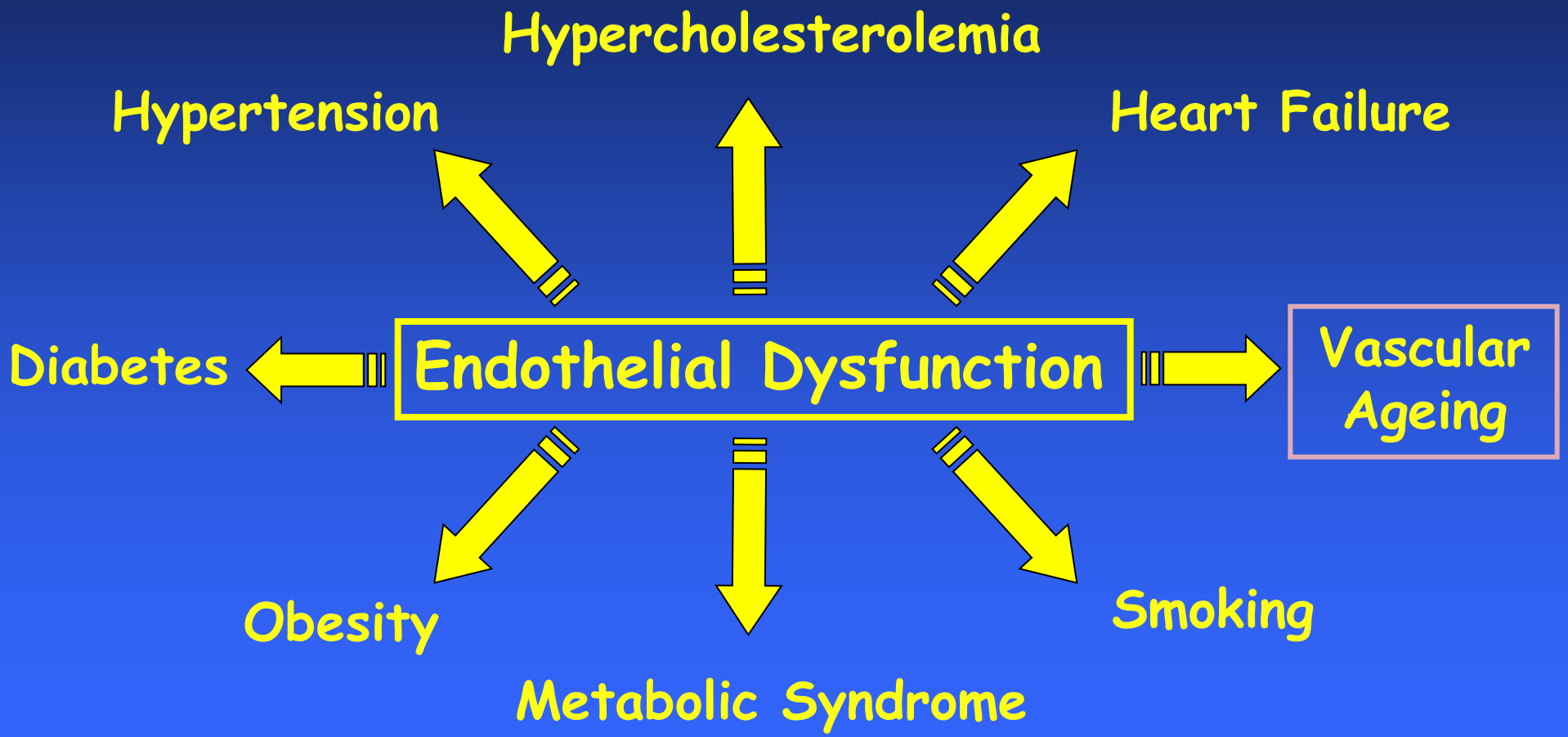


Auger et al., J Med Food 2014

Endothelium and the Control of Vascular Responses in Healthy and Diseased Blood Vessels

