



Gli alimenti nella prevenzione di malattie croniche e tumorali: casi studio

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Free Radicals



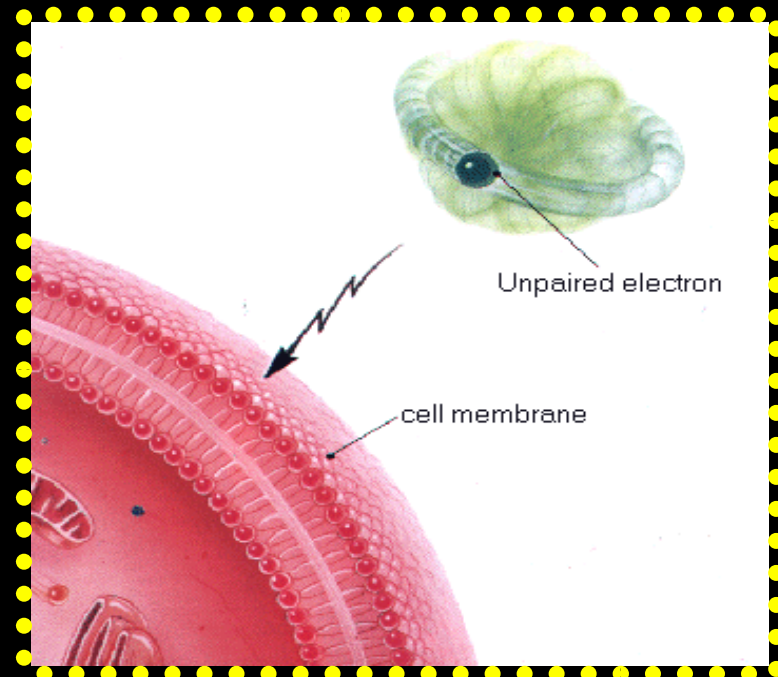
Free radicals attack all your vital cellular structures, such as cell membranes and stimulate processes that have been linked to accelerated cellular aging. An antioxidant's job is to neutralize the free radical cells thus protecting the cells in our body from accelerated aging.



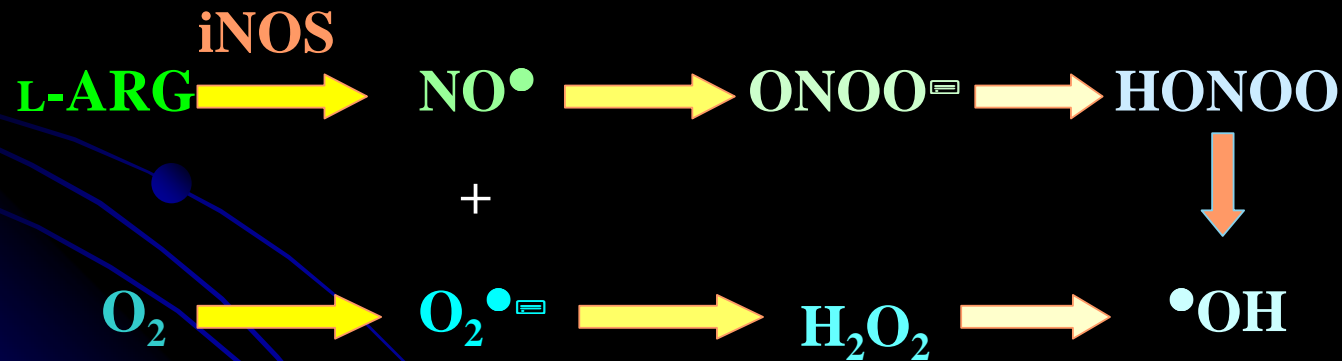
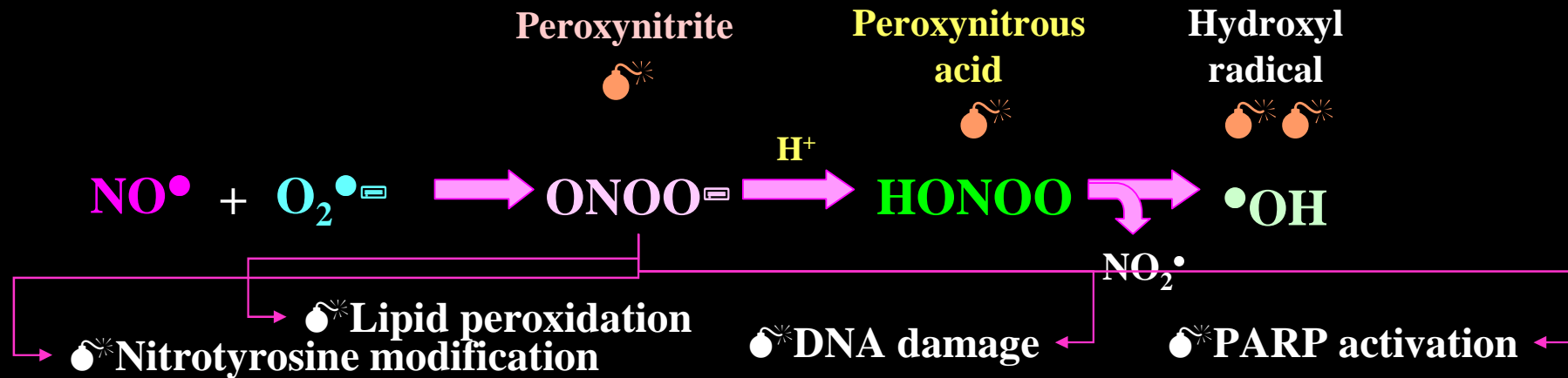
A free radical is defined as any atom or molecule possessing unpaired electrons

The biologically relevant free radicals derived from oxygen are:

- **superoxide anion (O_2^-)**
- **Hydrogen peroxide (H_2O_2)**
- **hydroxyl radical ($HO\cdot$)**
- **nitric oxide ($NO\cdot$)**



