Effect of novel plant antioxidant from *Aronia melanocarpa* on cardiovascular risk factors in patients after MI

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Proposed mechanism by which flavonoids may reduce risk for cardiovascular diseases

- **Oxidative stress**
  - ✓ Scavenge reactive oxygen and nitrogen species
  - ✓ Chelate redox-active transition metal ions
  - ✓ Spare and interact with other antioxidants
  - ✓ Inhibition of the redox-sensitive transcription factors
  - ✓ Inhibition of pro-oxidant enzymes
  - ✓ Induction of antioxidant enzymes

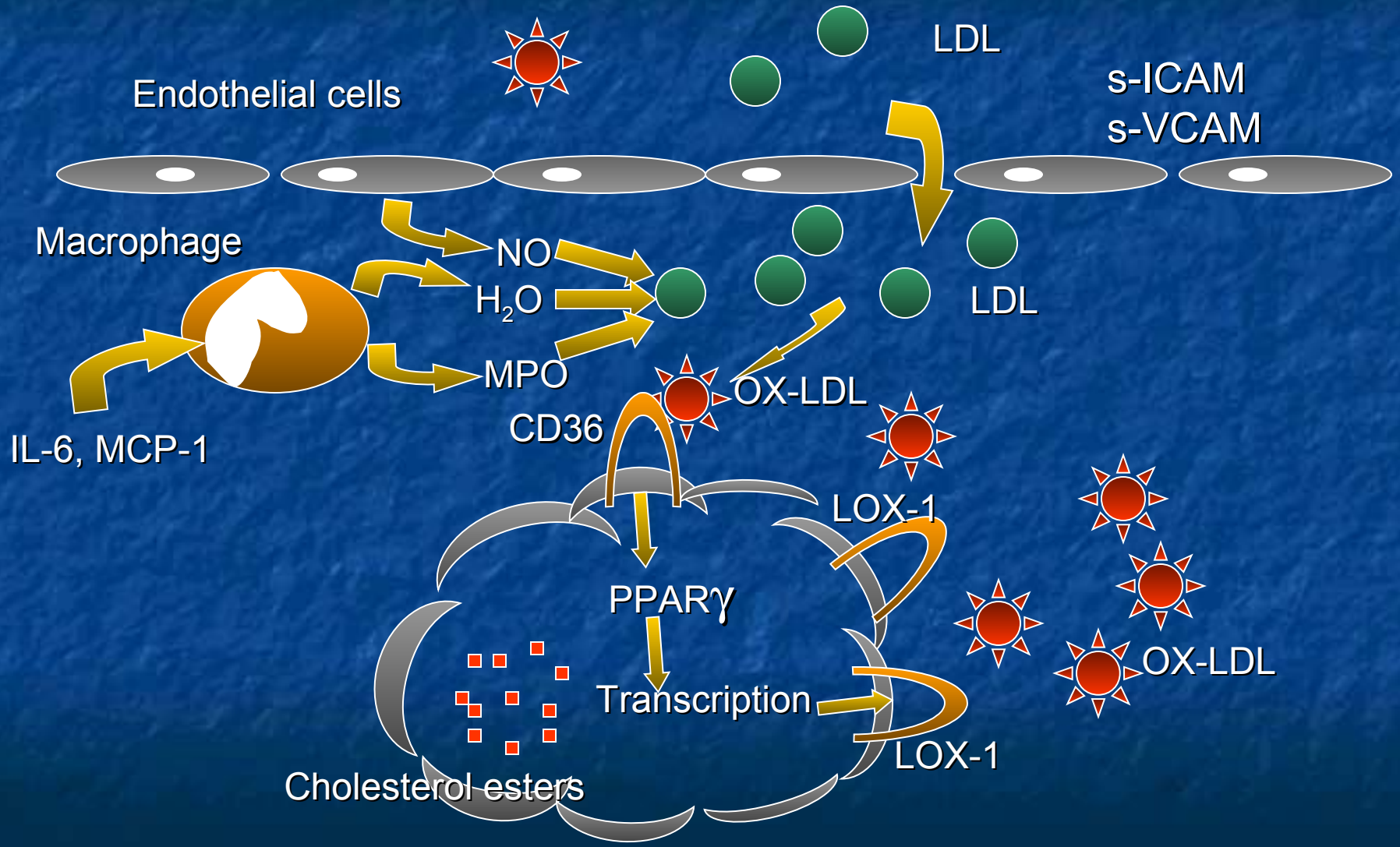
Proposed mechanism by which flavonoids may reduce risk for cardiovascular diseases

- **Growth of atherosclerotic plaque**
  - Reduce adhesion molecule expression
  - Anti-inflammatory
  - Reduce the capacity of macrophages to oxidatively modified LDL

Proposed mechanism by which flavonoids may reduce risk for cardiovascular diseases

- Platelet function and haemostasis
  - Inhibit platelet aggregation
- Blood pressure and vascular reactivity
  - Promote nitric oxide-induced endothelial relaxation

The role of CD36 and LOX-1 receptors in foam cell development



Aronia Berries

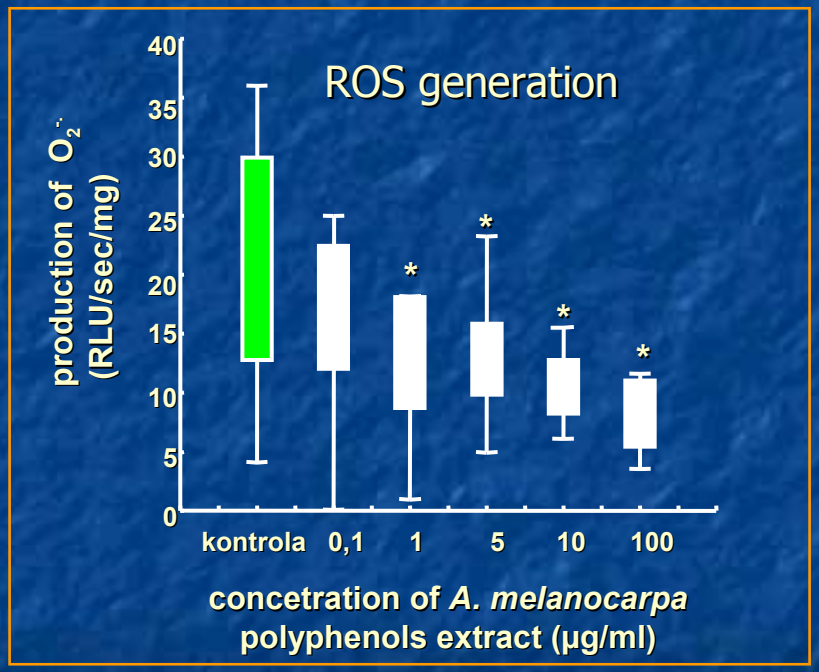
- Aronia (Photinia melanocaarpa, also known as Aronia melanocarpa and Aronia nigra), is a native American bush that has been successfully exported to Eastern Europe and is commercially grown in Denmark, Poland, Russia and elsewhere.
- Known commonly as "chokeberry" or "blak chokeberry", (Photinia melanocarpa) has at least two cousins worth mentioning. These are Photinia floribunda, also known as Aronia atropurpurea, the "purple chokeberry", and Photinia pyrofilia, also known as Aronia arbutifolia, the "red chokeberry". The former ranges from Mississippi to Wisconsin, Georgia into Canada, and all areas in between. The latter ranges from Texas-Oklahoma eastward through Tennessee to the Atlantic and from Florida northward into Canada. The Aronia berry has all of the healthy attributes of the cranberry, but also contains five to ten times the amount of anthocyanins and polyphenols of a cranberry.

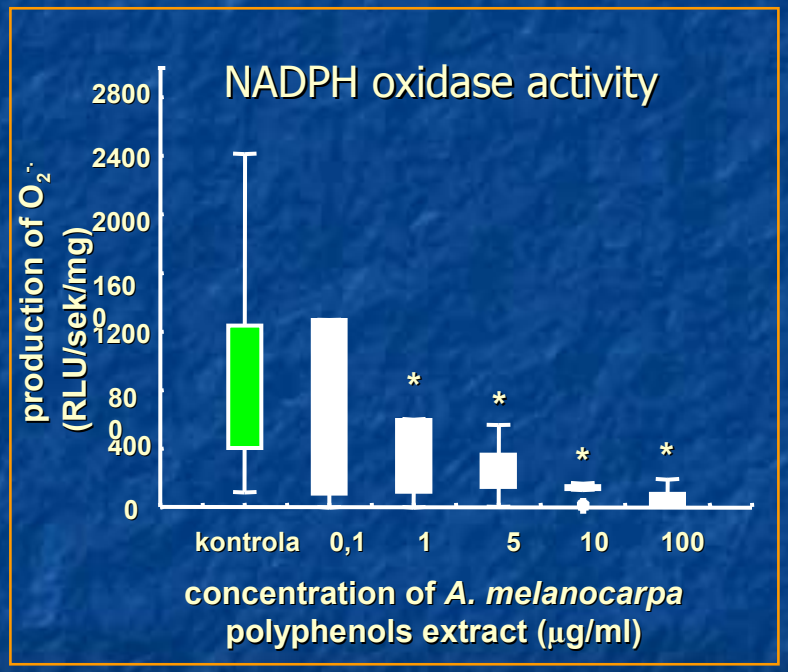
Antioxidant activity (ORAC), Anthocyanin Content and Phenolic Content in Fruit of Blueberry, Cranberry, Lingonberry and Chokeberry

species	ORAC (μmol of TE/g)	Anthocyanin (mg/g)	Total phenolic (mg/g)
Blueberry	28.9	1.20	4.12
Cranberry	18.5	0.32	3.15
Lingonberry	38.1	0.45	6.52
Chokeberry	**160.2**	**4.28**	**25.56**

W. Zheng, S.Y. Wang "Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries and lingonberries", J.Agric.Food Chem. 51, (2003) 501-509

Effect of *A. melanocarpa* extract on superoxide production by human arterial wall cells from patients with cardiovascular risk factors

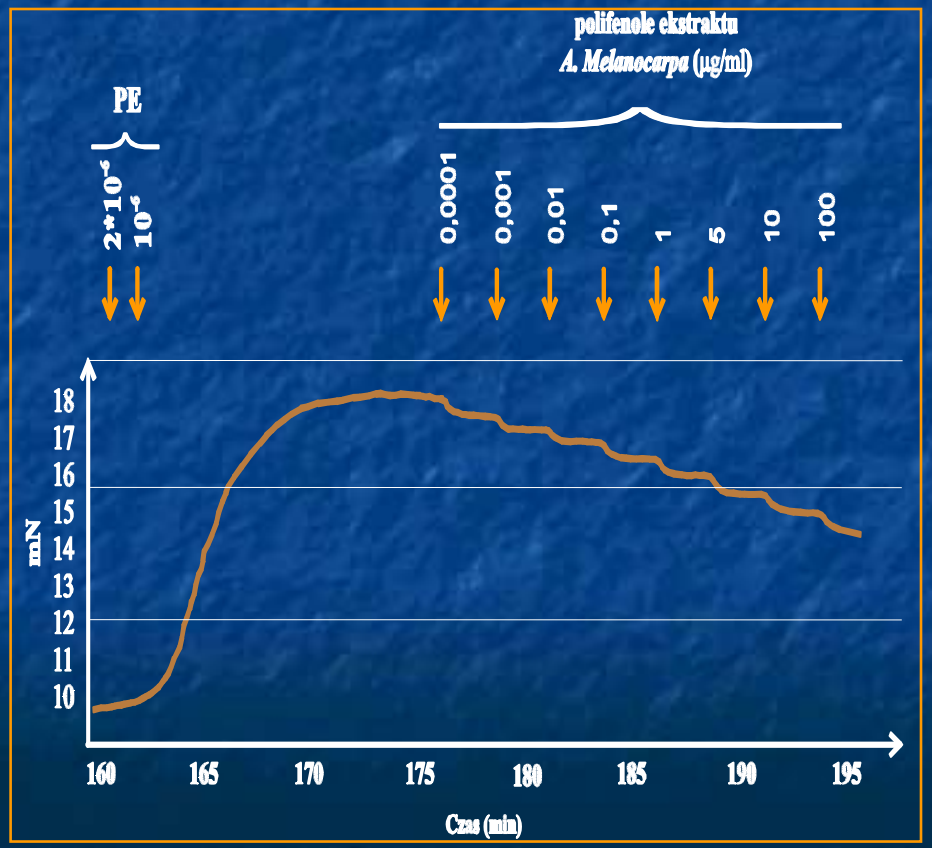




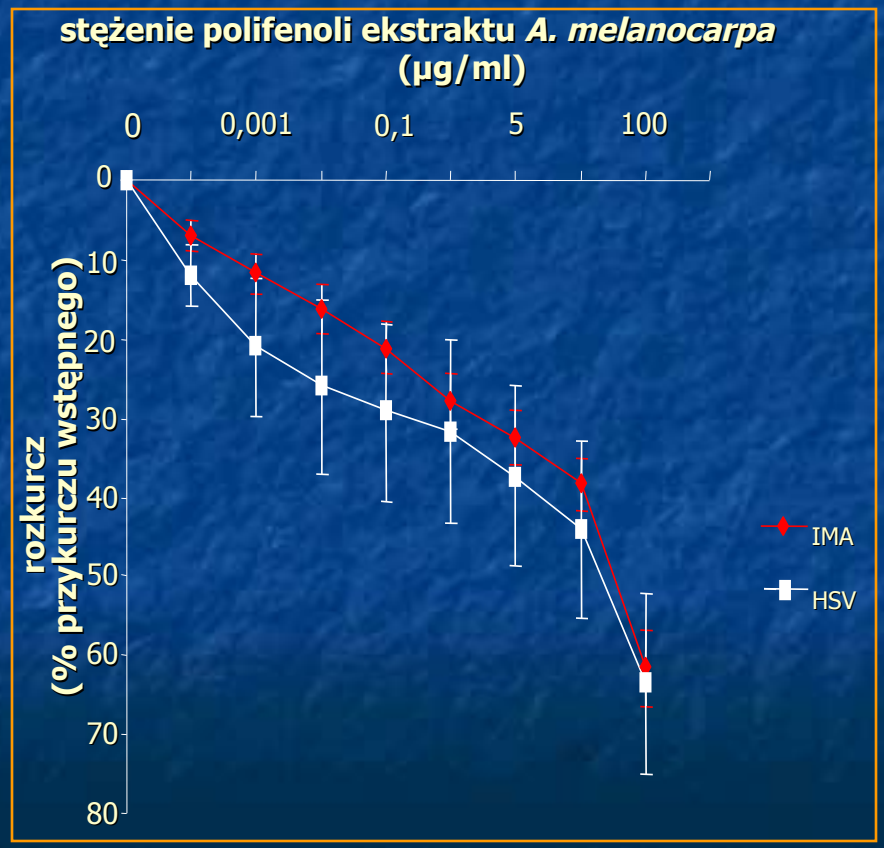
Data are shown as means +/-SEM, * - p<0,05 vs. native using appropriate tests depending on data distribution