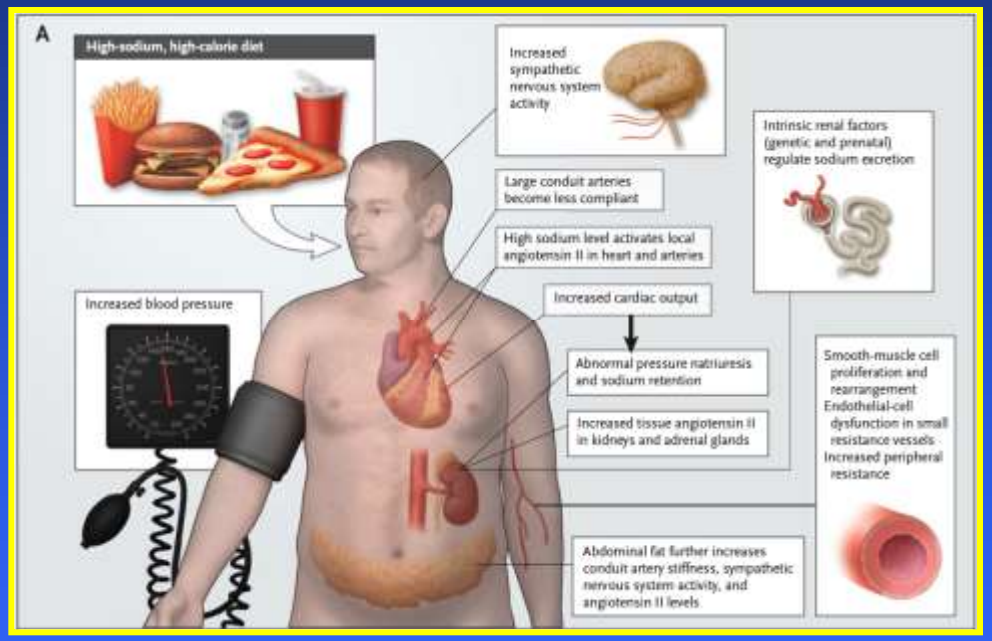


Oxidative Stress-related Endothelial Dysfunction in Cardiovascular Diseases

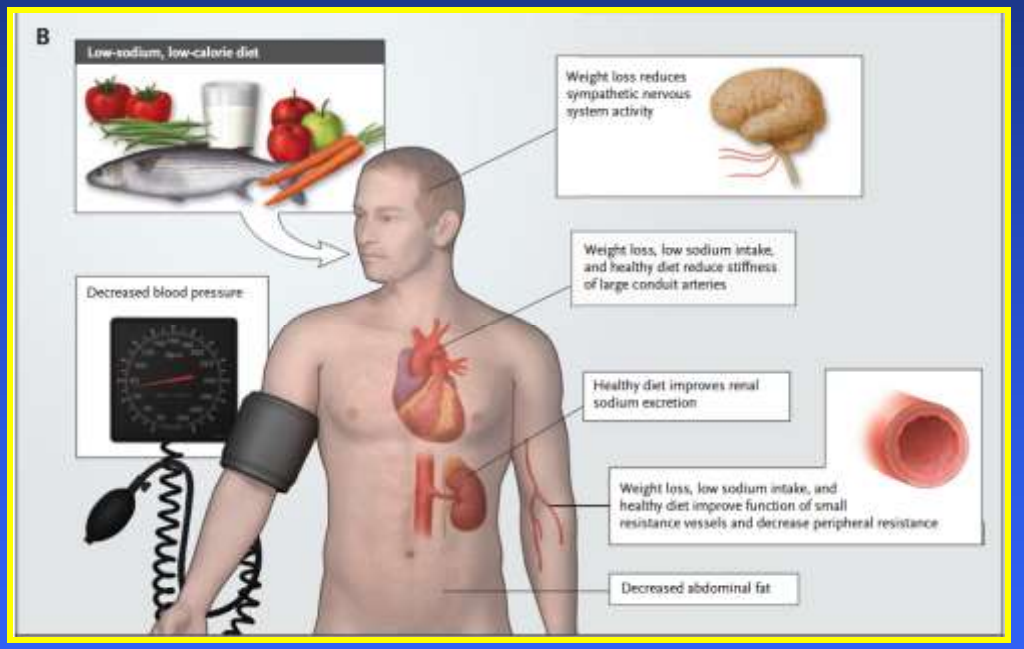


Cardiovascular Health and Diseases

Unhealthy diet



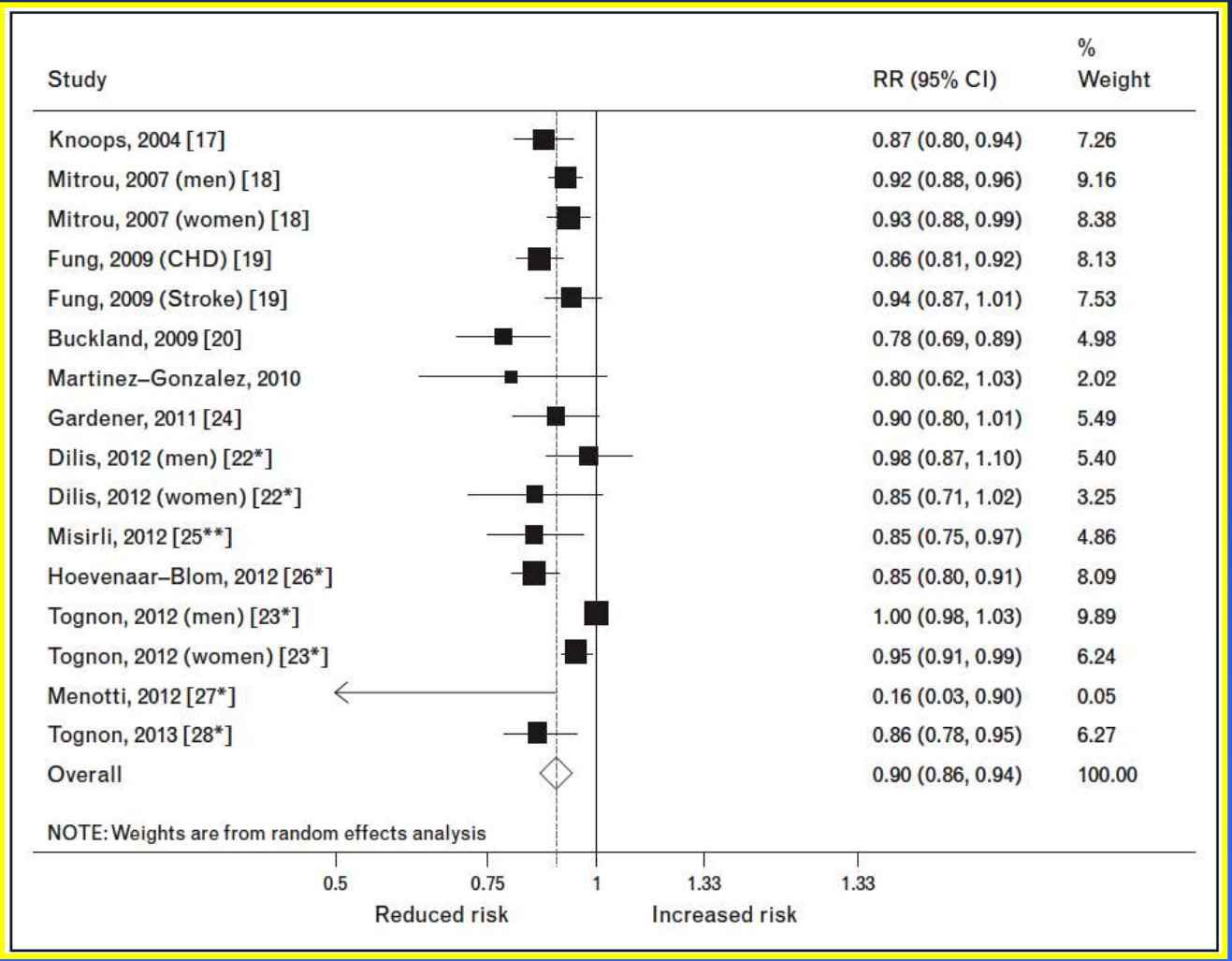
Healthful dietary patterns (DASH diet, Mediterranean diet)