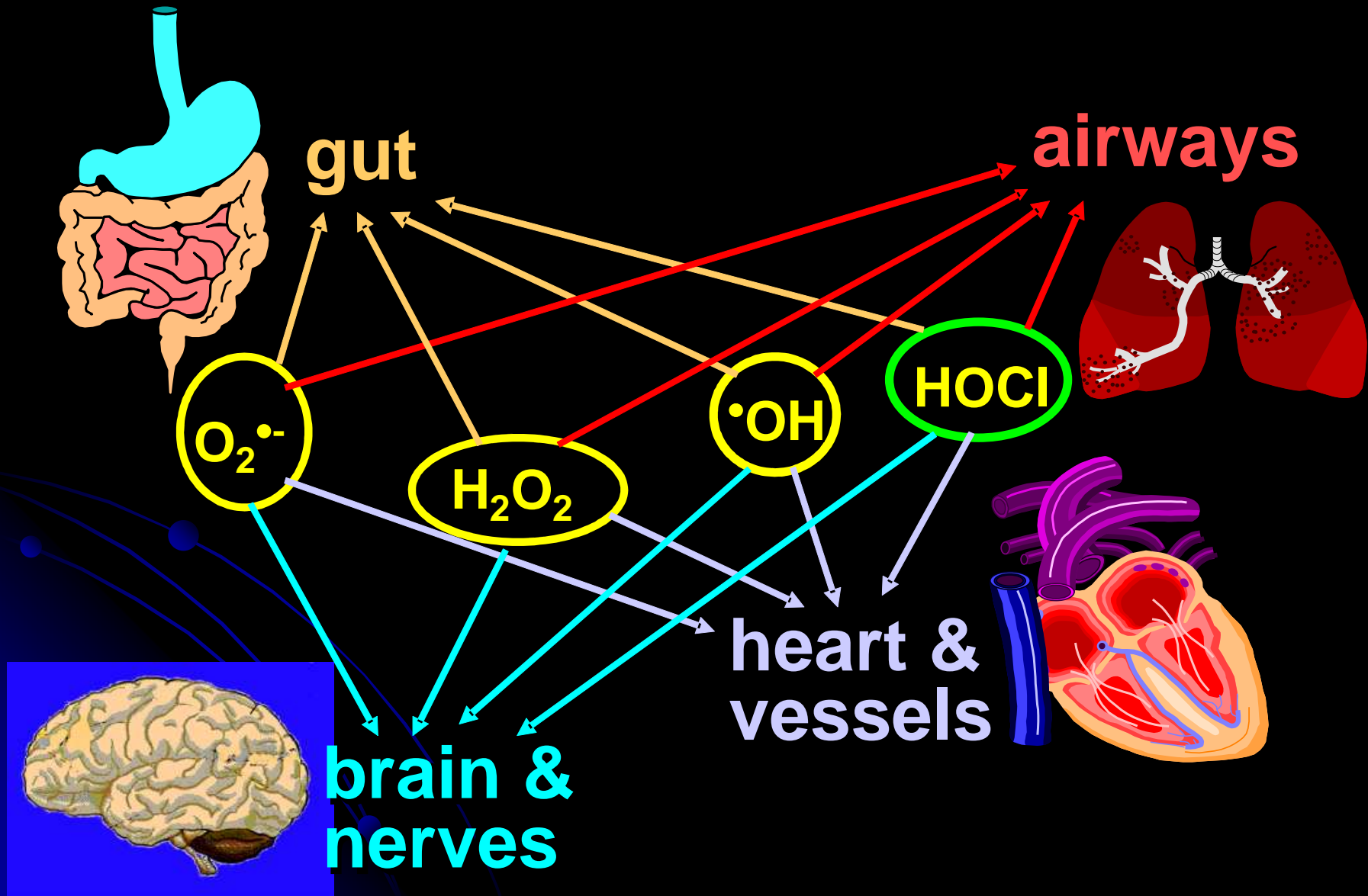
Production of reactive nitrogen species (RNS)



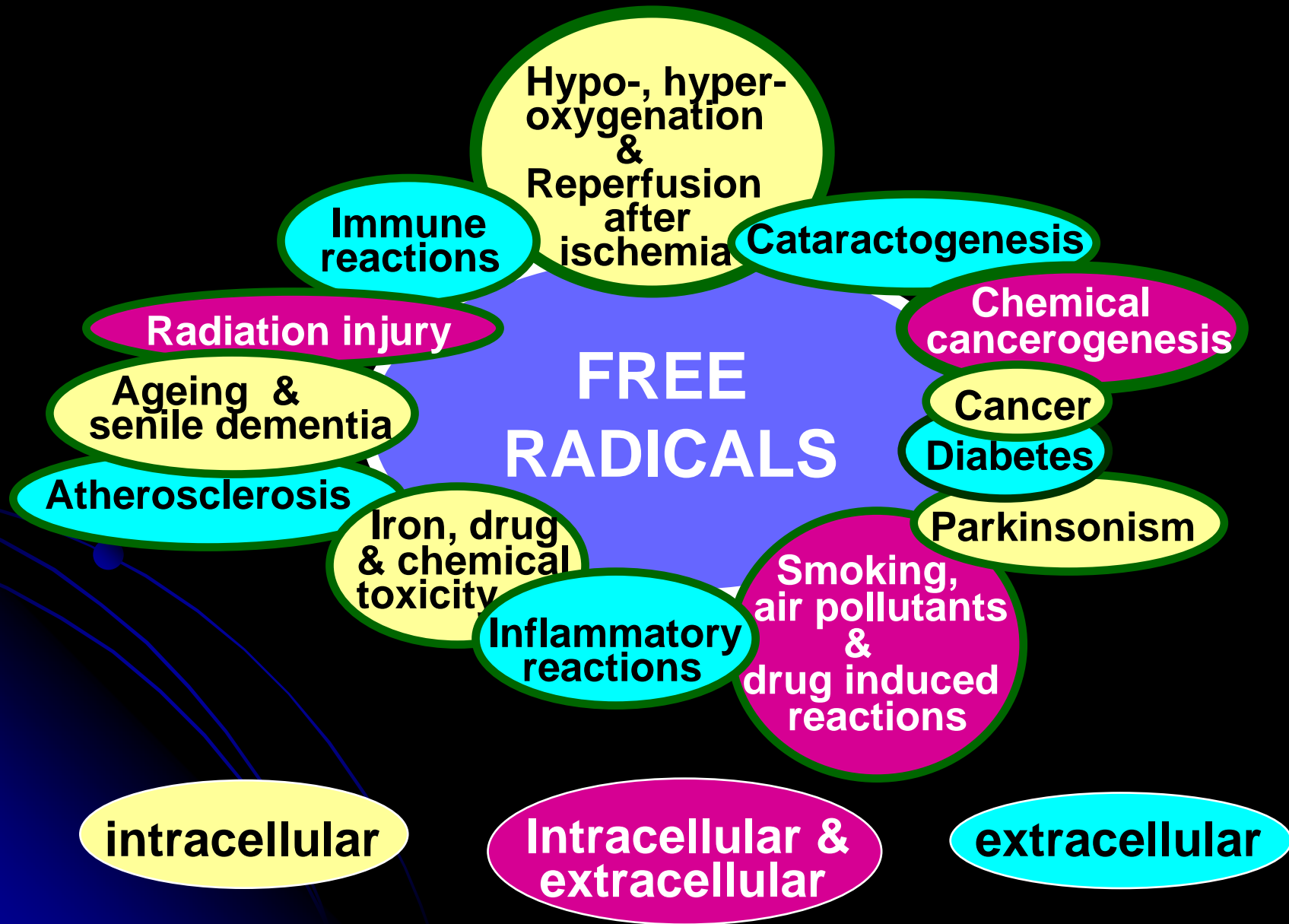
● Apparent Hydroxyl Radical Production by Peroxynitrite:

Implications for endothelial Injury from Nitric Oxide and Superoxide. Beckman *et al.*, *PNAS USA* 87:1620-1624, 1990