Effect of *A. melanocarpa* extract on vasoconstruction

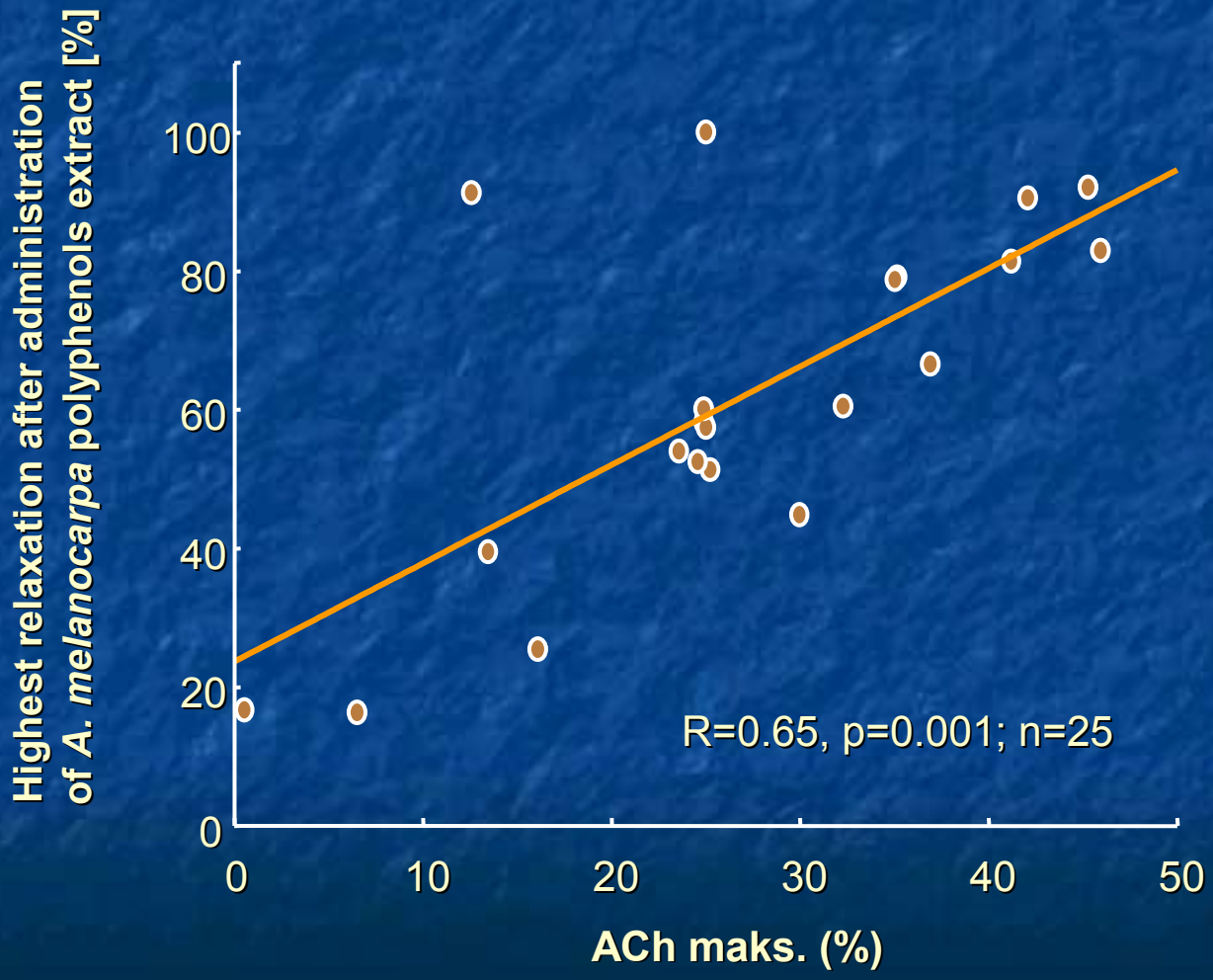
Increasing concentration of *A. melanocarpa extract*



Increasing concentration of *A. melanocarpa* extract

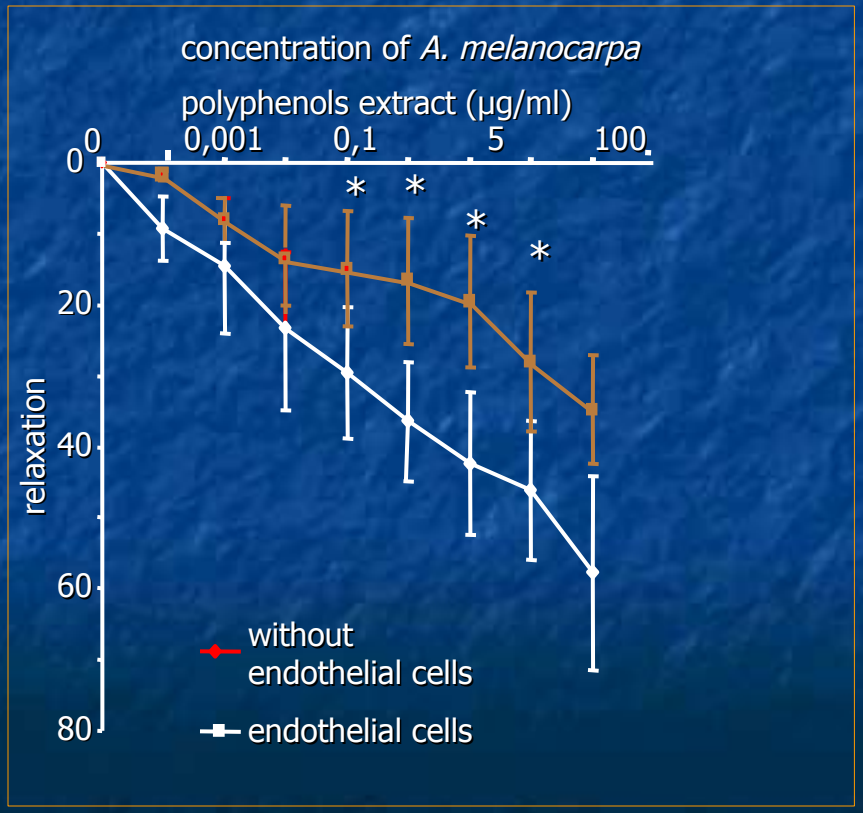


Correlation between endothelium function and vasorelaxation activity of *A. melanocarpa* extract

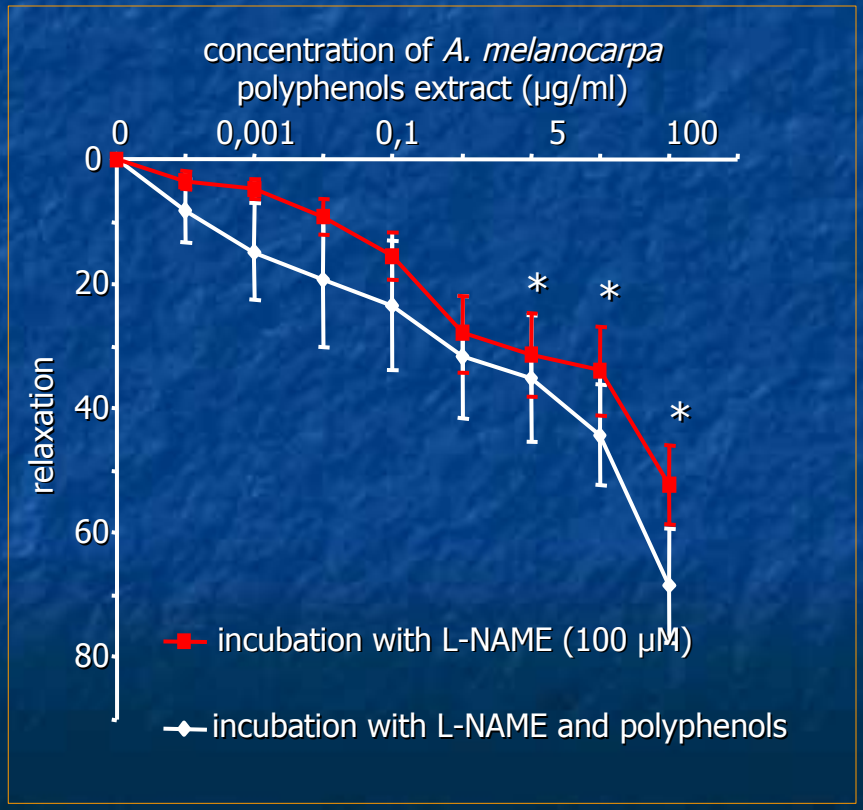


Mechanism of vasorelaxtion activity of *A. melanocarpa* polyphenols

Endothelium function



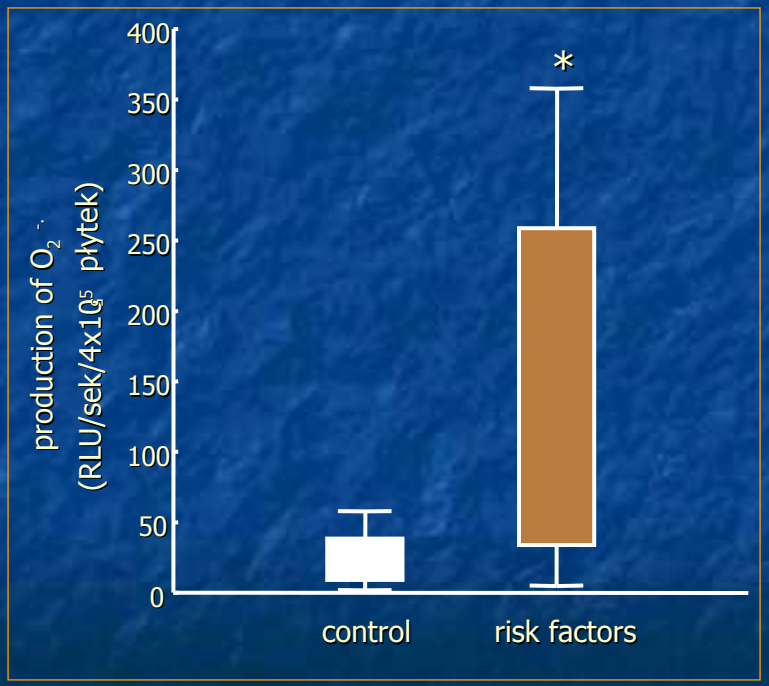
Role of eNOS (incubation with L-NAME)



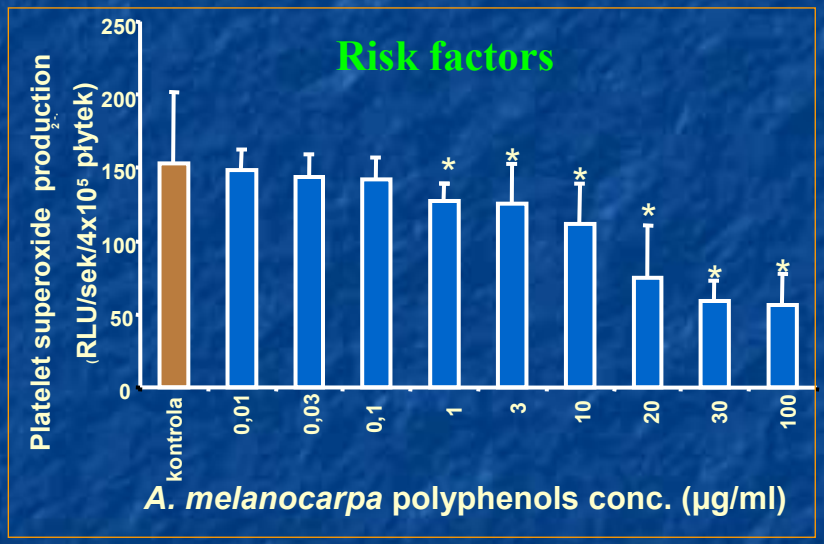
Superoxide production in platelets and effect of *A. melanocarpa* polyphenols