Sacks and Campos
NEJM 2010;362:2102-12

Adherence to the Mediterranean Diet and Human Health

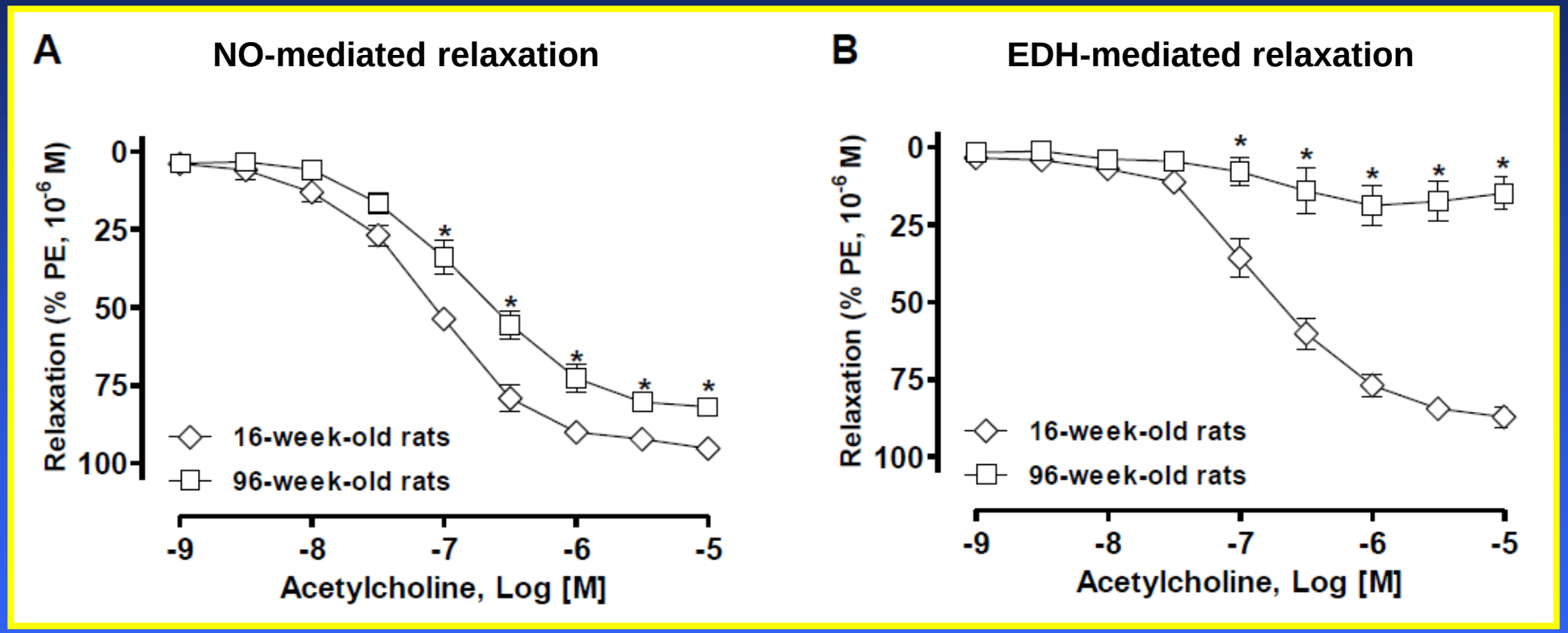
Meta-analysis of 16 prospective cohort studies



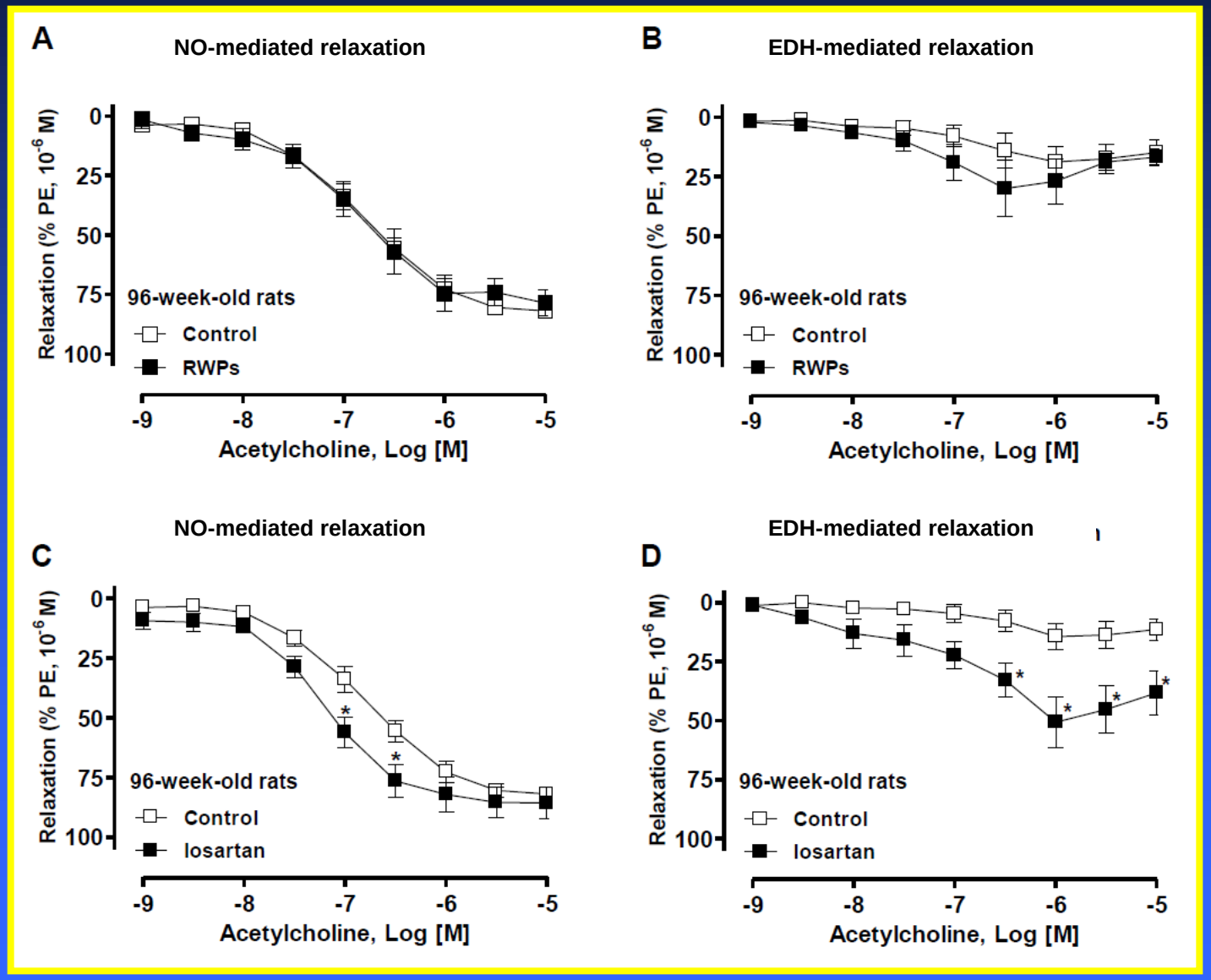
10% relative reduction in the risk of CVD