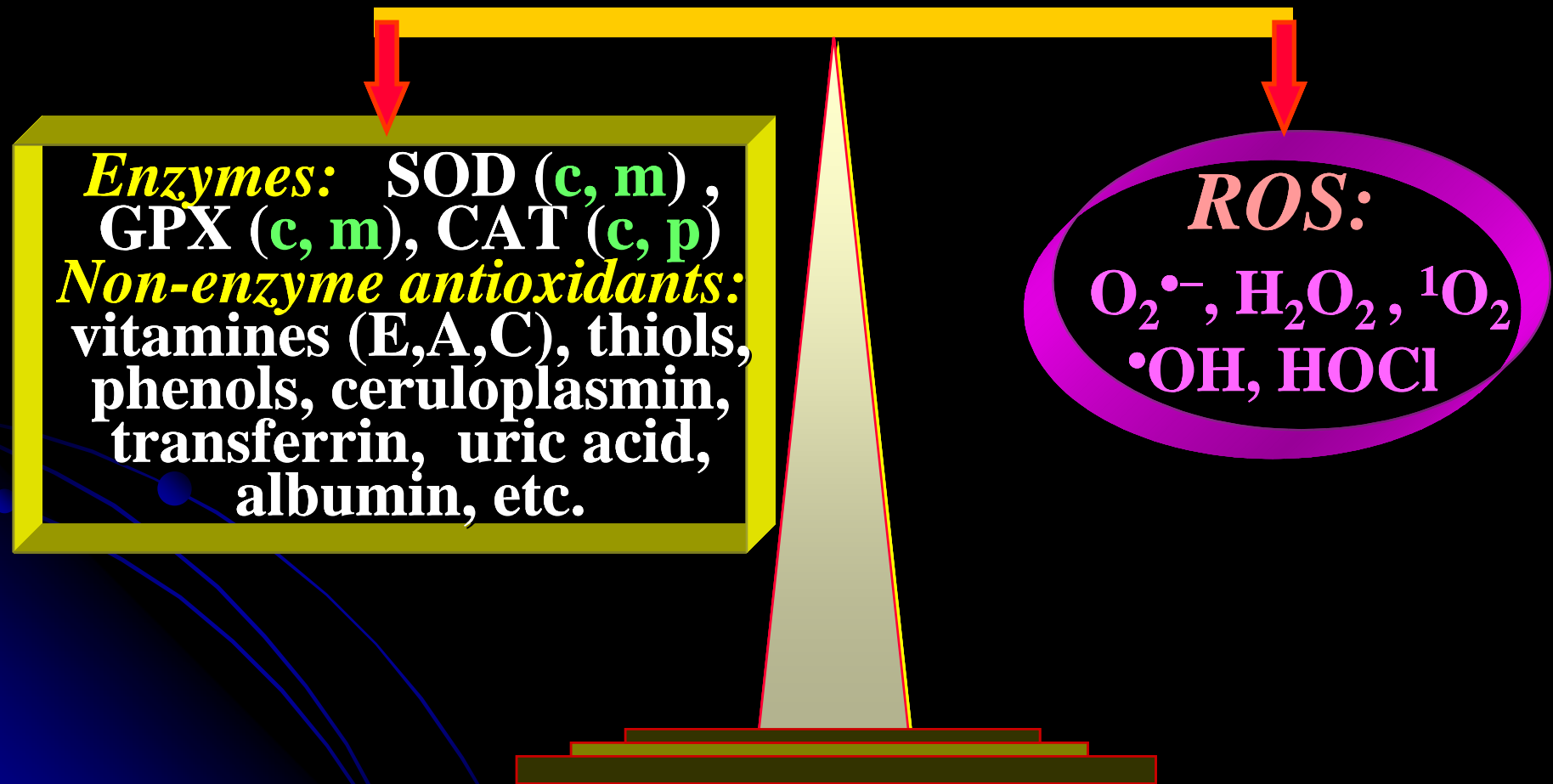
Frequent targets of ROS



Pathological conditions that may have a free radical component and sites of ROS actions



ROS are tightly controlled resulting in a physiological balance between their production and elimination



c-cytosolic, m-mitochondrial, p-peroxisomal

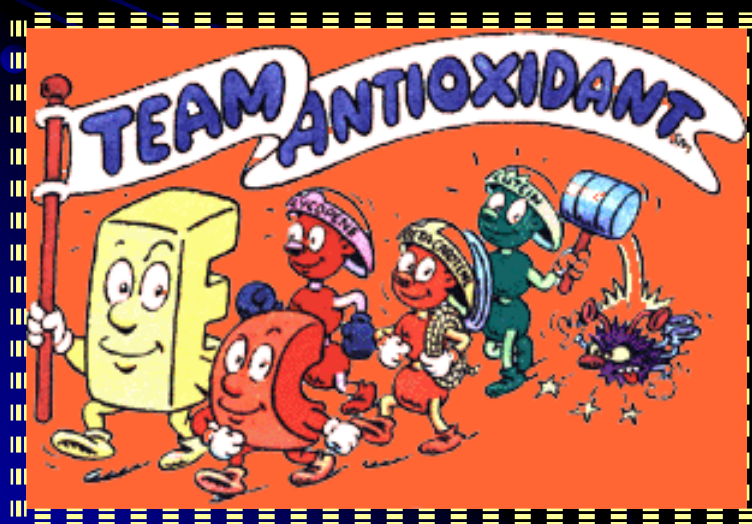
Under pathological condition the physiological balance is lost

Enzymes: SOD, GPX, CAT
Non-enzyme antioxidants:
vitamines (E, A, C), thiols,
uric acid, ceruloplasmin,
transferrin, phenols,
albumin, etc.

ROS:
 $O_2^{\bullet-}$, H_2O_2 , 1O_2 ,
 $\bullet OH$, HOCl

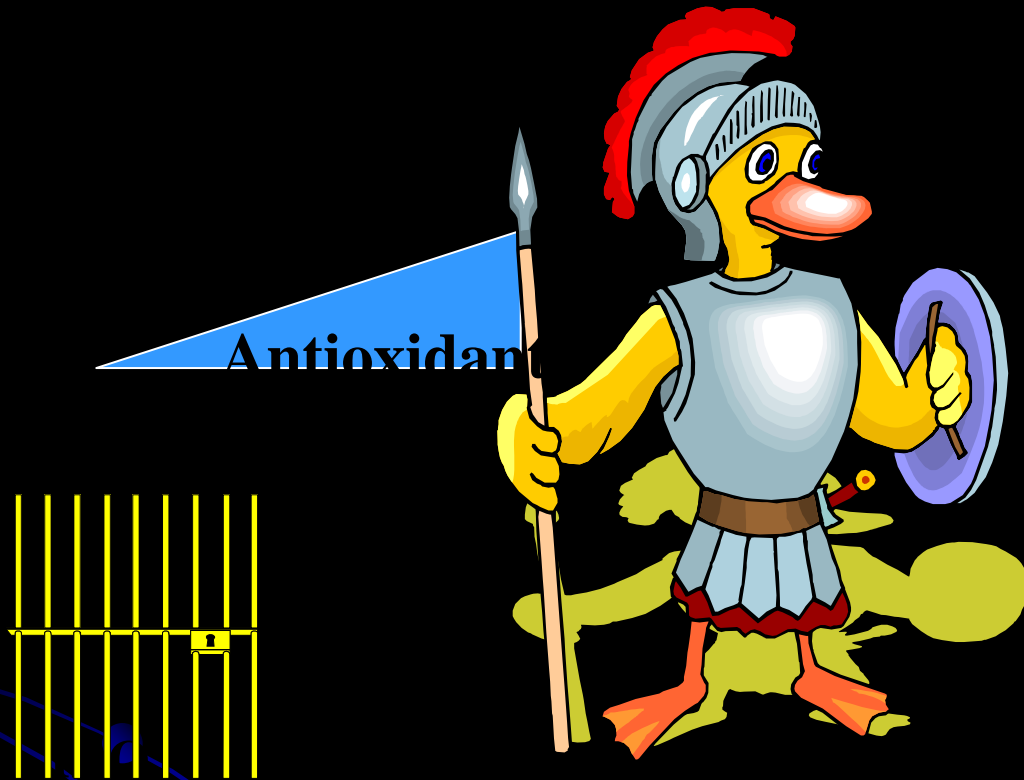
What are antioxidants?