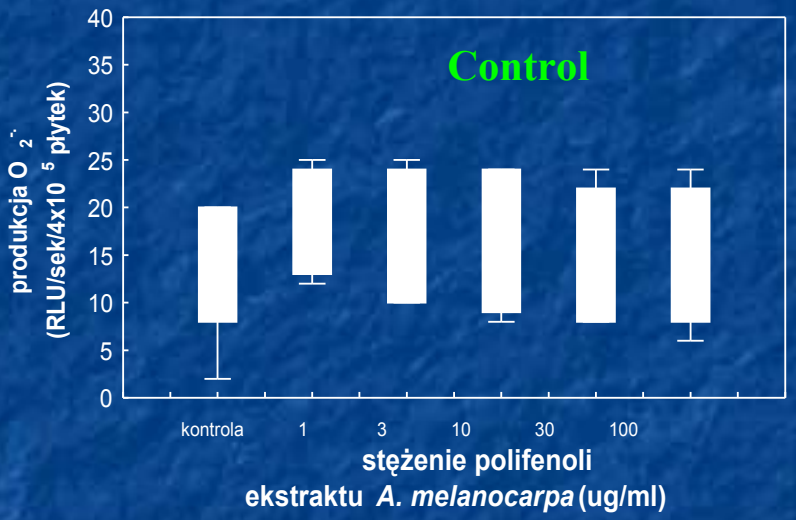
Production of $O_2^{-\cdot}$ in platelets

- correlation with risk factors

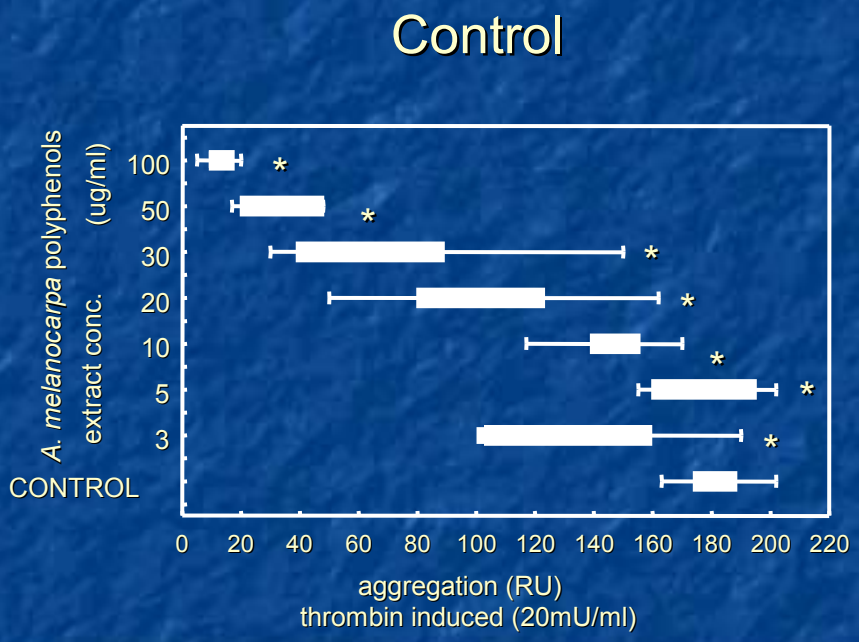


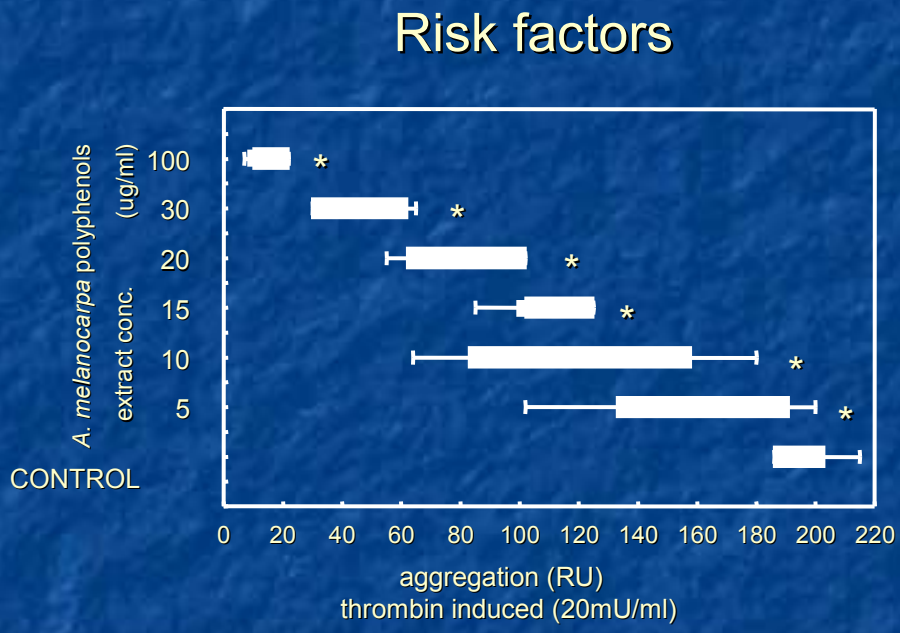
Superoxide production in platelets and effect of *A. melanocarpa* polyphenols



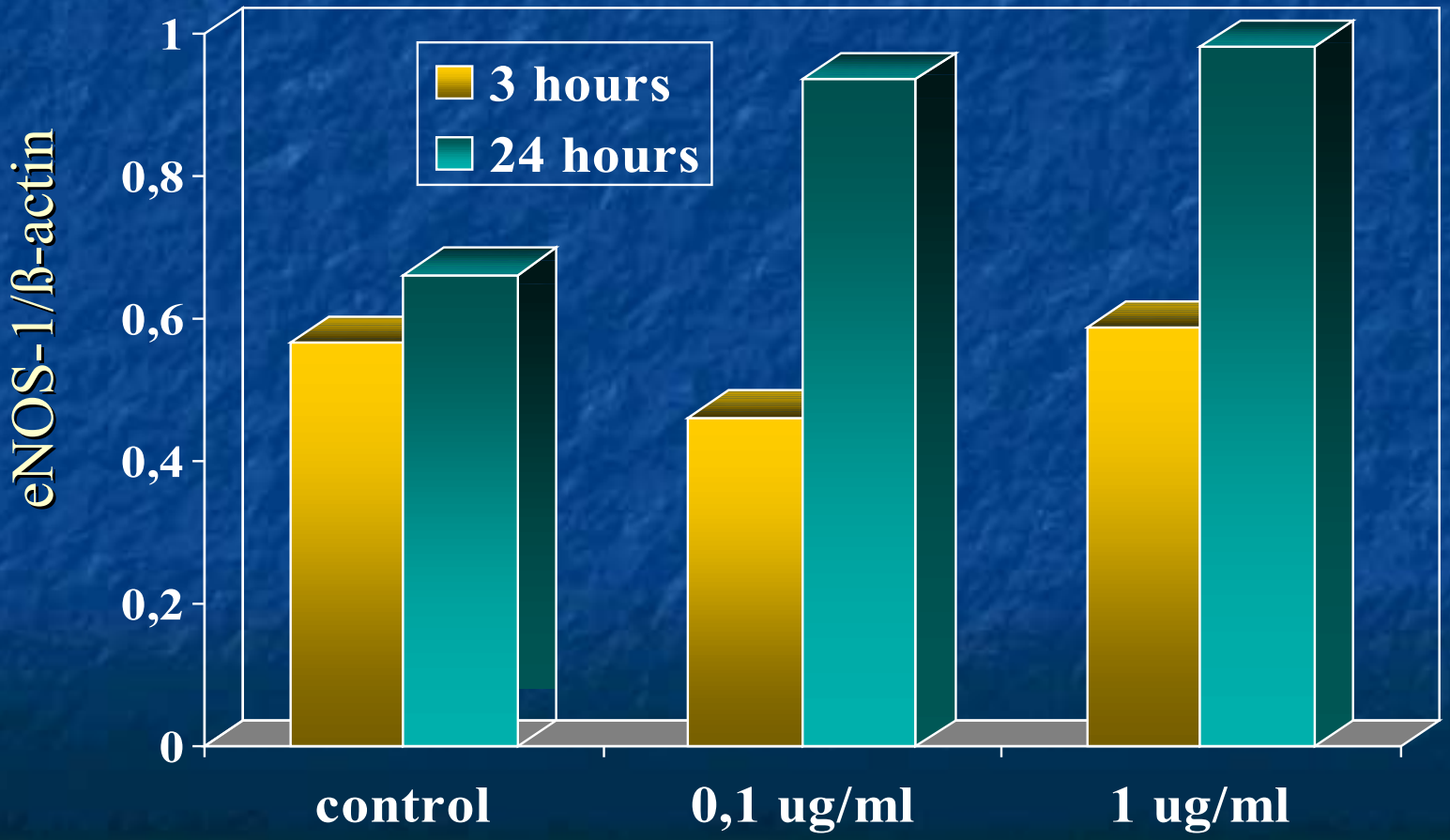


Effect of increasing *A. melanocarpa* polyphenols concentrations on platelet aggregation

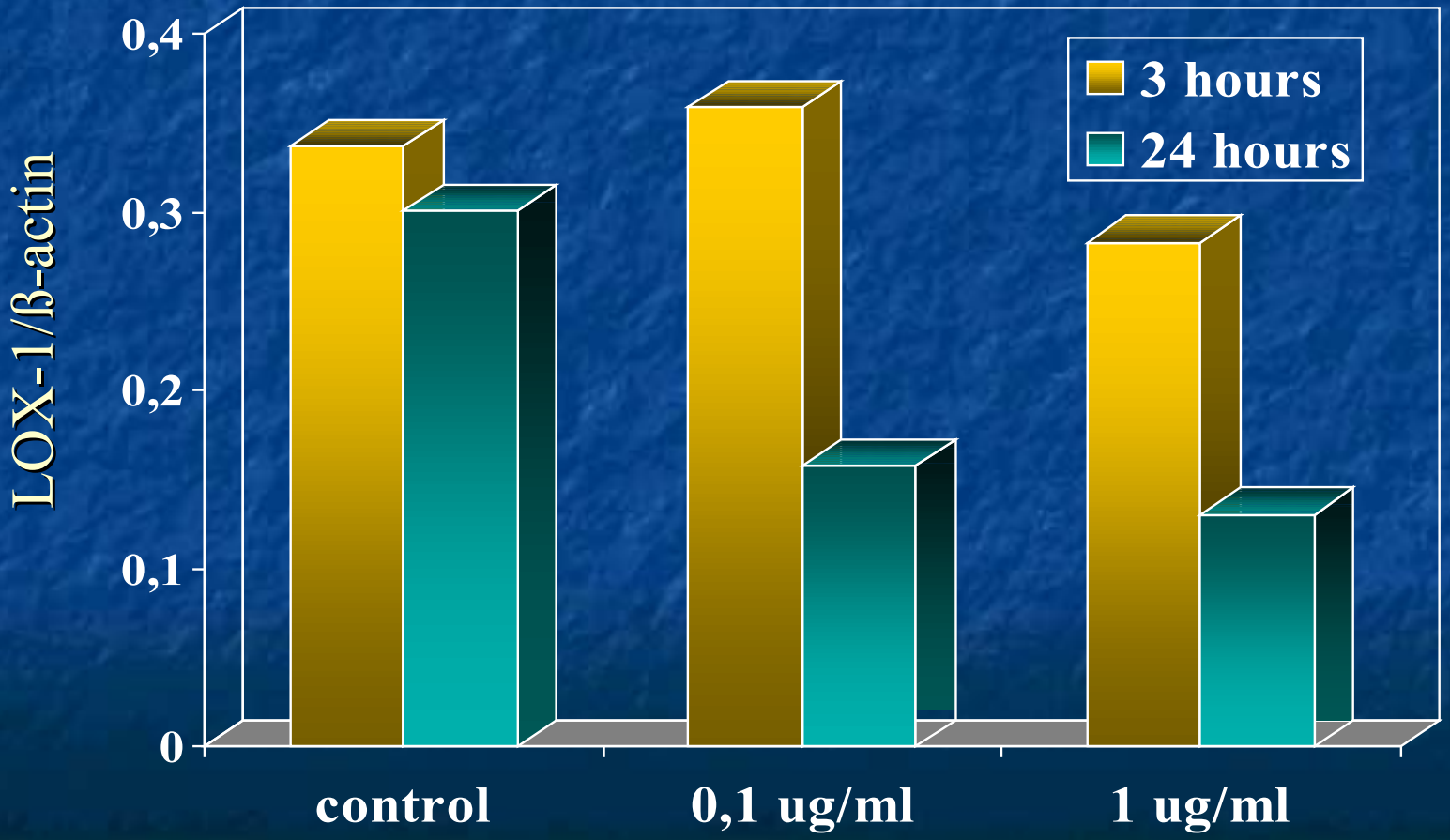




The effect of increasing concentrations of Aronia flavonoids from chokeberry on eNOS expression in HUVEC cells



The effect of increasing concentrations of Aronia flavonoids from chokeberry on LOX-1 expression in HUVEC cells



Product: Aronia fruits extract /ARONOX/ Scientific name: Aronia meelanocarpa (chokeberry)

Parameter	Result
Appearance	Powder
Colour	Red-brown
Humidity	max 8%
Anthocyanins Cy-3-O-Ga	20-25%
Polimeric procyanidins (+)(-) epicatechin	>55%
Phenolic acids	9%
Antioxidant activity (μM Trolox/g dried weight) DPPH radicals	118.7
ABTS radicals	106.1

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Combination therapy of statin with flavonoids rich extract from chokeberry fruits enhanced reduction in cardiovascular risk markers in patients after myocardial infraction (MI)

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Methods

- This was a double-blind, placebo-controlled, parallel trial. Forty-four patients (11 women and 33 men, mean age 66 years) who survived myocardial infarction and have received statin therapy for at least 6 months (80% dose of 40 mg/day simvastatin) were included in the study. The subjects were randomised to receive either 3 x 85 mg/day of chokeberry flavonoid extract or placebo for a period of 6 weeks.