Martinez-Gonzalez and Bes-Rastrollo
Curr Opin Lipidol.
2014;25:20-26

Ageing-related Endothelial Dysfunction



Ageing-related Endothelial Dysfunction



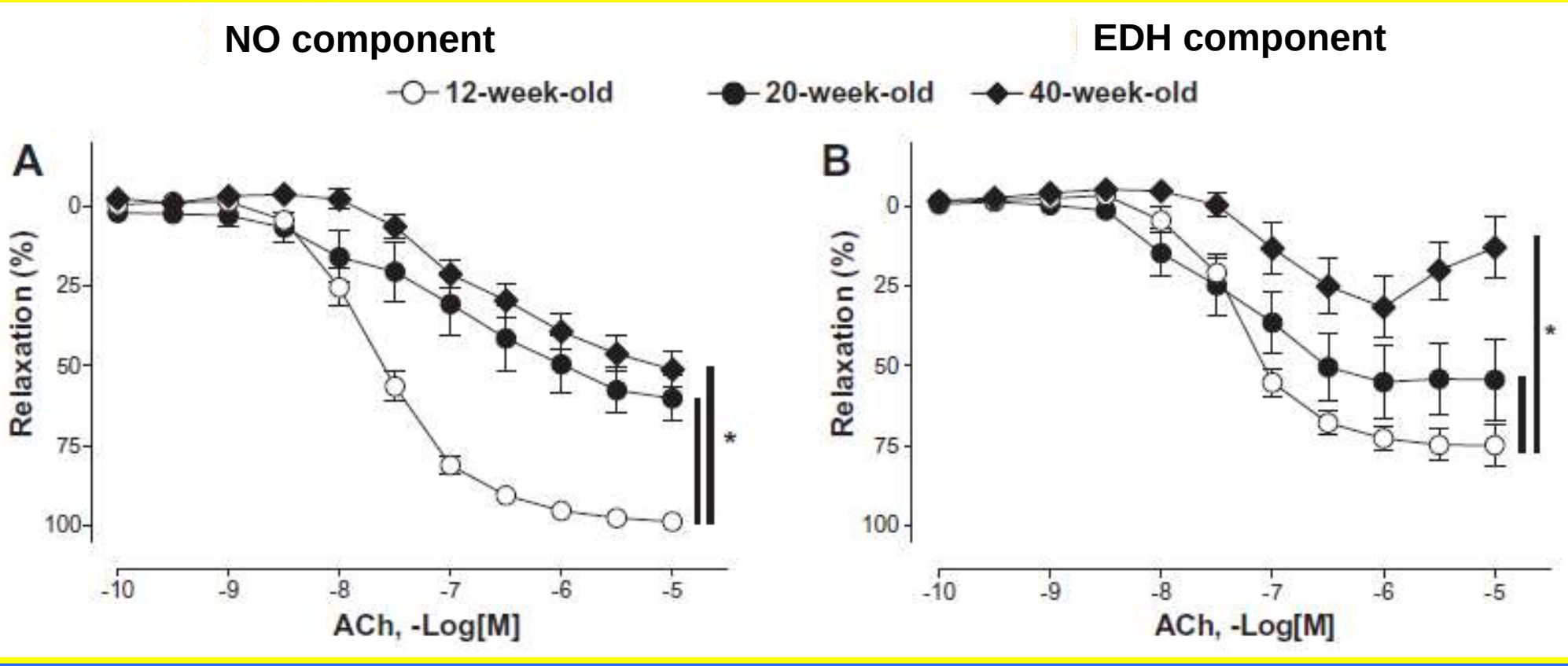
Ageing-related Endothelial Dysfunction

Male Wistar rats (inbred strain)

Mesenteric artery

(in the presence of indomethacin, charybdotoxin and apamin)

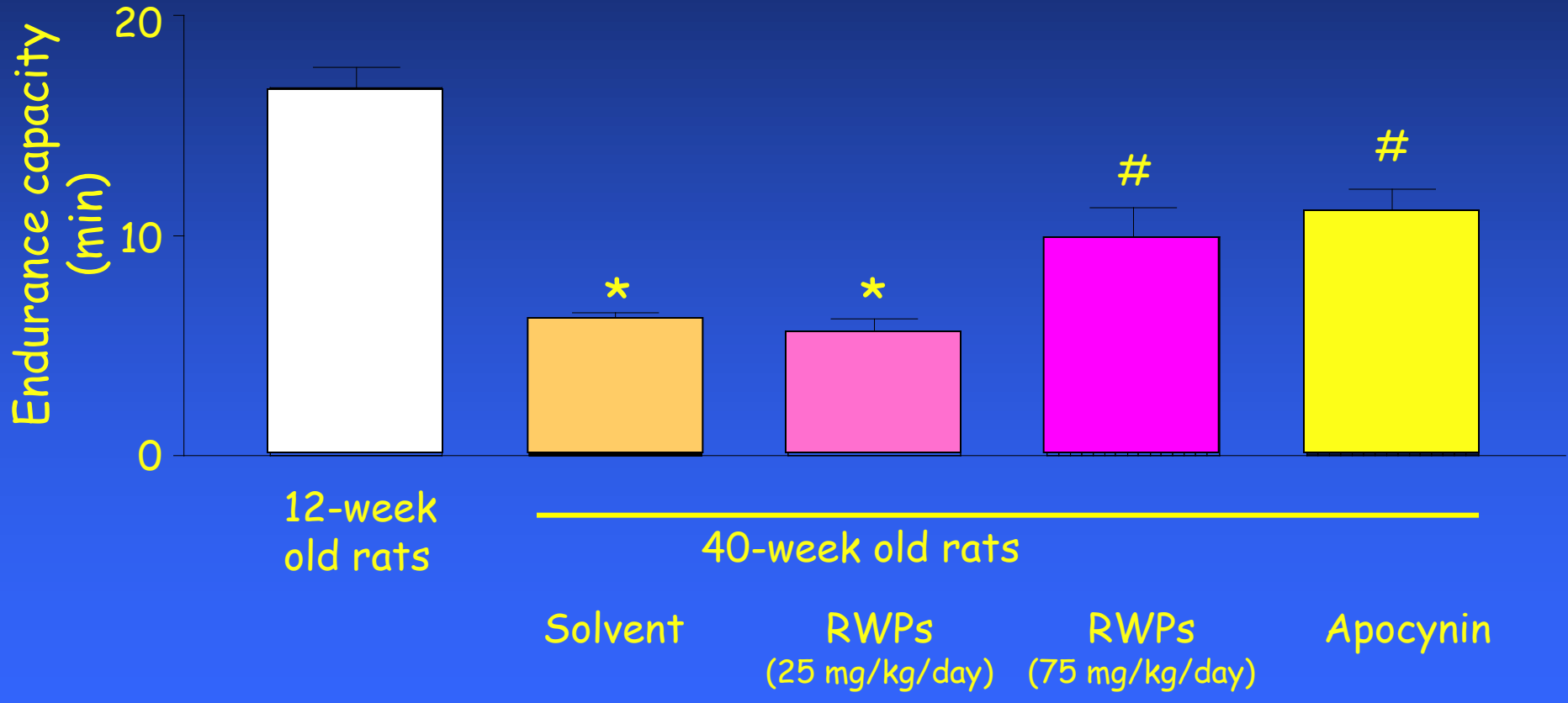
(in the presence of indomethacin, N^G-nitro-L-arginine)