Antioxidants come in different shapes and sizes: they are nutrients (vitamins and minerals) or enzymes.



These tiny superheroes counteract the negative effects of oxidation in animal tissue.

How do anti-oxidants work?



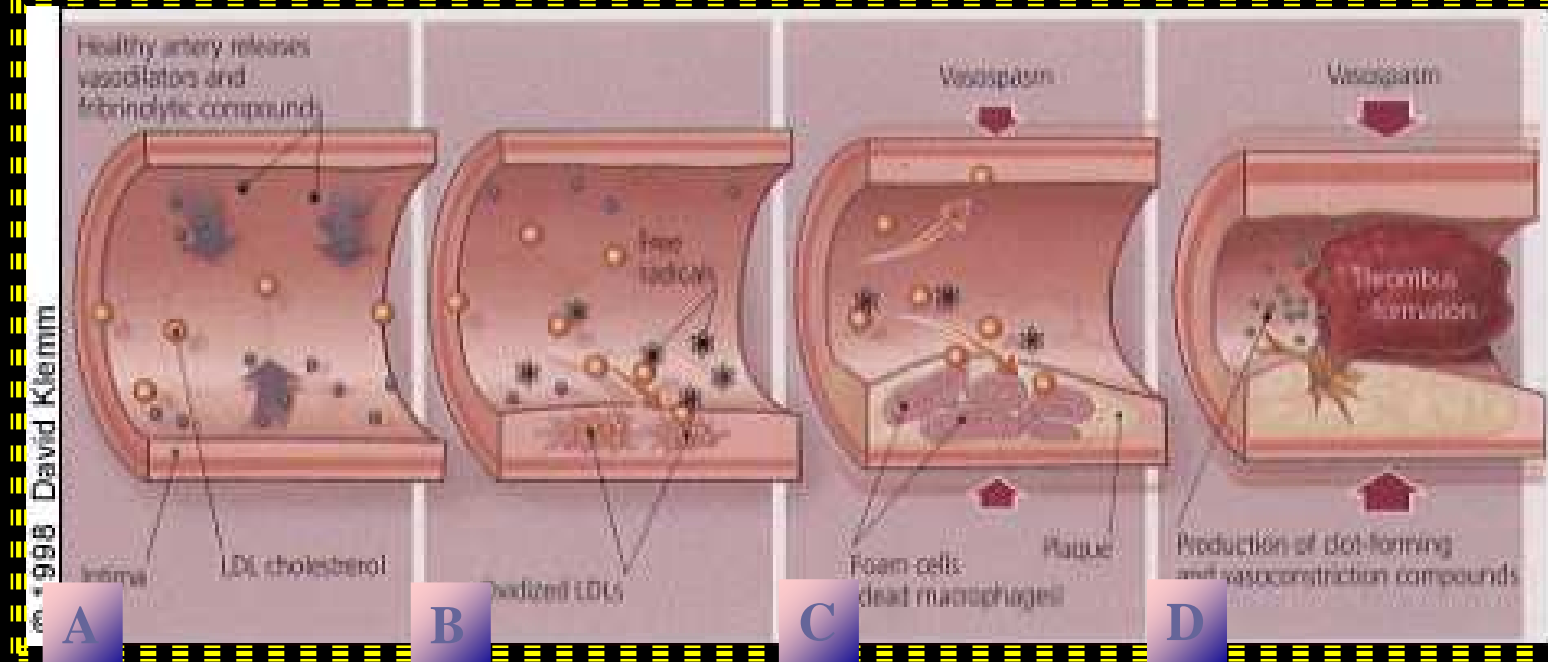
The free radical tug-of-war for electrons damages cells, proteins and DNA. If Wright's antioxidant vitamins are developed, they may be able to shorten the battle time between the two molecules. He is targeting Vitamin E since this is where he has detected a weakness in the body

Antioxidants prevent or treat

- ✓ Cancer
- ✓ Diabetes
- ✓ Heart disease
- ✓ High blood pressure



Prevention of disease shown in populations having a high consumption of fruits and vegetables



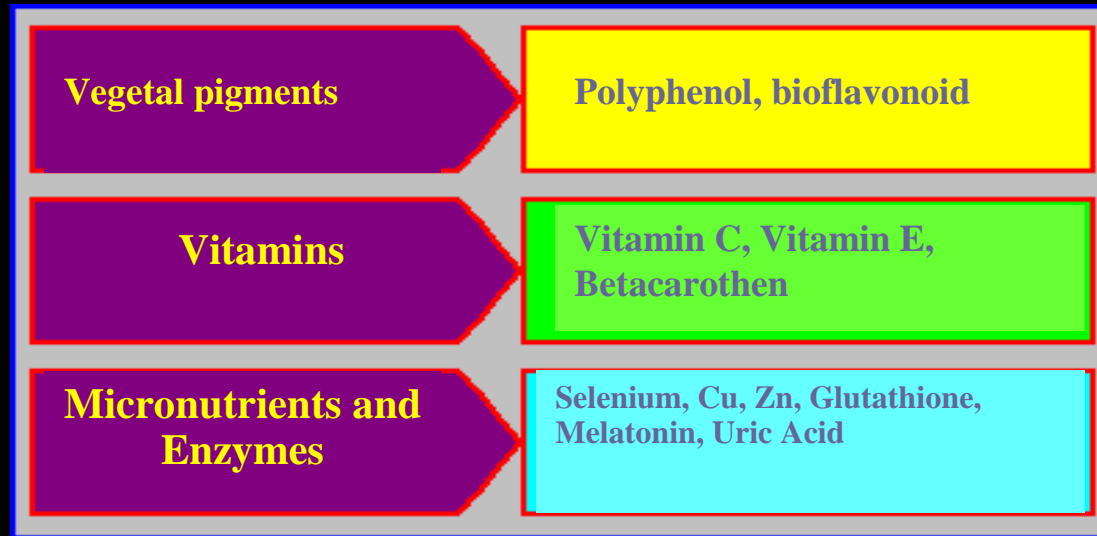
(A) An antioxidant-enriched diet maintains healthy arteries that release vasodilators and fibrinolytic compounds. (B) An antioxidant-inadequate diet results in free radical proliferation and LDL oxidation. Macrophages engulf oxidized LDL, die and form foam cells in the arterial intima. (C) Increased LDL oxidation and foam cell proliferation forms plaque and blocks the formation of fibrinolytic compounds and vasodilators. (D) A clinical event occurs when a 20-30% lumen-obstructing plaque ruptures. The plaque rupture causes immediate release of clot-forming and vasoconstriction compounds. Lumen obstructions lead to myocardial infarction or death. (LDL=low-density lipoprotein)