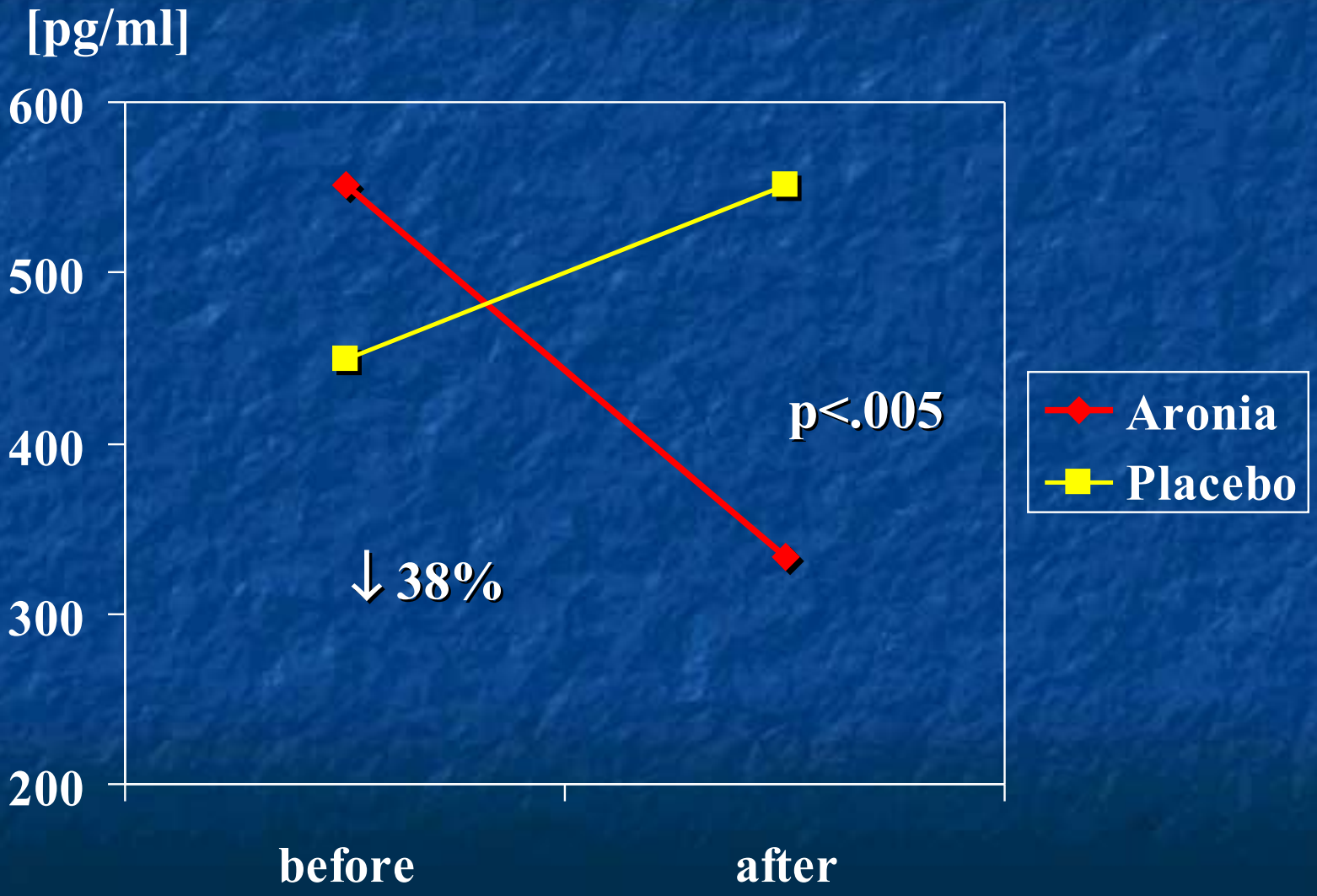
Clinical and Demographic Characteristics of MI Patients

	Aronia flavonoids (n=22)	Placebo (n=22)
Age	65.87 ± 8.3	66.1 ± 7.9
Sex (women, men)	6/16	5/17
BMI (kg/m^2)	26.5 ± 3.5	26.9 ± 2.5
MI (years after)	5.2 ± 2.0	5.4 ± 2.1
Diabetes (%)	19	23
Hypertension (%)	32	36
Current smokers (%)	14	19
Medication		
Statins (%)	100.0	100.0
simvastatin 40 mg	81	86
atorvastatin 20	19	14
Aspirin (%)	81	73
ACE inhibitors (%)	54	50

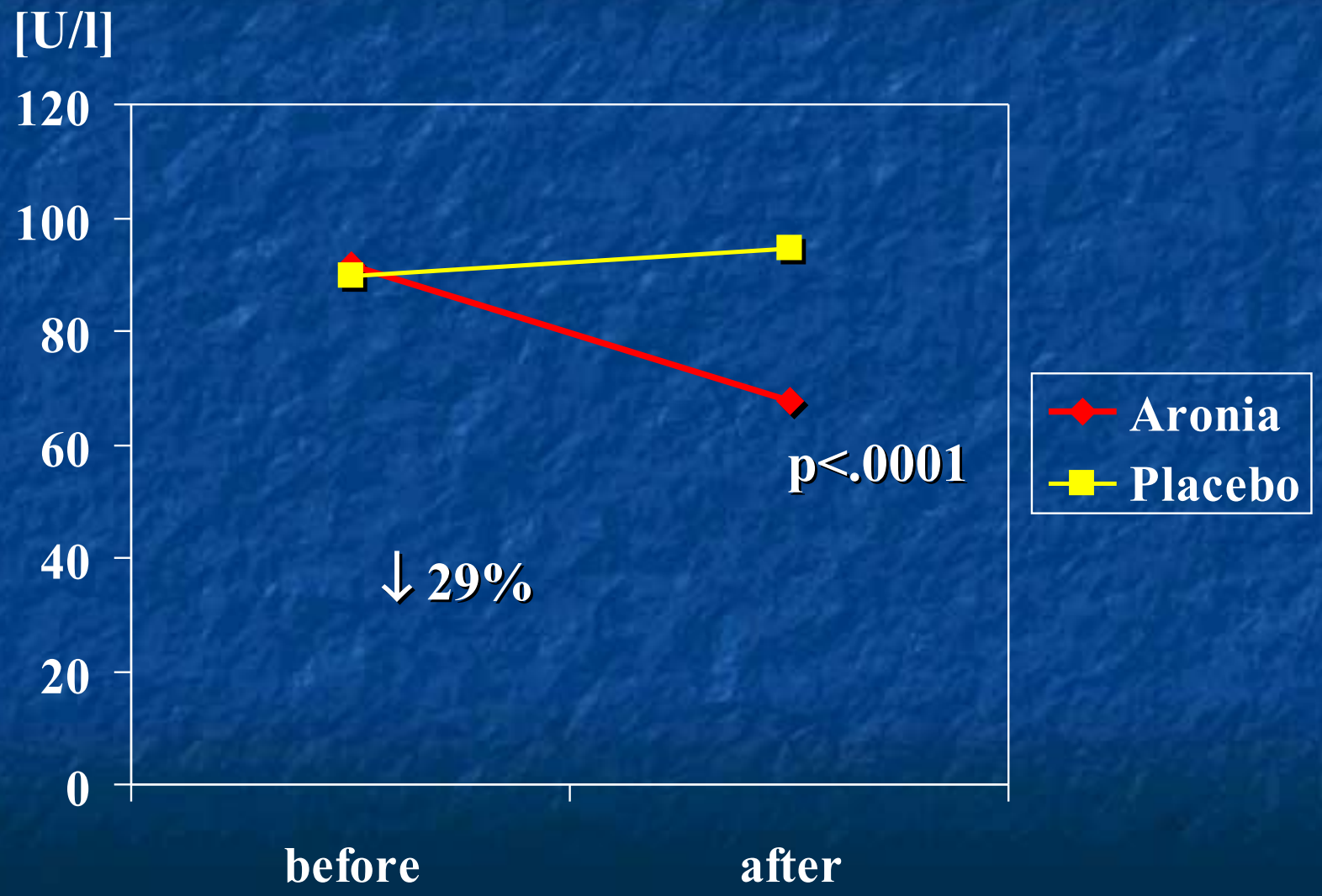
Effect of Aronia flavonoids or placebo on lipids, lipoproteins and homocysteine levels in patients with a history of MI

	Anthocyanins (n=22)		Placebo (n=22)		
	before	after	before	after	ANOVA
TG [mg/dl]	162.7 ± 66.2	152.7 ± 55.5	131.8 ±	127.2 ± 36.5	ns
Chol [mg/dl]	198.0 ± 25.6	199.8 ± 28.2	202.2 ±	196.0 ± 42.6	ns
LDL [mg/dl]	117.3 ± 25.9	116.9 ± 27.9	116.8 ±	110.0 ± 32.4	ns
HDL [mg/dl]	42.2 ± 9.56	43.4 ± 9.7	45.6 ± 9.2	46.4 ± 9.57	ns
Lp(a) [mg/dl]	27.3 ± 33.6	28.2 ± 37.0	25.2 ± 36.4	25.3 ± 36.3	ns
Homocysteine [□mol/l]	17.2 ± 7.3	17.1 ± 8.2	16.0 ± 7.0	16.2 ± 5.9	ns

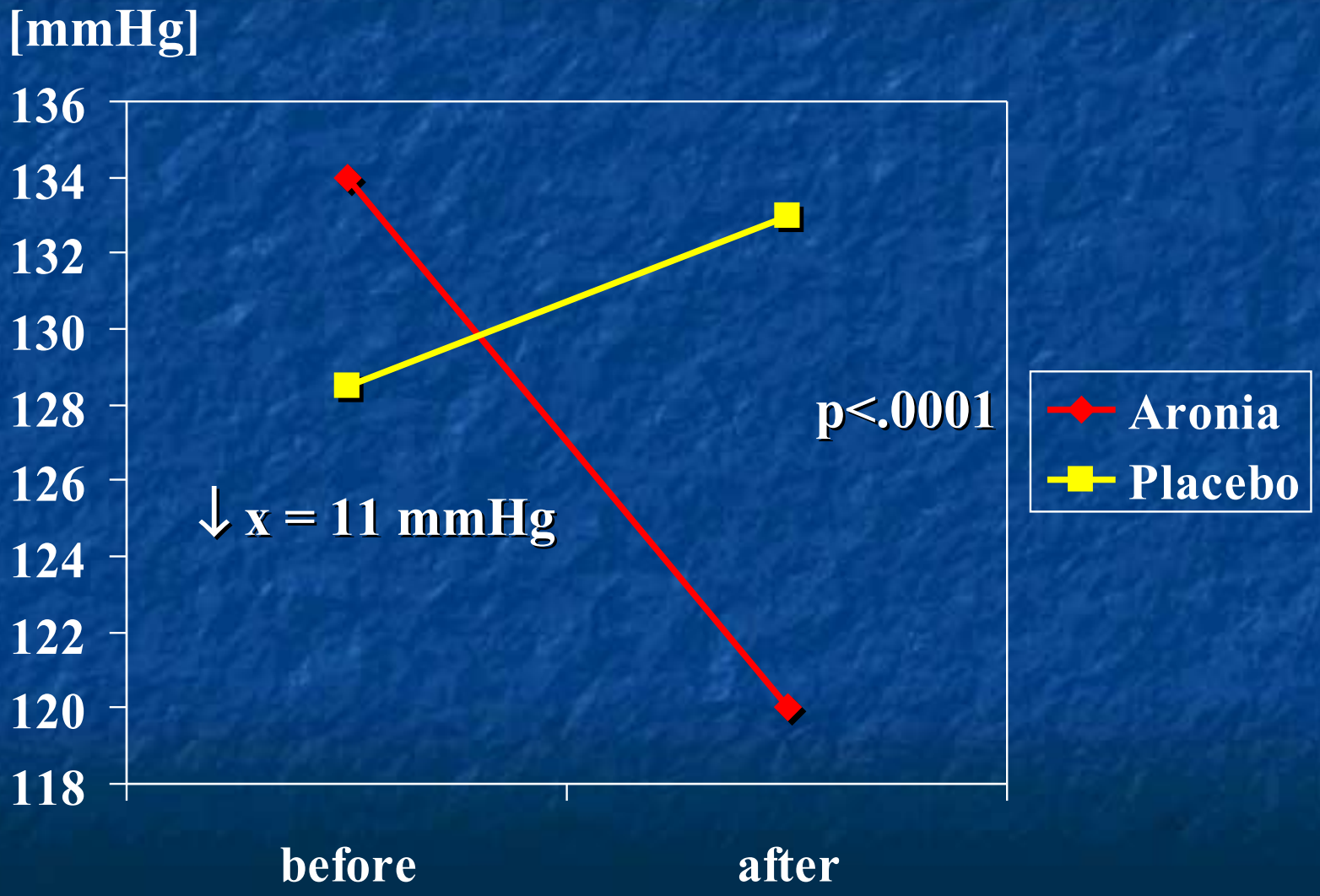
The effect of Aronia flavonoids on plasma total F2-isoprostanes level