Dal-Ros et al., BBRC 2011;404:743-749

RWPs and Endothelial Dysfunction in Ageing

Treadmill experiment



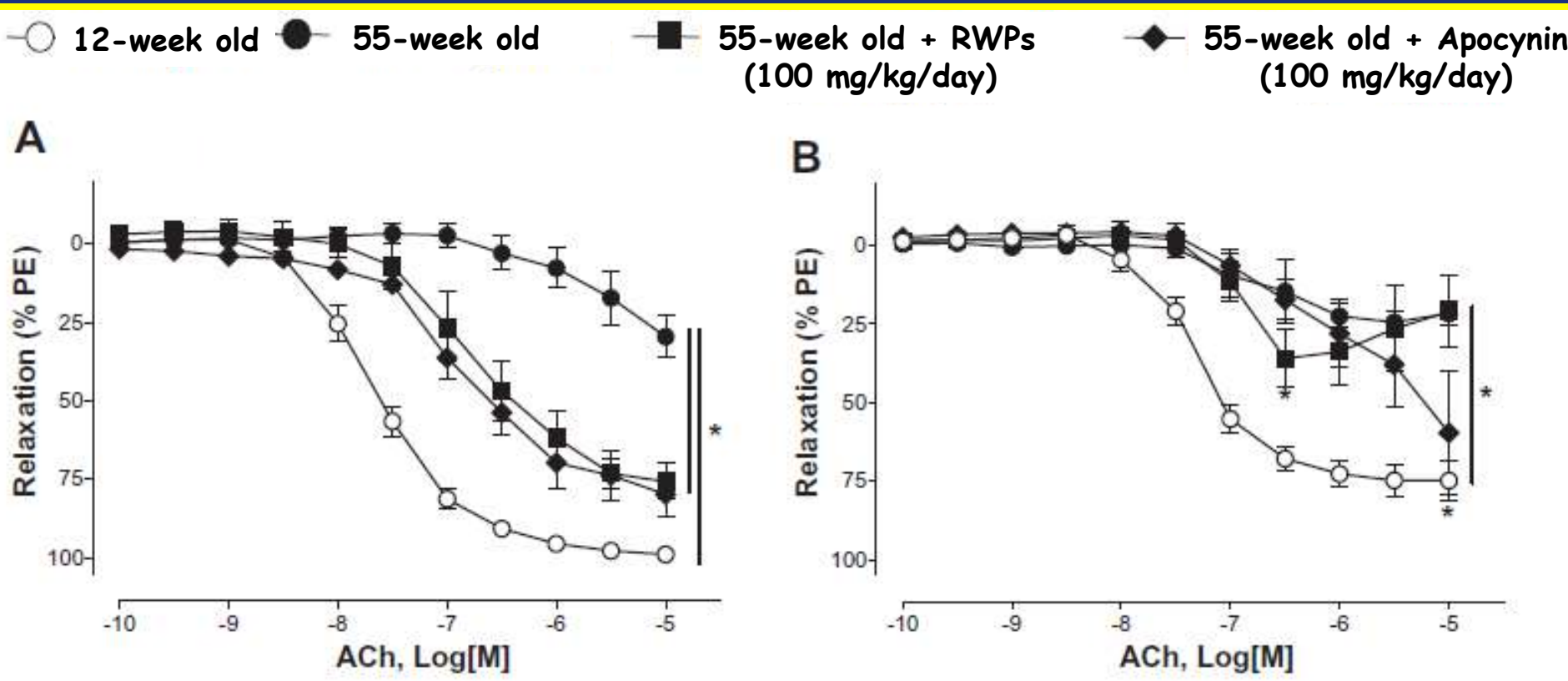
Dal-Ros et al., BBRC, 2011;404:743-749

RWPs improve an Established Ageing-related Endothelial Dysfunction

Mesenteric artery

NO component

EDH component



Dal-Ros et al., BBRC 2012;419:381-387

RWPs and Endothelial Dysfunction in Ageing

Preventive study

16

40 week

- Vascular reactivity
- Immunohistochemistry
- Physical exercise capacity

RWPs
(25 or 75 mg/kg/day)

Apocynin
(100 mg/kg/day)

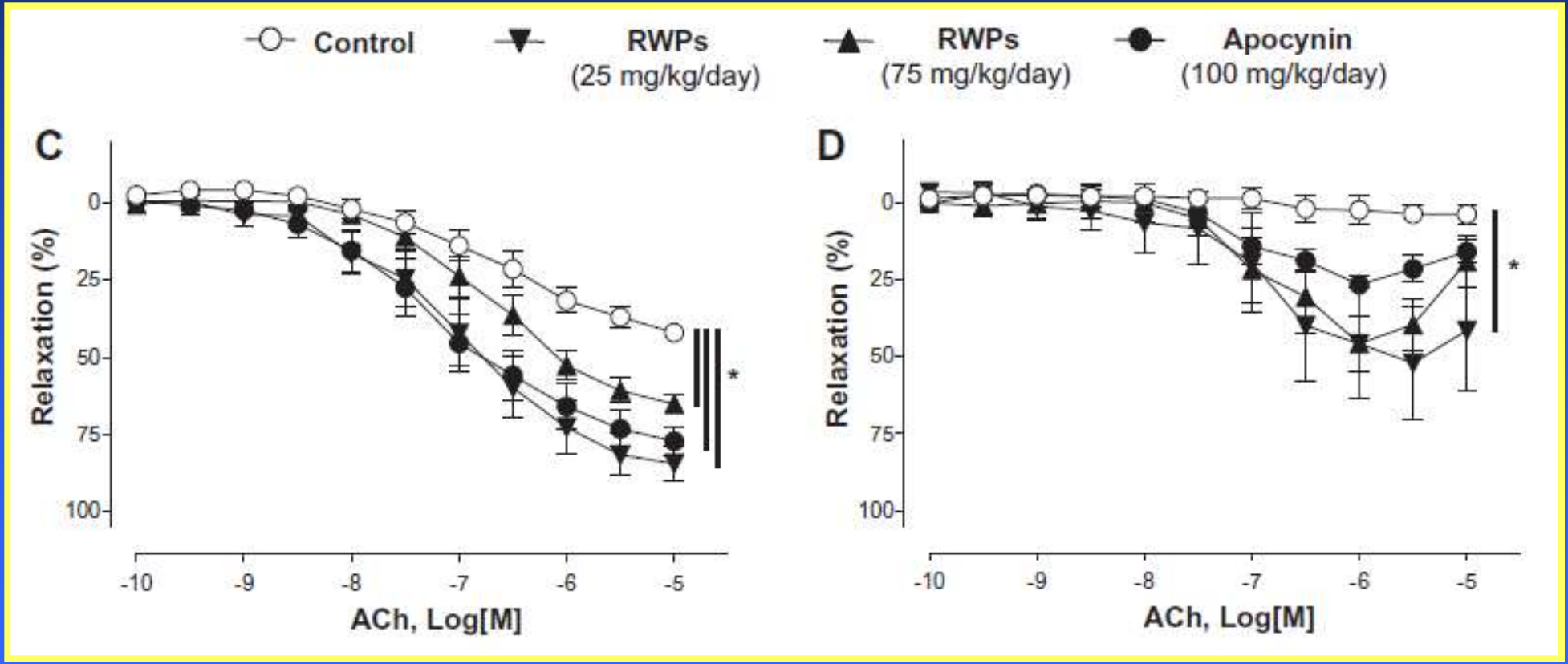
Solvent

Chronic Intake of RWPs by Young Rats Prevents Ageing-induced Endothelial Dysfunction