Superfoods

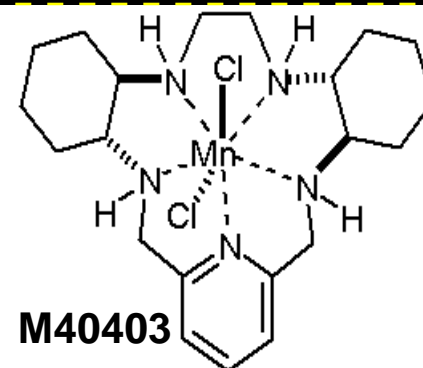
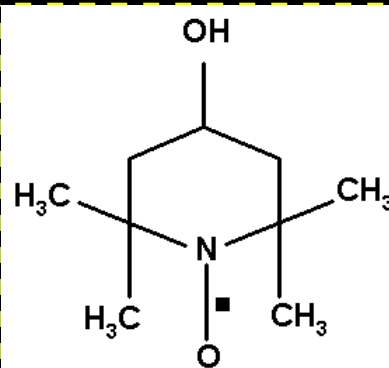
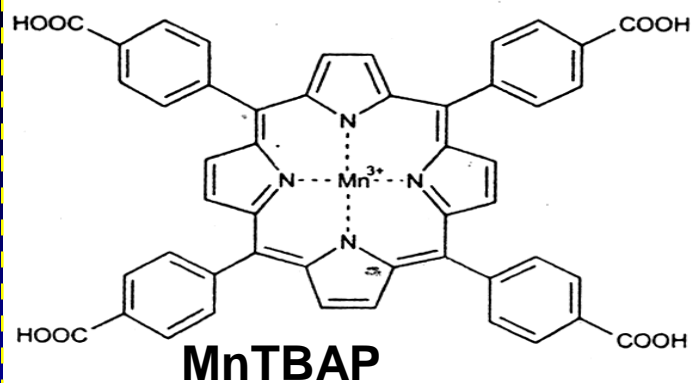
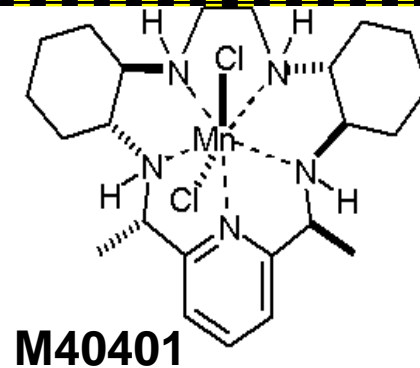
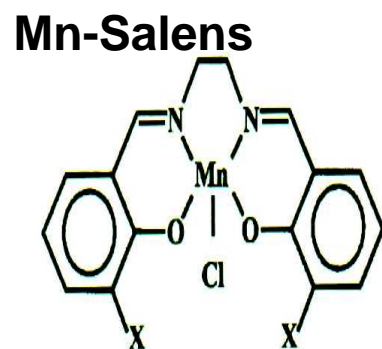
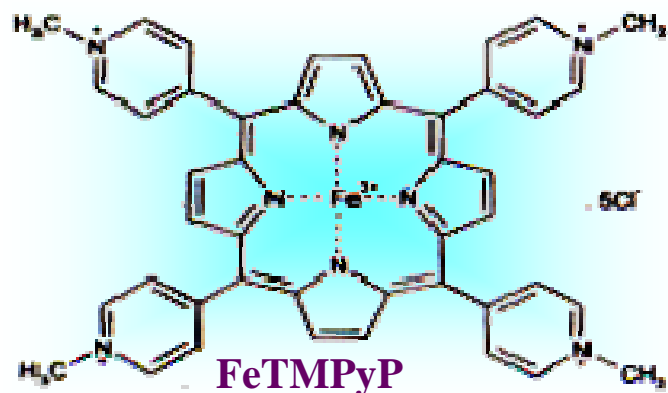
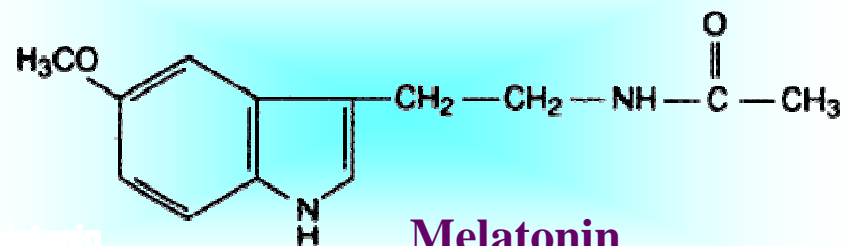
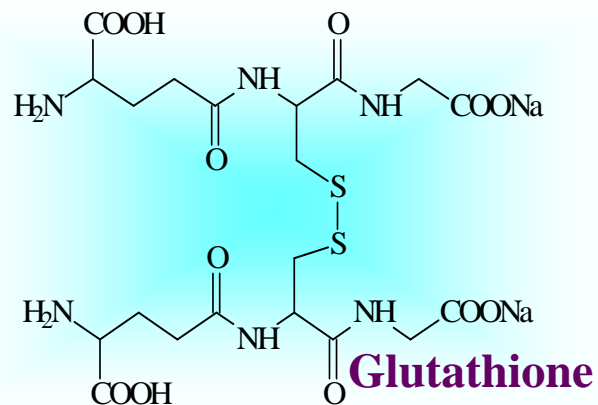
Sure, everyone knows that an apple is a better snack than potato chips, but do you know that a daily handful of walnuts or a bowl of blueberries can actually improve your well-being and longevity?



Antioxidants in Diet



~~Free Radicals~~



Evidence That Antioxidant Flavonoids in Tea and Cocoa Are Beneficial for Cardiovascular Health

By

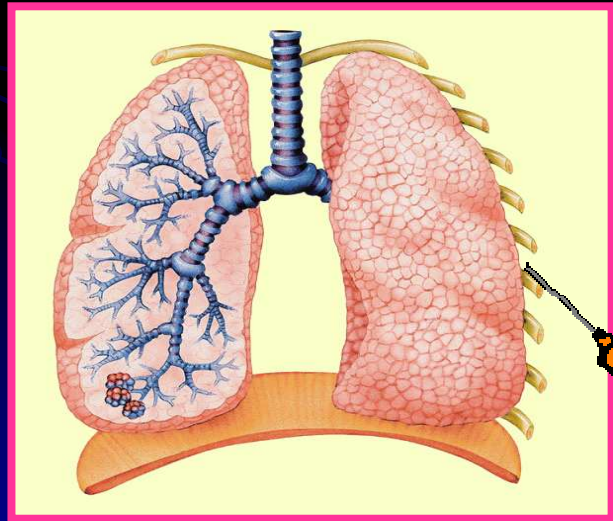
Penny M. Kris-Etherton and Carl L. Keen



Current Opinion in Lipidology 2002, 13:41-49

Anthocyanins

Evaluation of antioxidant and antinflammatory activity in vivo and in vitro sperimental model of pulmonary damage in rat



Antioxidant vitamin C

Food sources:

- ✓ Citrus fruit
- ✓ Tomatoes
- ✓ Peppers
- ✓ Broccoli
- ✓ Melons
- ✓ Strawberries



Antioxidant vitamin E

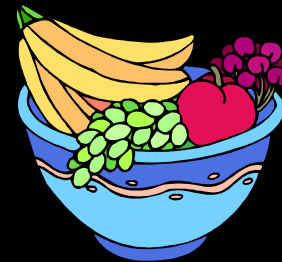
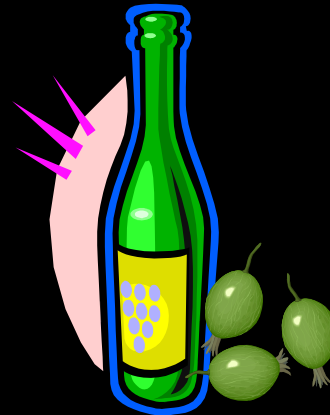
Food sources:

✓ Oil (60%)

✓ Fruits and veggies, esp. dark green leafy (10%)

✓ Grains

✓ Nuts and seeds



Antioxidant-beta carotene

Food sources:

- ✓ Carrots
- ✓ Sweet potatoes
- ✓ Oranges
- ✓ Cantaloupe
- ✓ Tomatoes
- ✓ Dark green leafy vegetables





Researchers find red wine's secret



■ White: no help fighting hardening of the arteries

LONDON (AP) — Researchers say they have discovered the key component in red wine that explains the so-called French Paradox, or the way the French can eat lots of cheese, buttery sauces and other rich foods and still suffer less heart disease than people in other countries.