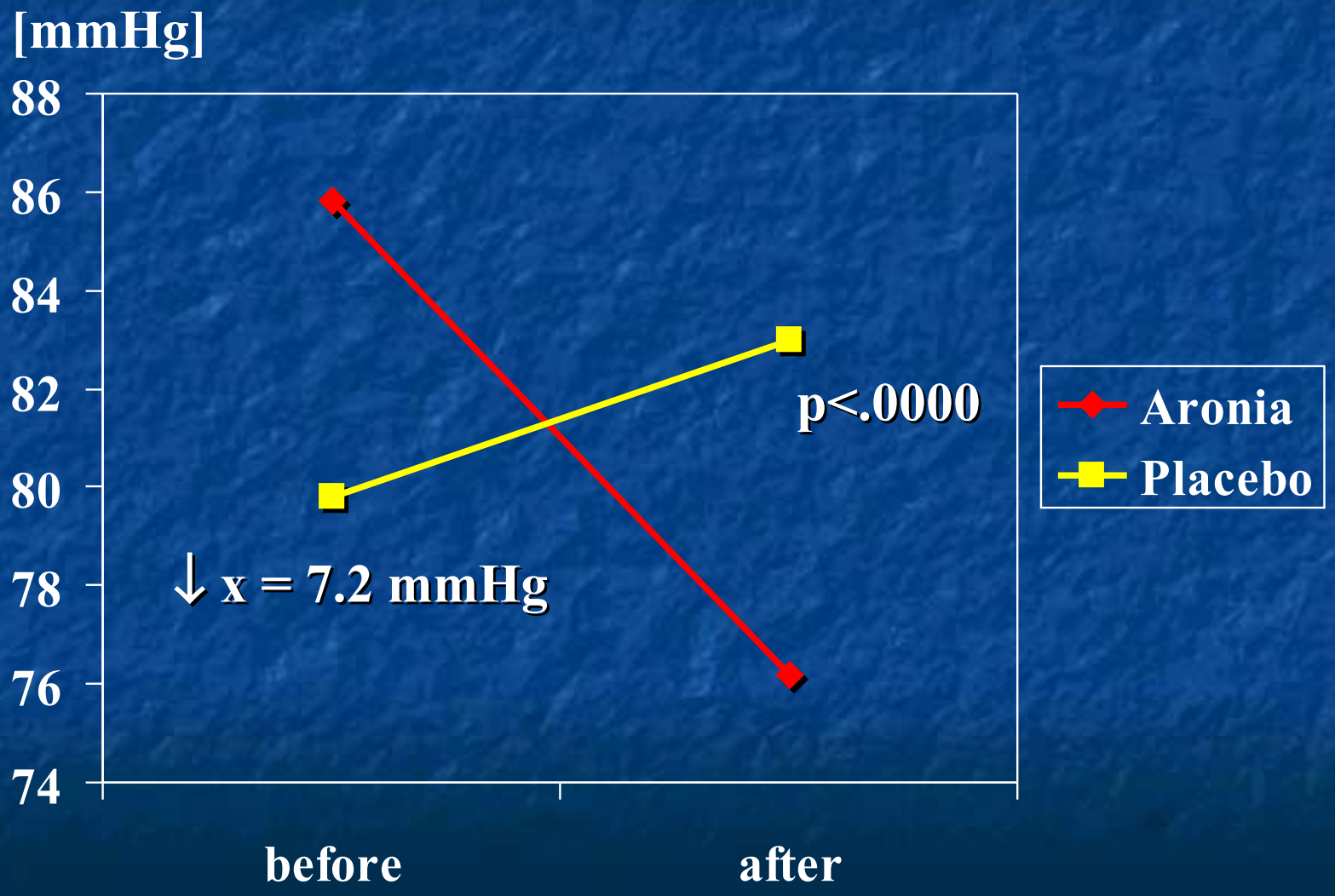
The effect of Aronia flavonoids on plasma OX-LDL level



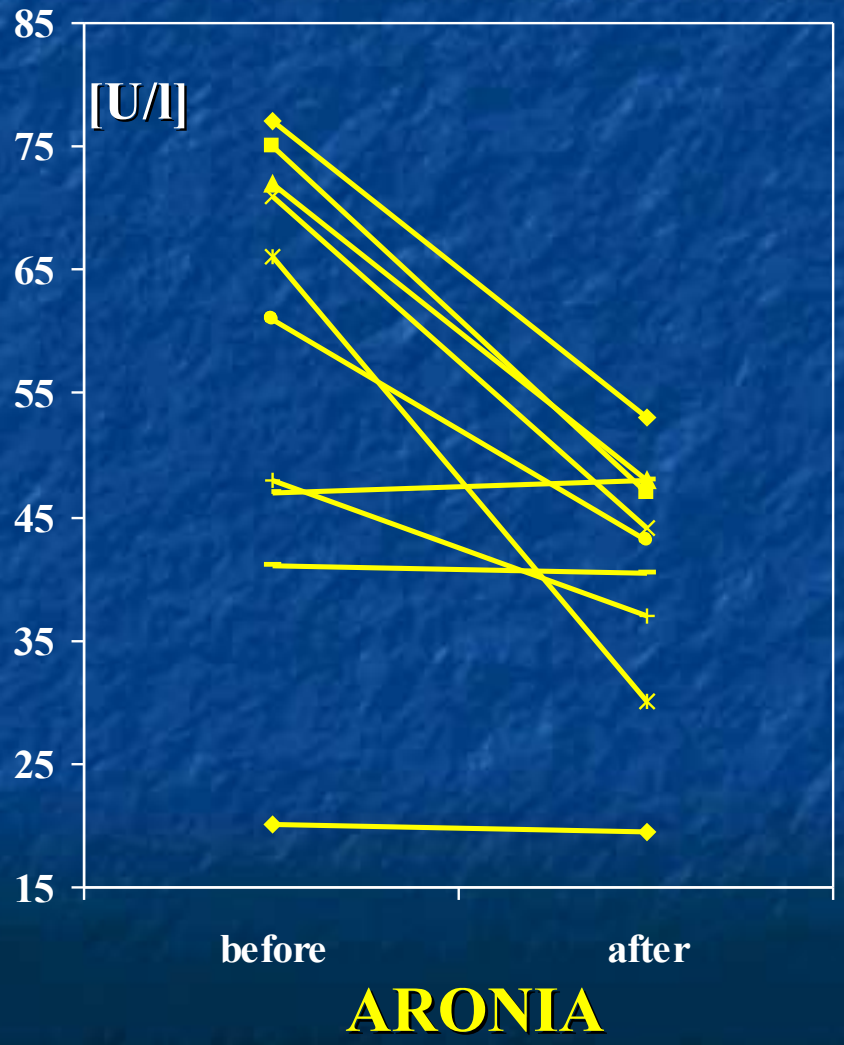
The effect of Aronia flavonoids on systolic blood pressure