Mesenteric artery 40-week old rats

NO component

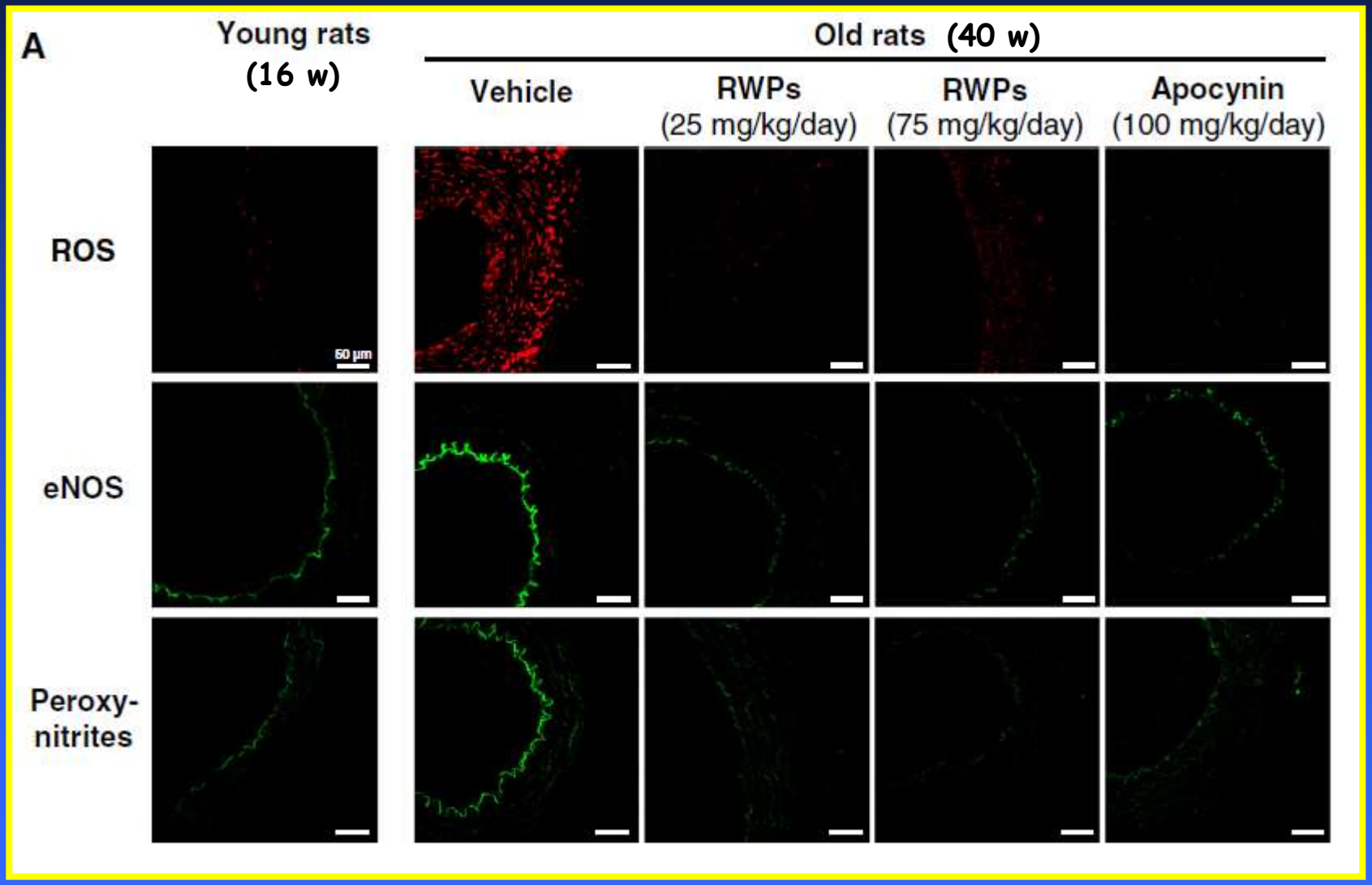
EDH component



Dal-Ros et al., BBRC, 2011;404:743-749

RWPs and Endothelial Dysfunction in Ageing

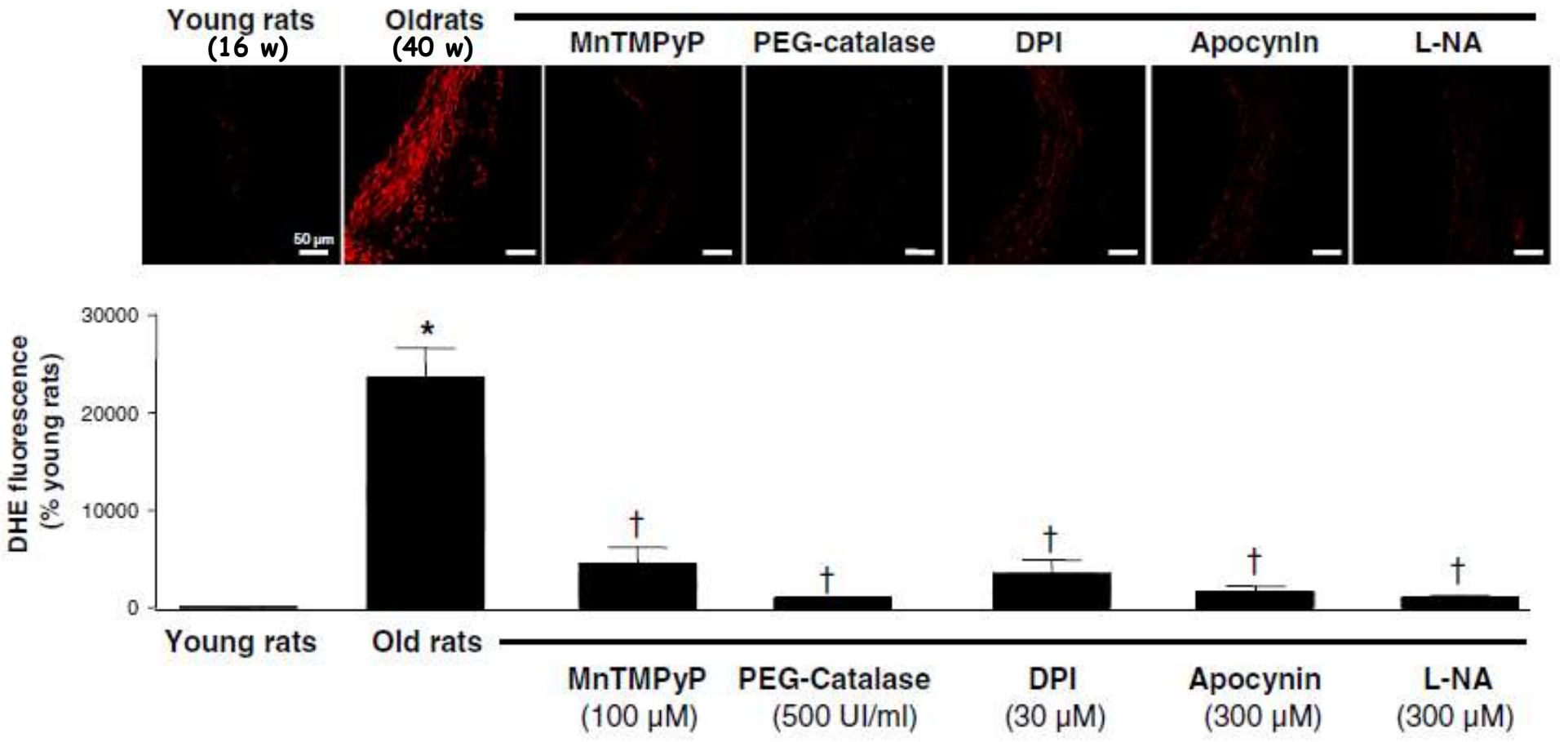
Mesenteric artery



Dal-Ros et al., BBRC, 2011;404:743-749

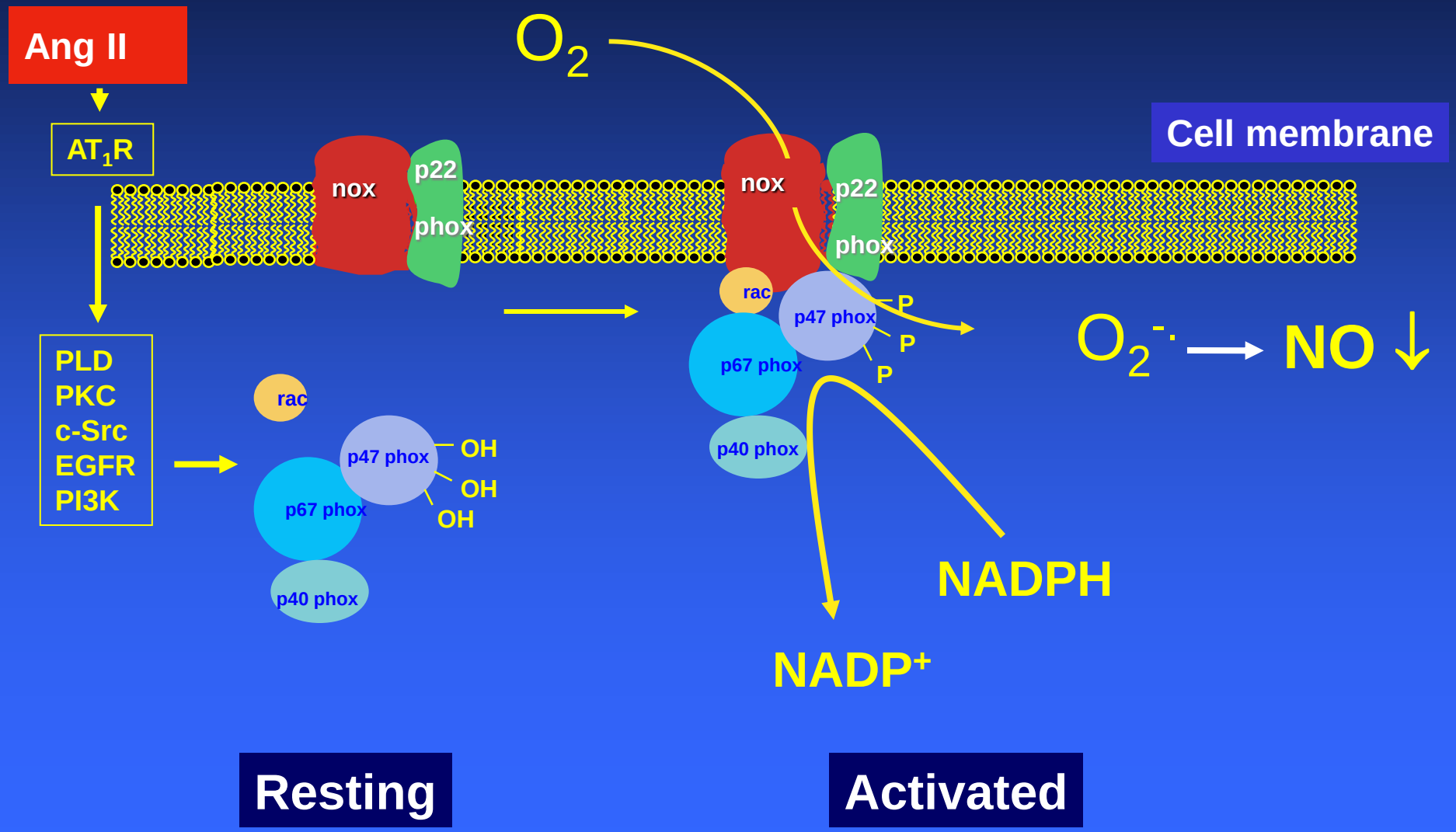
Vascular Oxidative Stress in Ageing

Mesenteric artery