The explanation is pigments known as polyphenols.

The pigments are not present in white wine or rose, and they seem to be less potent when they are present in grape juice.

Polyphenols inhibit the production of a peptide that contributes to hardening of the arteries, researchers report in the latest issue of the journal *Nature*.

In laboratory dish experiments, polyphenols in red wine decreased the amount of the peptide endothelin-1 produced by cells taken from the blood vessels of cows.

Endothelin-1 is a potent blood vessel constrictor, and overproduction of the compound is thought to be a key factor in why arteries clog with fatty deposits, said the researchers from the William Harvey Research Institute at the London

School of Medicine and Dentistry.

In the study, the cow cells were exposed to extracts from 23 red wines, four white wines, one rose and one type of red grape juice.

Researchers found the decrease in endothelin-1 levels was related to the amount of polyphenols in the wines.

The white and rose wines — which contain little or none of the pigment — had no effect on endothelin-1 levels.

Red grape juice, which has plenty of the pigment, was markedly less potent in reducing endothelin-1 than red wine.

The researchers said that suggests that something in the wine-making process changes the pigment's properties.

Researchers believe the pigment comes from red wine skins. In white wine and rose, the grape skins are taken out before fermentation.

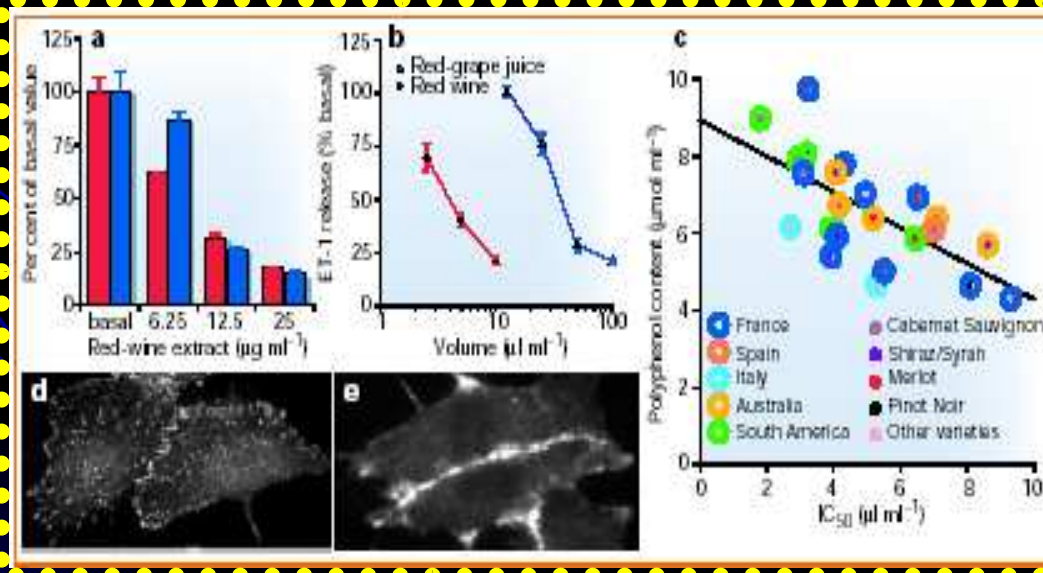
The type of grape also appeared to matter. Four of the six most effective red wines used in the study were made entirely or partially from cabernet sauvignon grapes.

"The key message is moderate consumption of red wine is likely to prevent heart disease, but we have no evidence that white wine or rose would have a similar benefit," said Roger Corder, who led the study.

To drink moderately and regularly attenuates stroke risk

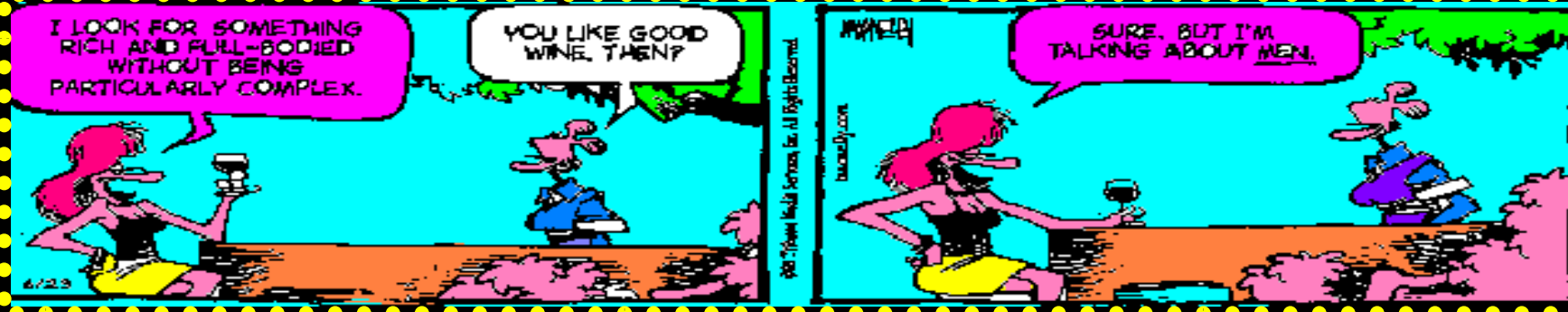
Recently on Nature review it was published that wine has beneficial effect on safety. Prof. R.Corder, of London school of Medicine, showed that polyphenols, bioflavonoid and proanthocyanins can have beneficial effect on arteries and veins, stopping endothelin-1 production.

Polyphenols, are substances so powerful that a moderately assumption, can be very efficacy.





Grape Nuts Extract



Used like as:

- Antioxidant
- Allergy, asthma
- Vein fragility, arteriosus disfunction

Mechanism of Action:

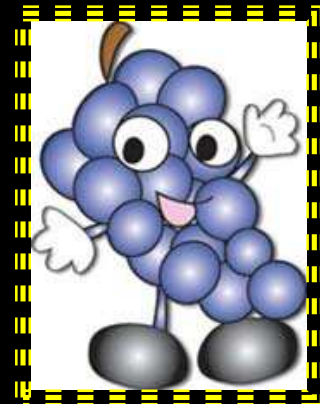
- Antioxidant
- Stabilitazion of 1-antitrypsine
- Inibition of inflammation mediator release (Hystamine and PGS)
- Inibition of platelet aggregation

Precaution of use:

- People with evidence of present or past emorrhagic, alterations of hemostatic components
- Anticoagulator and antiaggregator drugs

General Warming:

- Caution with children under 2 years
- Caution with pregnant or lactating women



Antioxidant on exhaustive exercise



Antioxidant restricted diet increases oxidative stress during acute exhaustive exercise.

Watson TA, Callister R, Taylor R, Sibbritt D, MacDonald-Wicks LK, Garg ML.