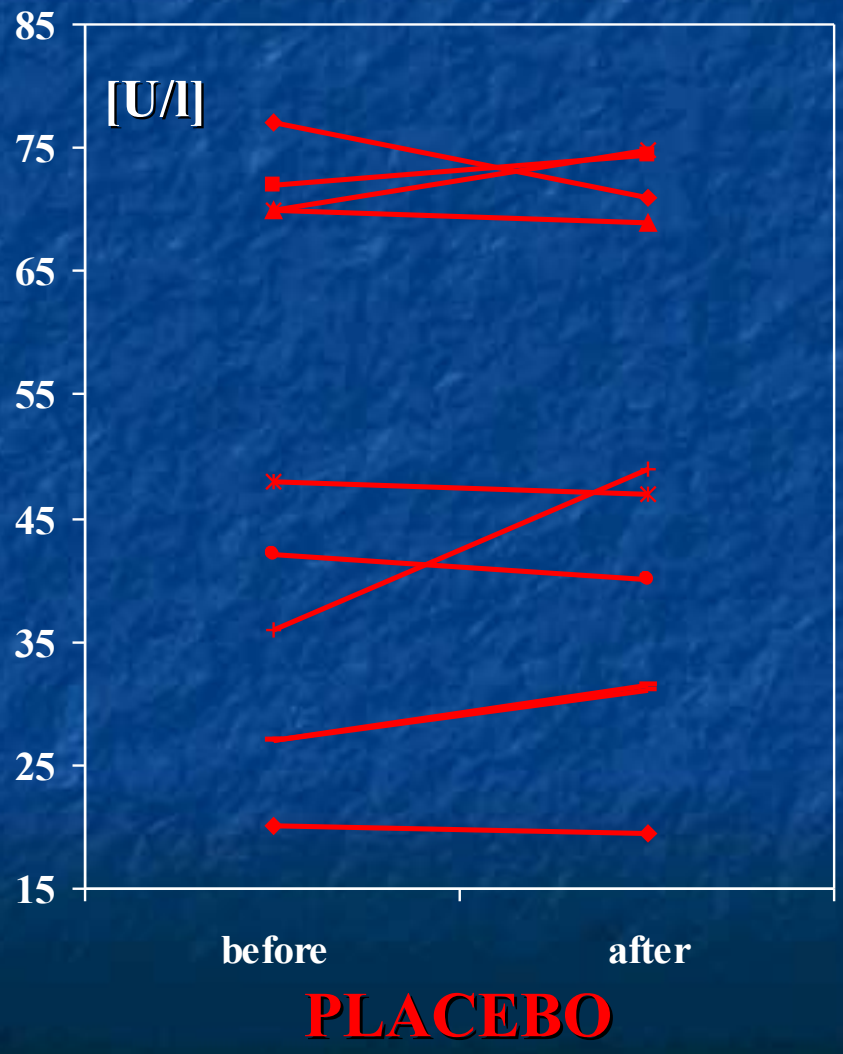


The effect of Aronia flavonoids on diastolic blood pressure

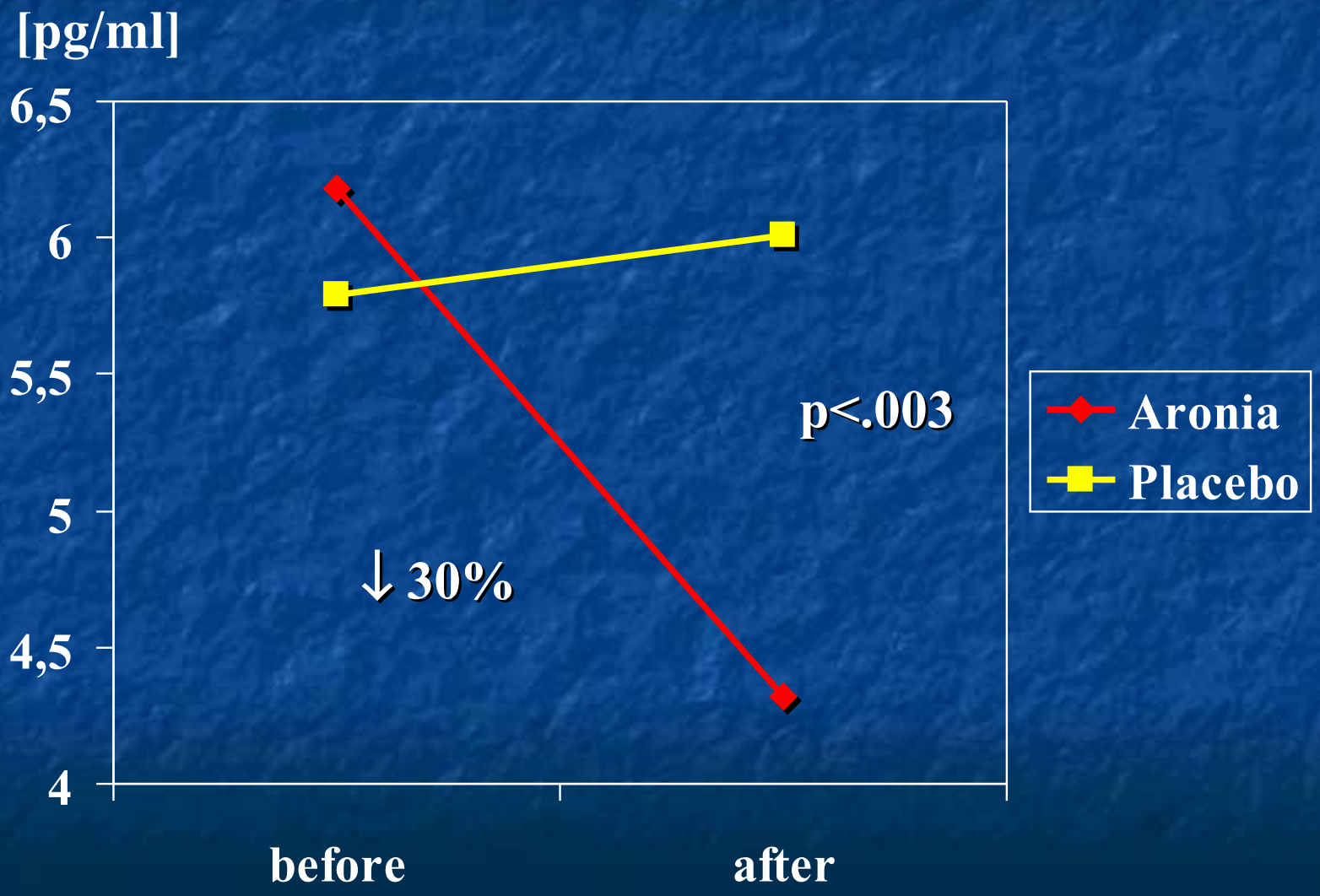


The effect of Aronia flavonoids or placebo on plasma ACE activity

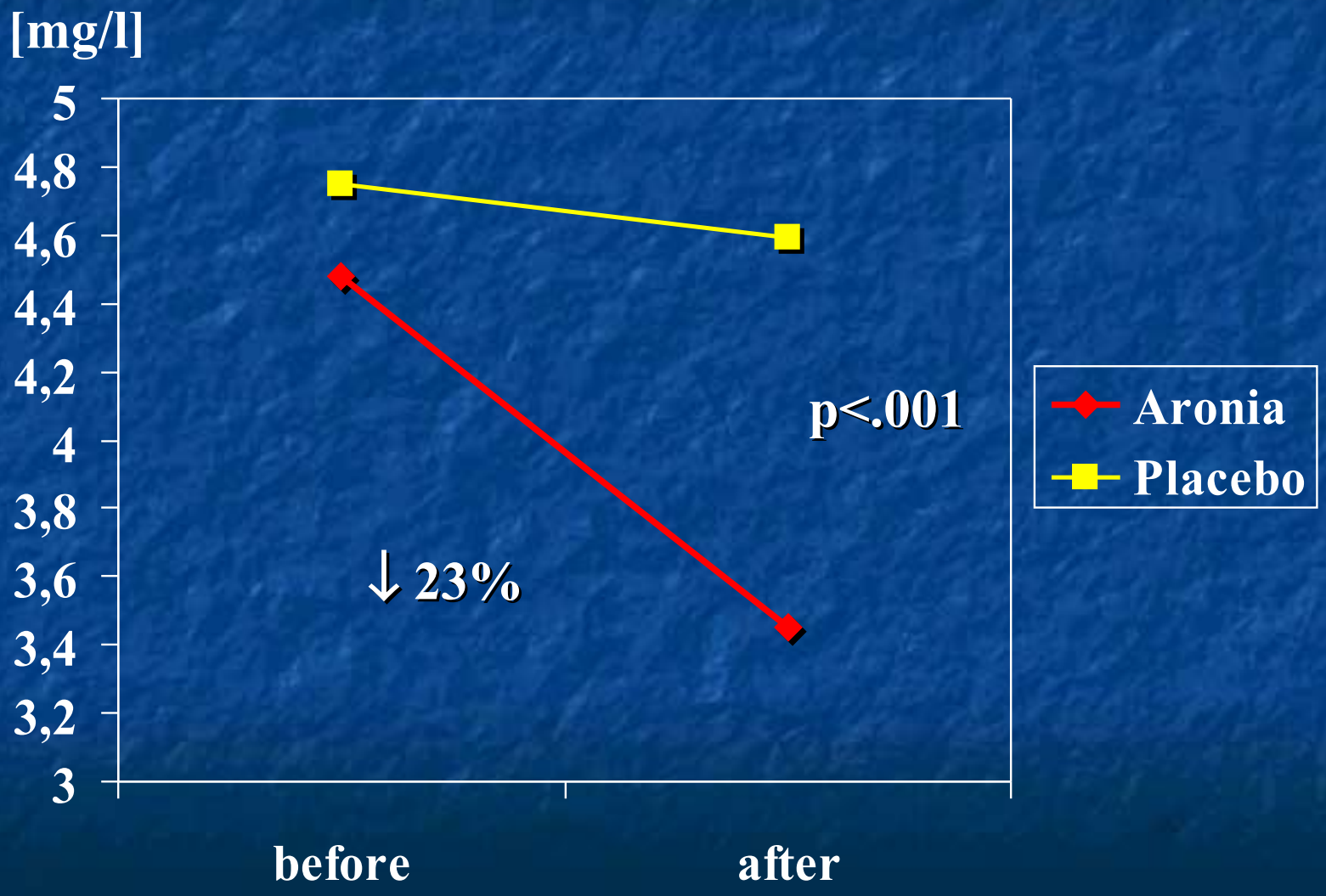




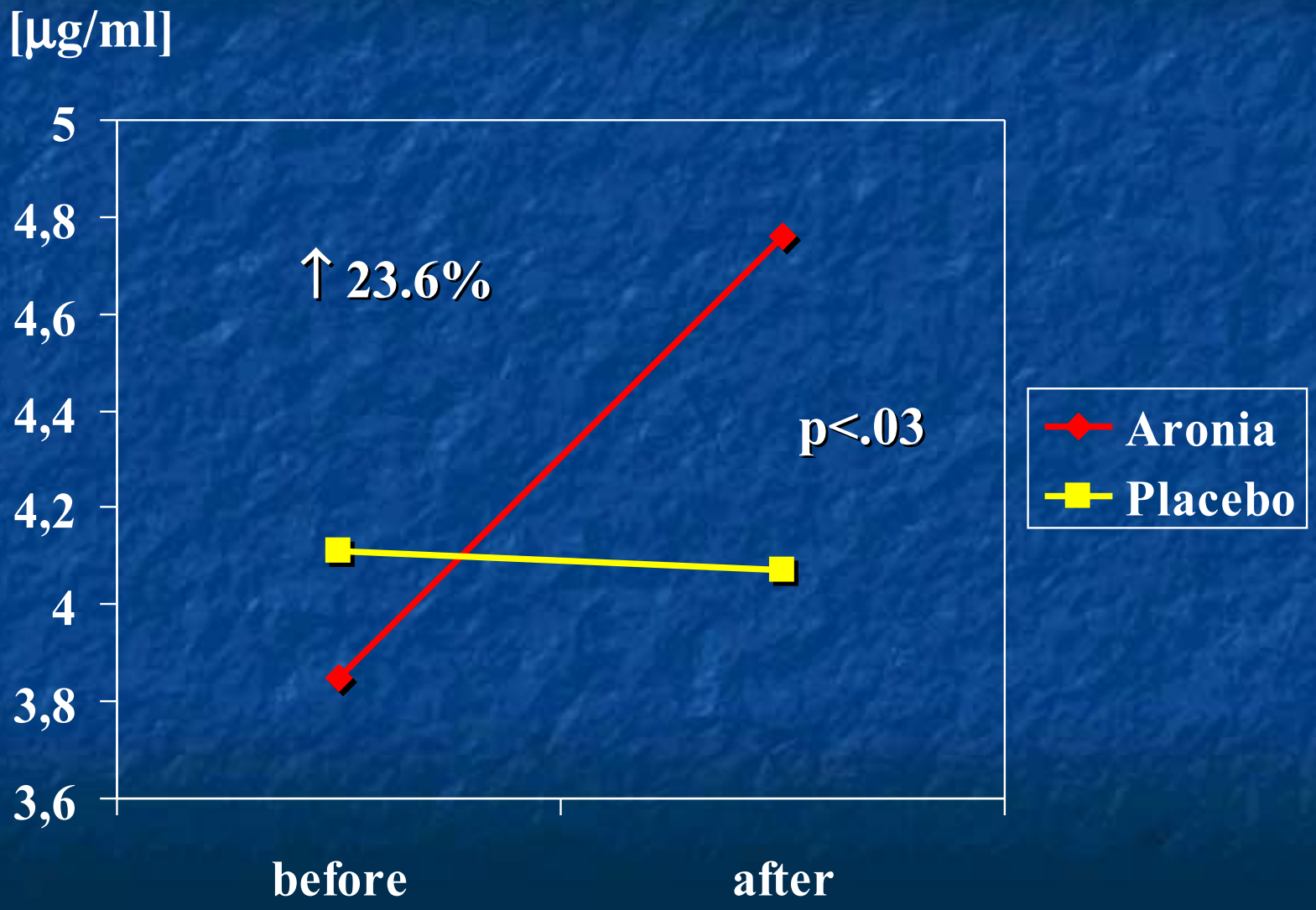
The effect of Aronia flavonoids on plasma IL-6 level



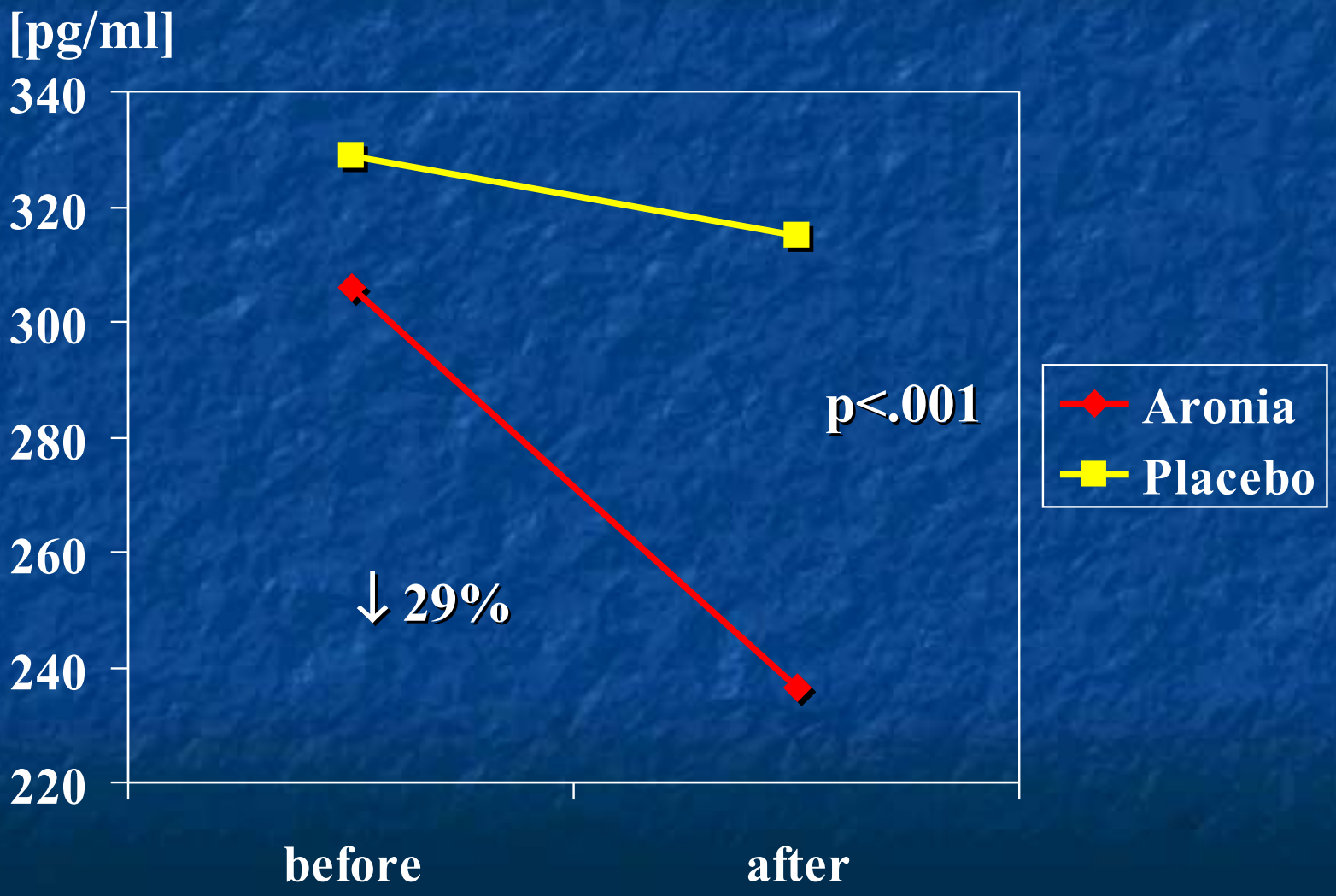
The effect of Aronia flavonoids on plasma hs-CRP level