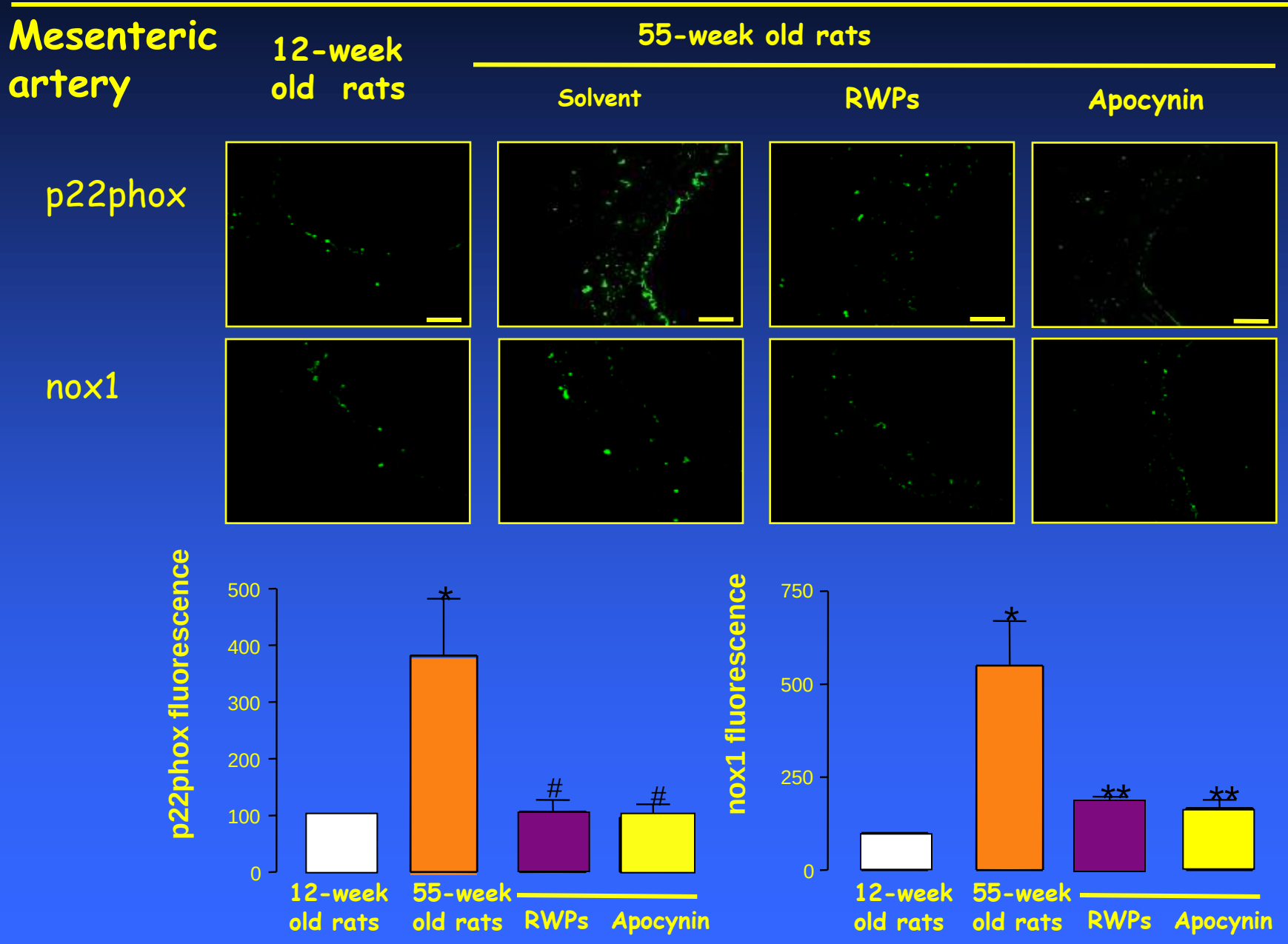


Dal-Ros et al., BBRC, 2011;404:743-749

Vascular NADPH oxidase

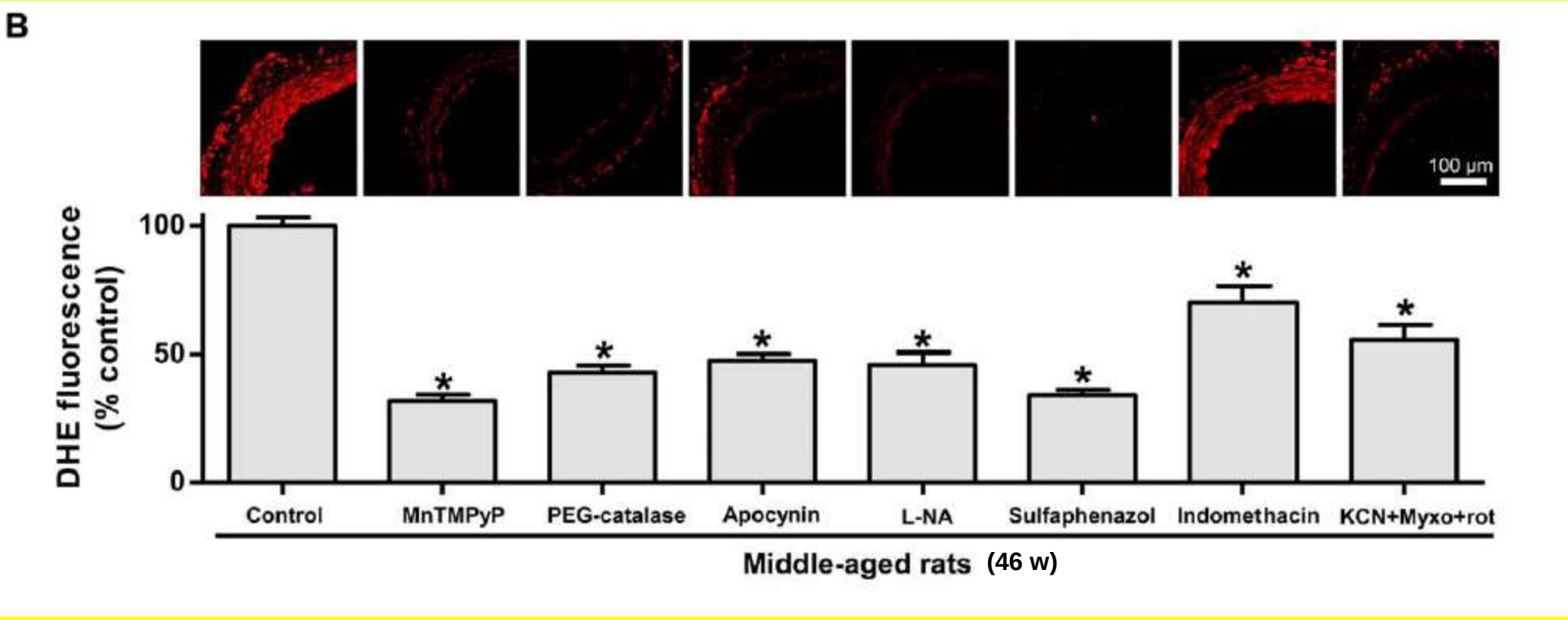


Vascular Oxidative Stress in Ageing: Role of NADPH oxidase



Dal-Ros et al., 2012

Vascular Oxidative Stress in Ageing



Idris Khodja et al., PLoS ONE 2012;7(2):e32039

Viniflhor
OFFICE NATIONAL INTERPROFESSIONNEL DES FRUITS, DES LEGUMES, DES VINS ET DE L'HORTICULTURE

Red Wine Polyphenolic Extract (RWPs)

French Red Wine (Corbières A.O.C.)

1 liter of wine produced 2.9 g of RWPs

-Flavanol:
- Catechin 8.6 mg/g
- Epicatechin 8.7 mg/g

-Anthocyanin:
- Malvidin-3-glucoside 11.7 mg/g
- Peonidin-3-glucoside 0.66 mg/g
- Cyanidin-3-glucoside 0.06 mg/g

-Phenolic acid:
- Gallic acid 5.0 mg/g
- Caffeic acid 2.5 mg/g
- Caftaric acid 12.5 mg/g