Asia Pac J Clin Nutr. 2003;12 Nutrition and Dietetics, University of Newcastle

Exercise – Antioxidant manipulation



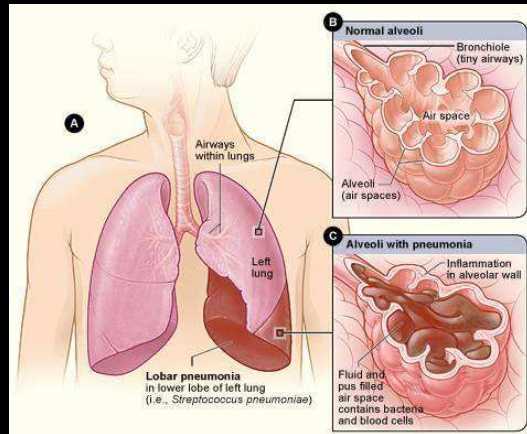
Diet

- Little research
- Antioxidant deficiency reduces exercise capacity

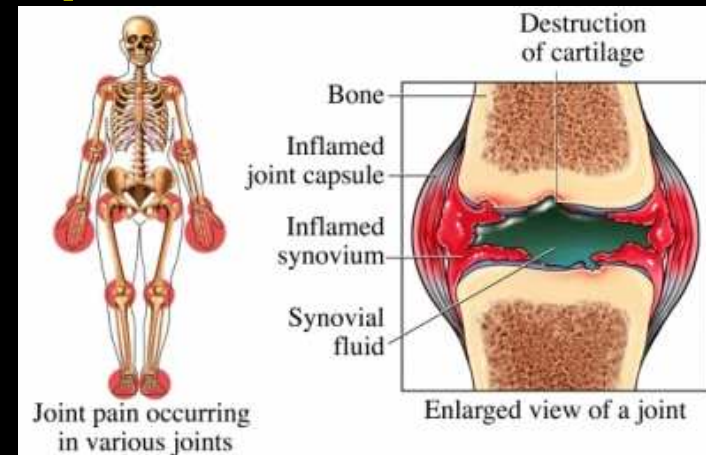
• Supplementation

- Mixed findings
- Reduced oxidative stress markers
- No impact on performance

Acute disease: Carrageenan-induced pleurisy (CAR)



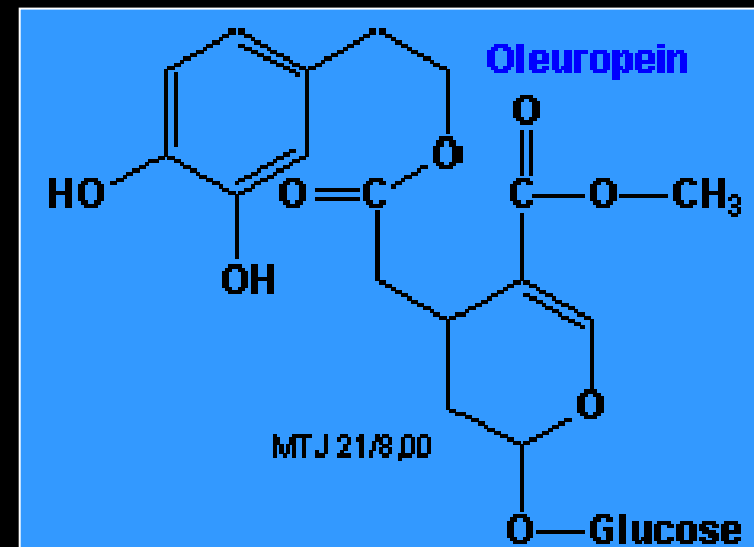
Chronic disease: Type II collagen-induced arthritis (CIA)



Olive oil is an integral ingredient of the traditional Mediterranean diet and several studies attribute many of the healthy advantages of this diet to olive oil's unique characteristics.



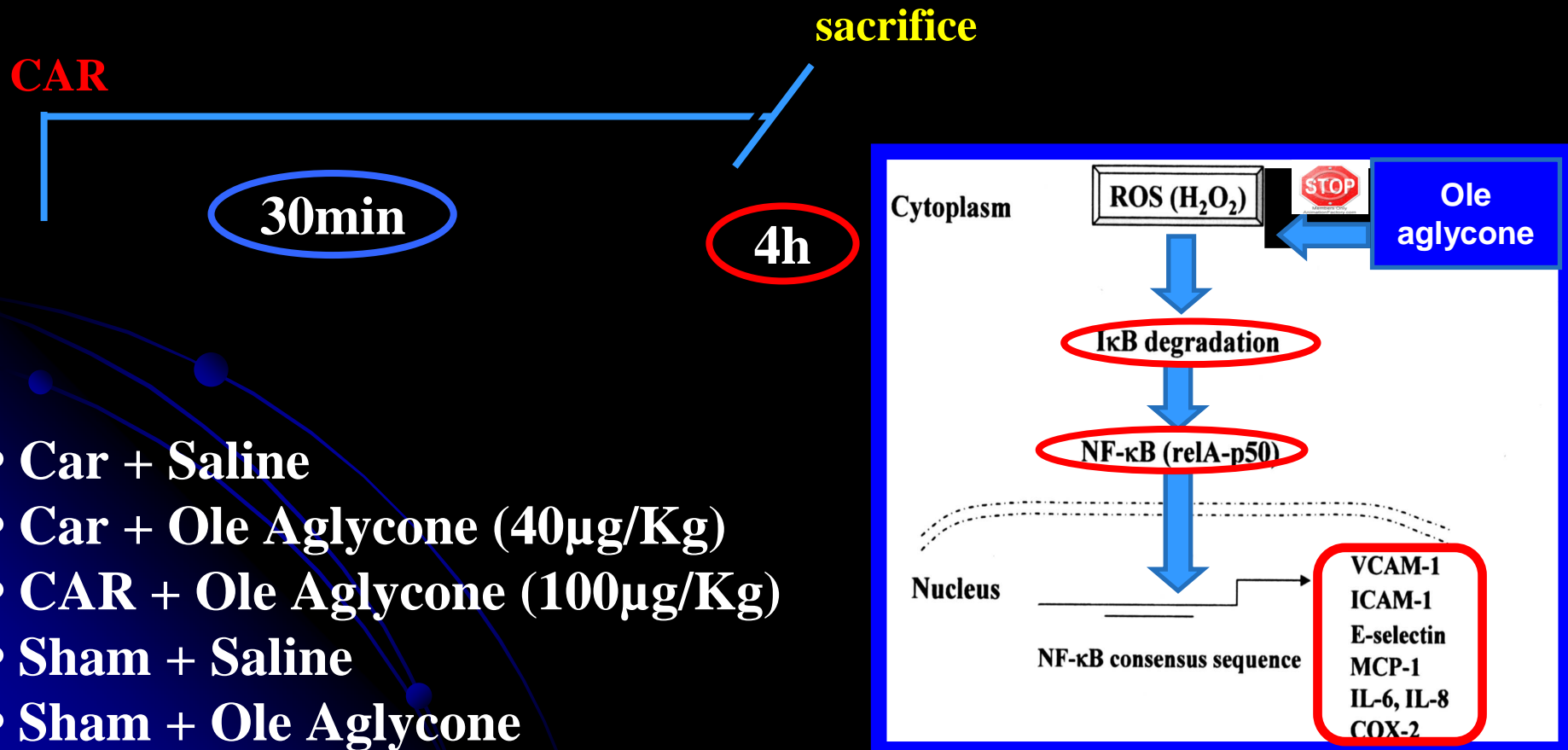
Disease	Protective Role
Cardiovascular disease	Inhibition of neuroinflammation and oxidative stress; inhibition of platelet aggregation; reduction of high cholesterol levels, ↓ LDL and ↑ HDL
Alzheimer disease	Inhibition of neuroinflammation and oxidative stress
Type II diabetes	Inhibition of neuroinflammation and oxidative stress; ↓ NF-kappa B activation; ↓ PGE2 production
Lung tumor	and inactivation of Erk cascade
Breast cancer	Downregulation of the expression of Her-2/neu gene



The major constituent of the leaves and unprocessed olive drupes of "*Olea europaea*" is **oleuropein** and the majority of polyphenols found in olive oil or table olives are derived from its hydrolysis.