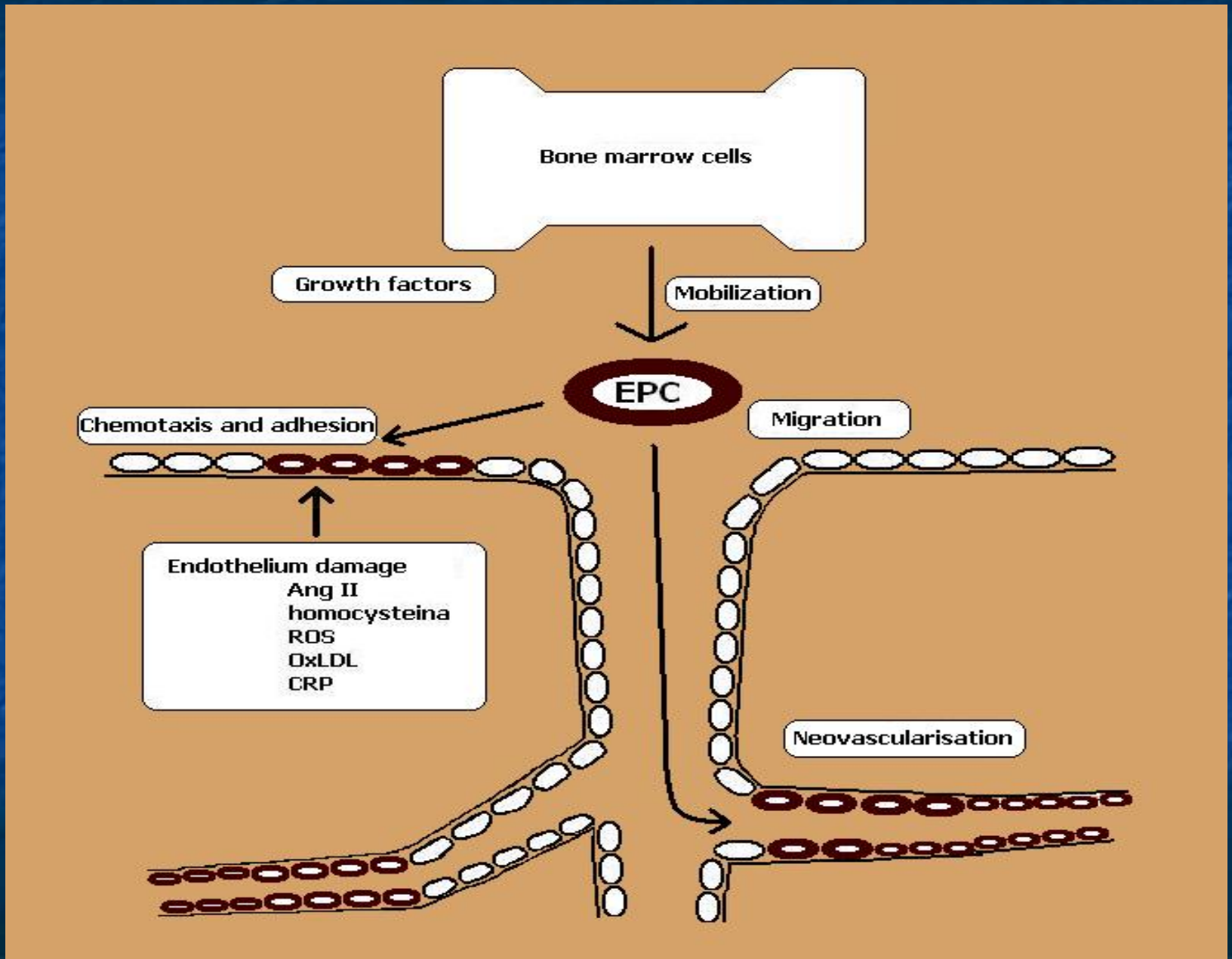
The effect of Aronia flavonoids on plasma adiponectin level



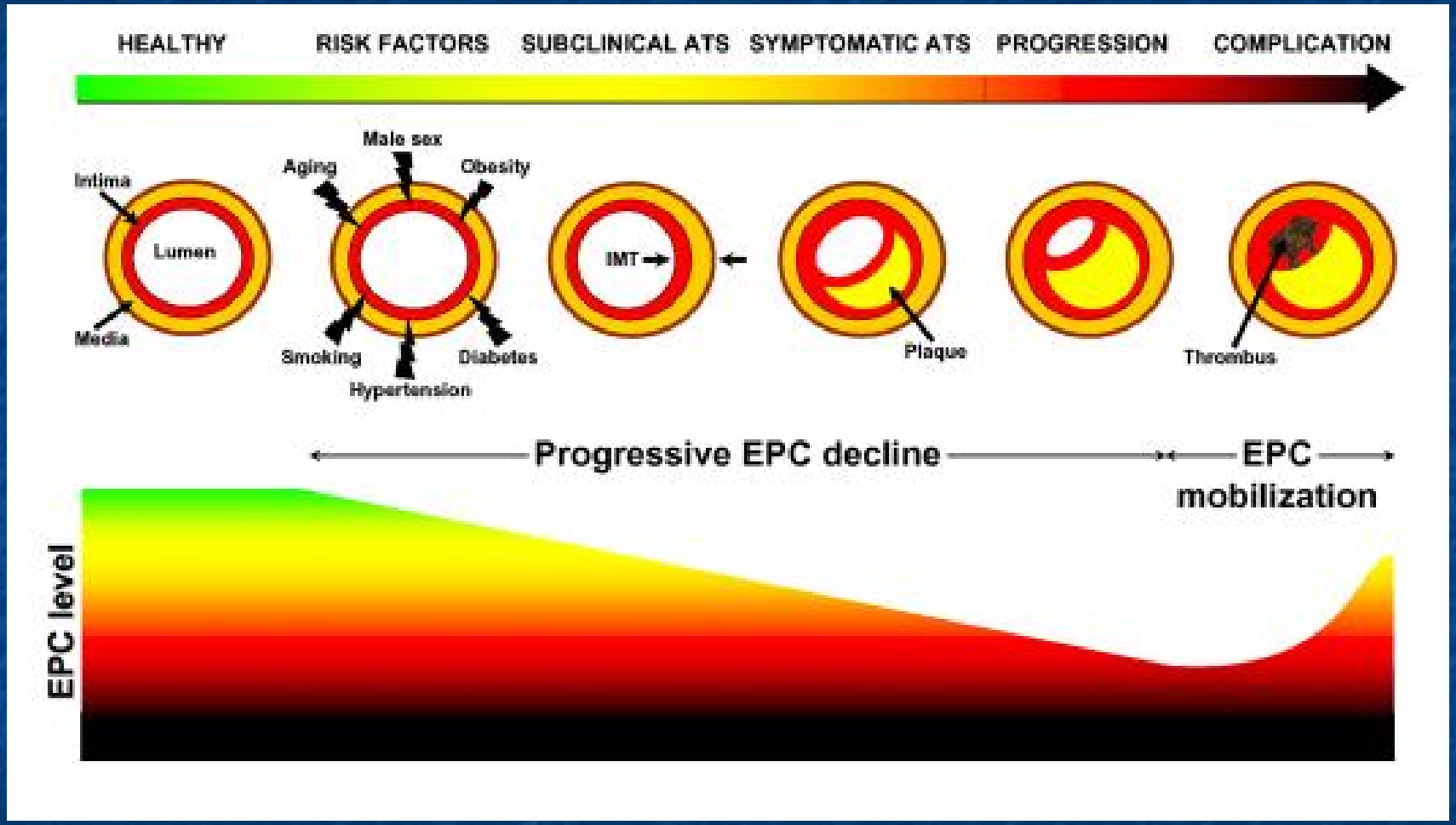
The effect of Aronia flavonoids on plasma MCP-1 level



Role of EPC in reendothelisation and neovascularisation



Regulation of EPCs following the natural history of atherosclerosis

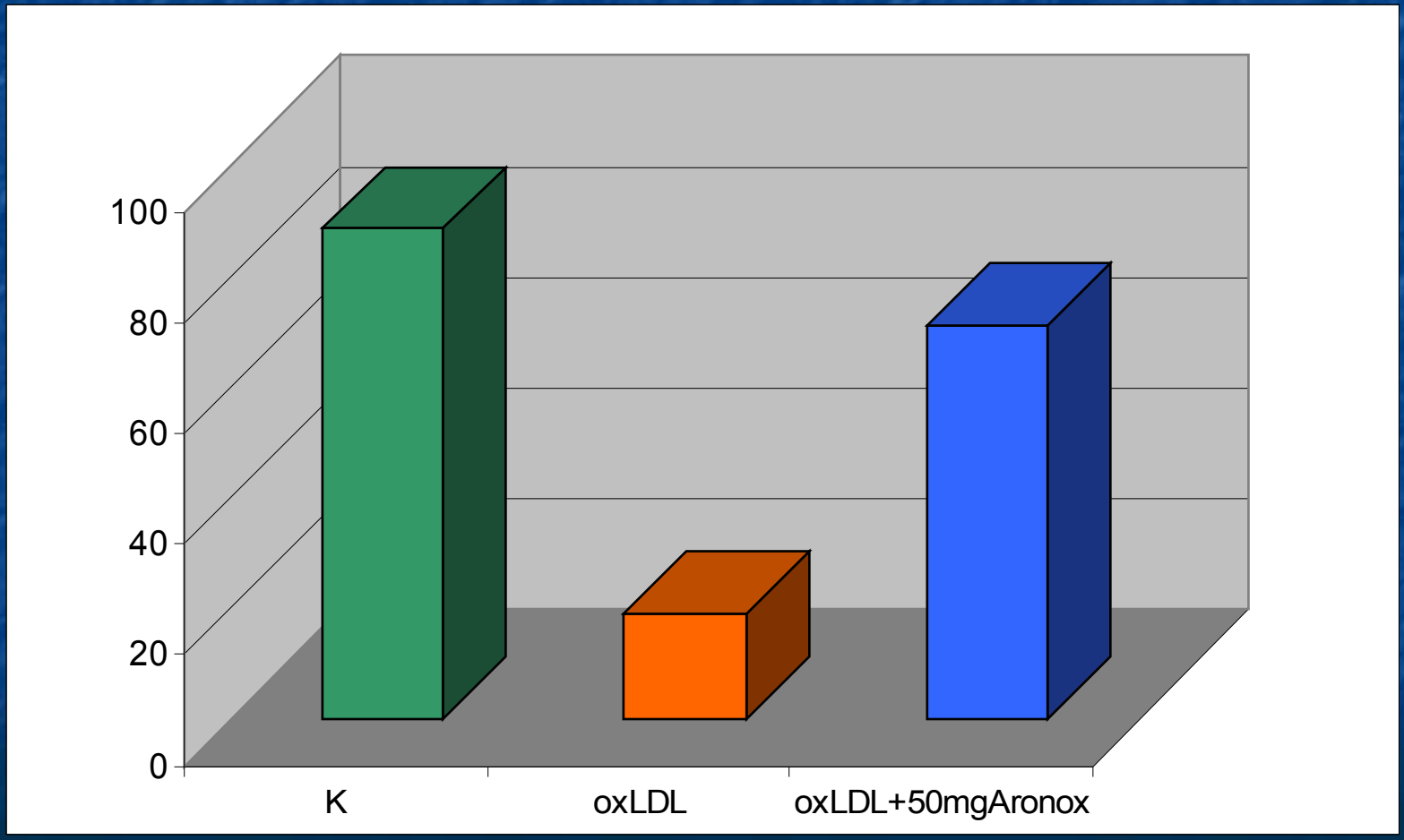


G. P. Fadini et al., Atherosclerosis 194 (2007) 46-54.

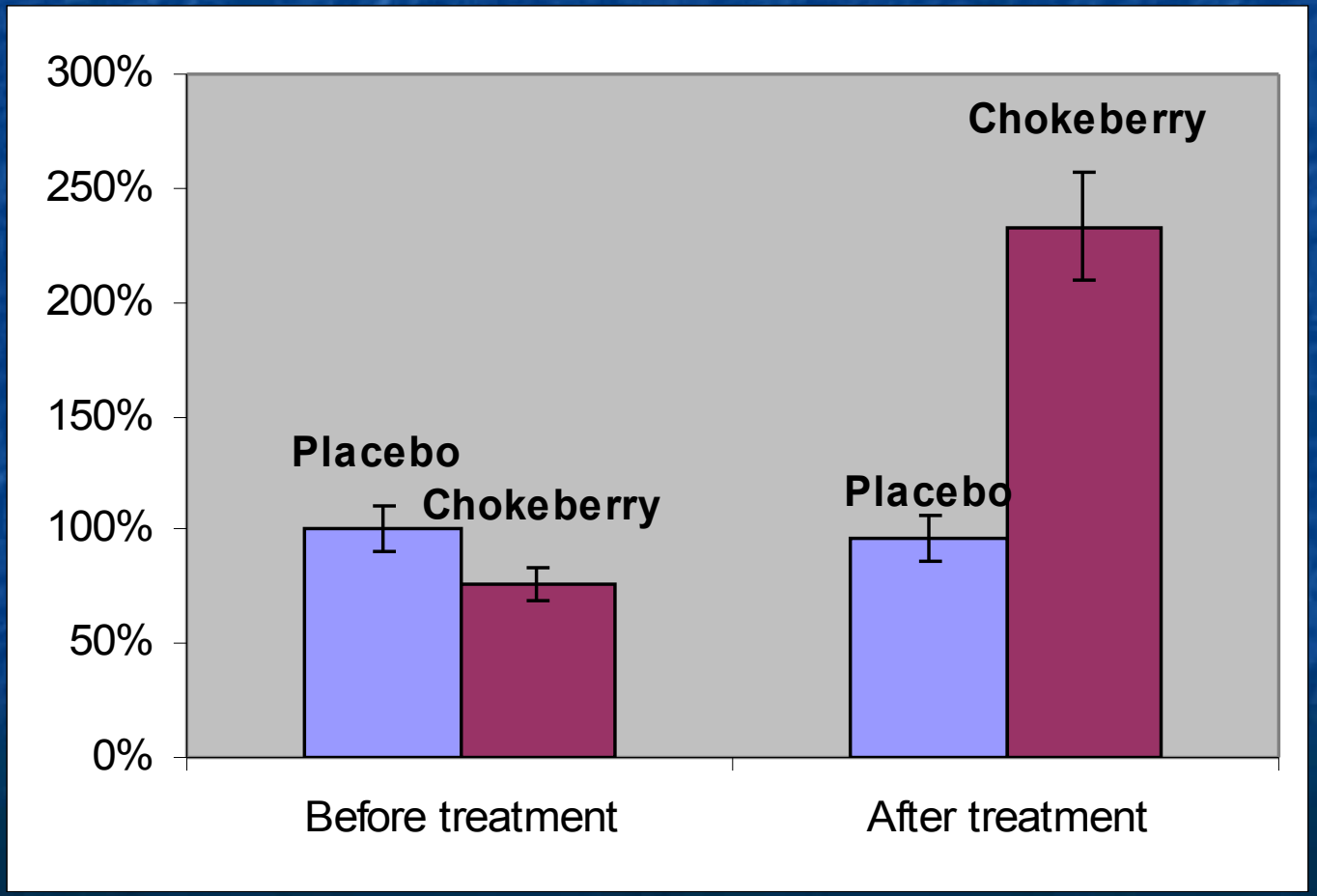
Endothelial progenitor cells and atherosclerosis

- EPCs are a circulating bone marrow-derived cell population that express surface CD34, CD133 and vascular endothelial growth factor receptor 2 (VEGFR-2).
- EPCs are incorporated into the sites of endothelial denudation and provide an endogenous repair mechanism to endothelial injury.
- EPCs from subject with CVD showed in vitro accelerate senescence and reduction in telomerase activity. This effect was partially through increase of oxidative stress and inhibiting eNOS.

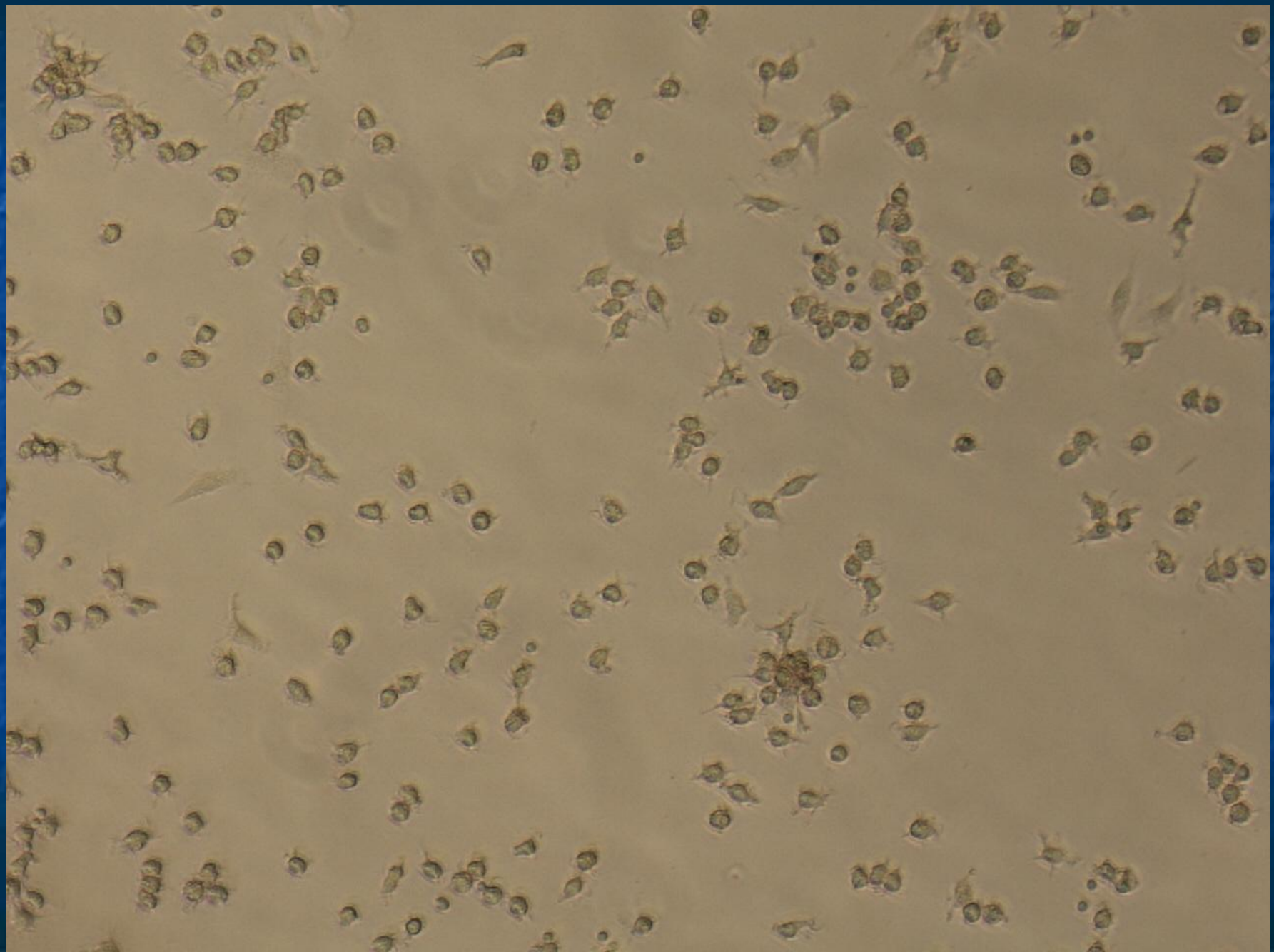
Effect of *Aronia melanocarpa* polyphenols on telomerase activity in EPC



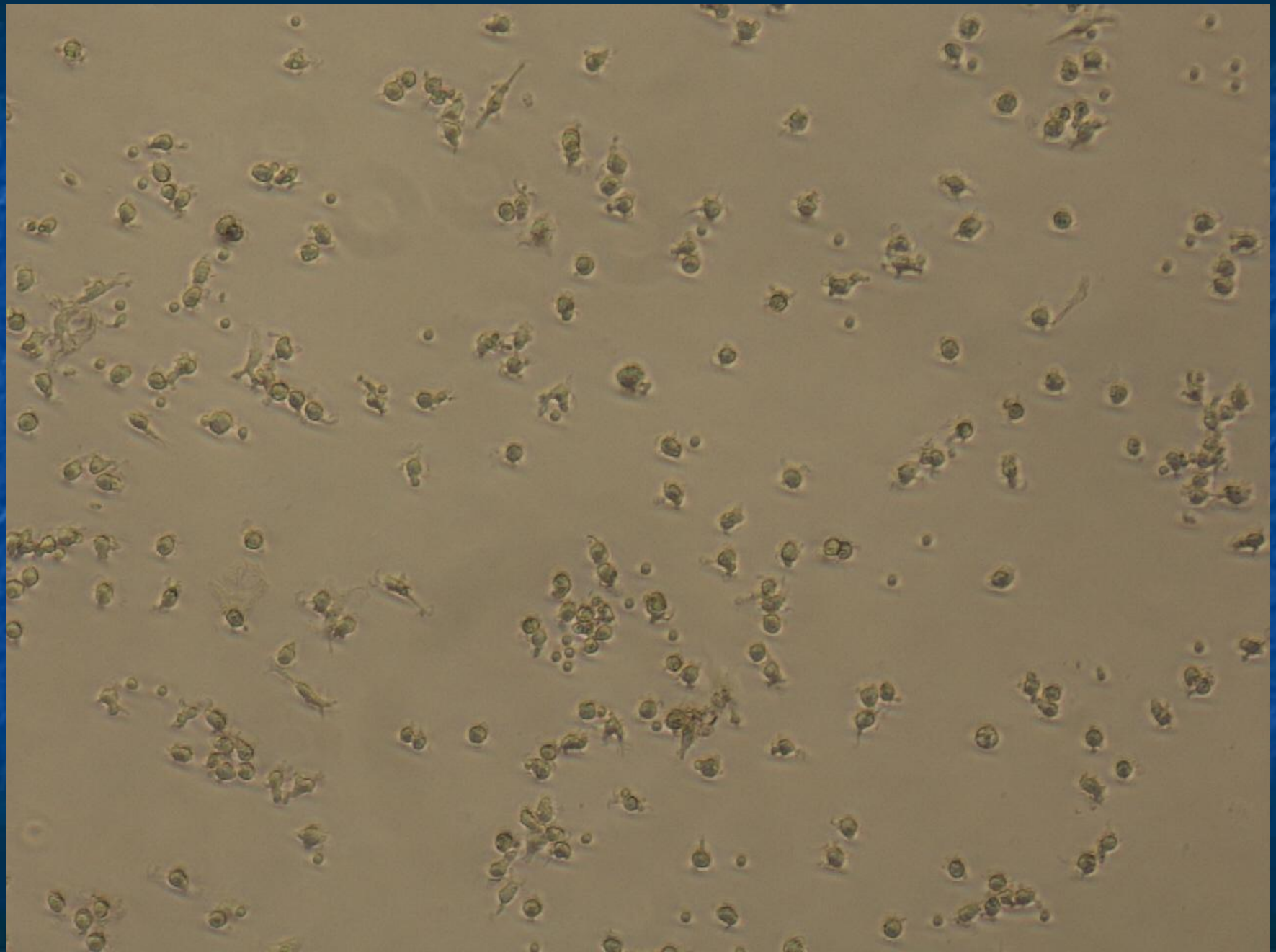
Effect of chokeberry extract on telomerase activity in vivo in patients with CVD



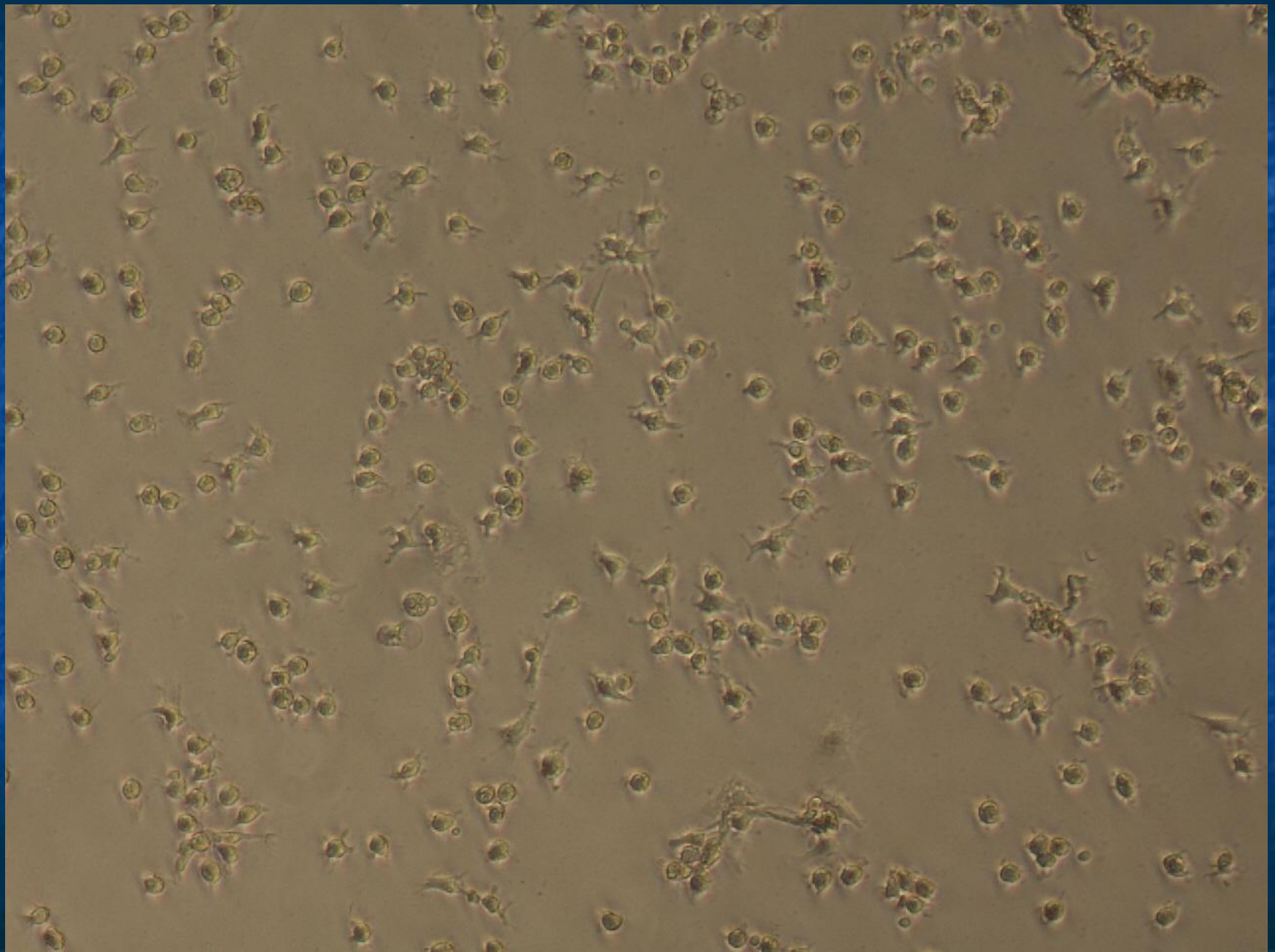
Cells incubated with 50ug of Aronia extract



Cells incubated with oxLDL



Cells incubated with Aronia extract and oxLDL



Conclusions

- These results confirm the potential usefulness if natural antioxidants in the treatment of atherosclerosis, also through their effect on EPC senescence inhibition.
- Funding. This work was supported by non-restricted grants from Polish Society for Athrosclerosis Research and from Agropharm

Conclusion

- In view of the fact that chokeberry flavonoids reduce the severity of inflammation, regardless of statins, they can be used clinically for secondary prevention of ischaemic heart disease.
- Funding. This work was supported by non-restricted grants from Polish Society for Athrosclerosis Research and from Agropharm