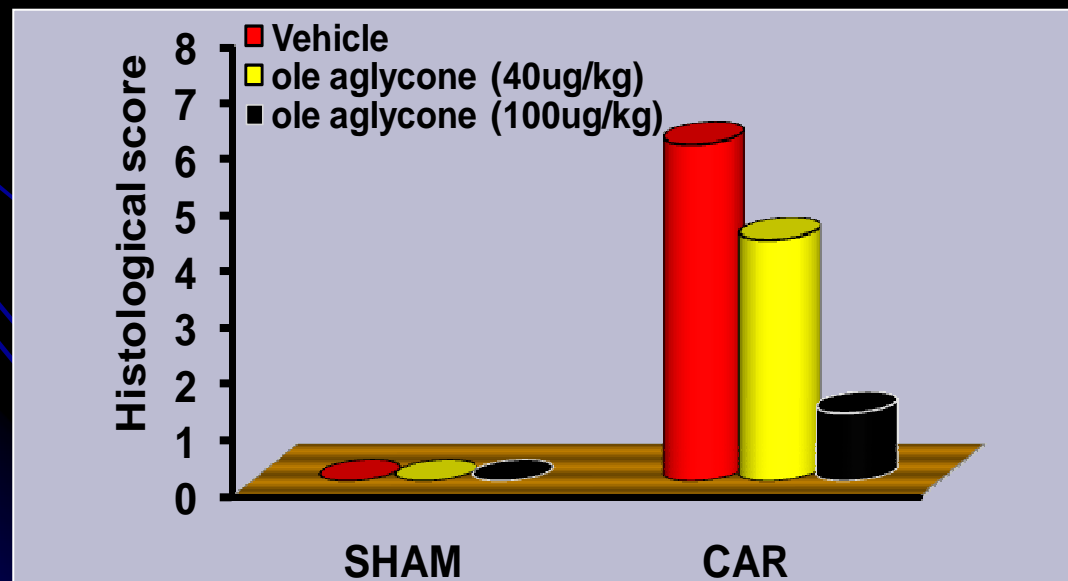
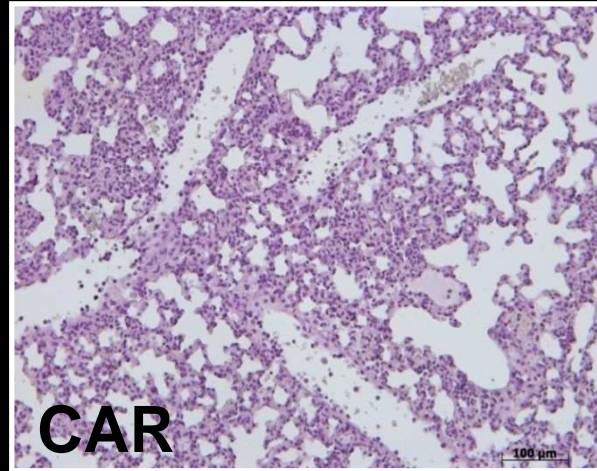
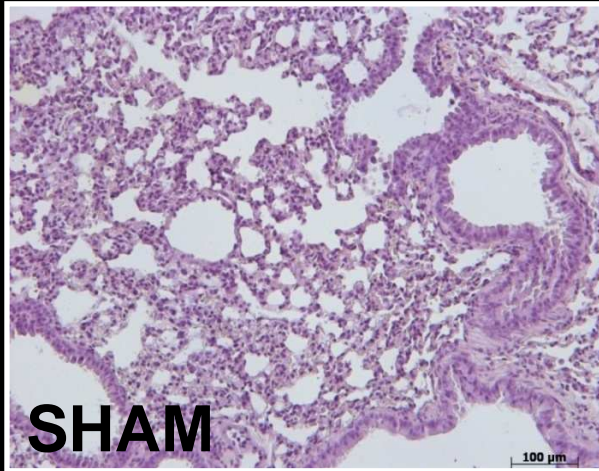
Experimental design – “CAR” Model

Mice were anaesthetized and subjected to a skin incision at the level of the left sixth intercostals space. The underlying muscle was dissected and saline or saline containing 2% λ -carrageenan (0.1 ml) was injected into the pleural cavity.



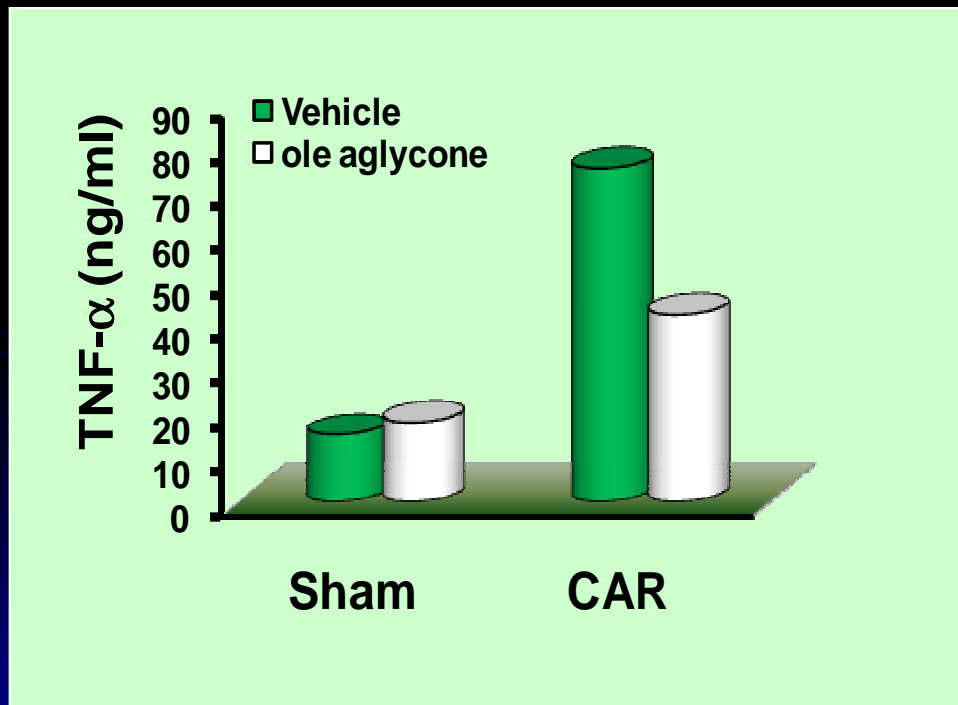
RESULTS ACUTE INFLAMMATION-1

HISTOLOGICAL EVALUATION

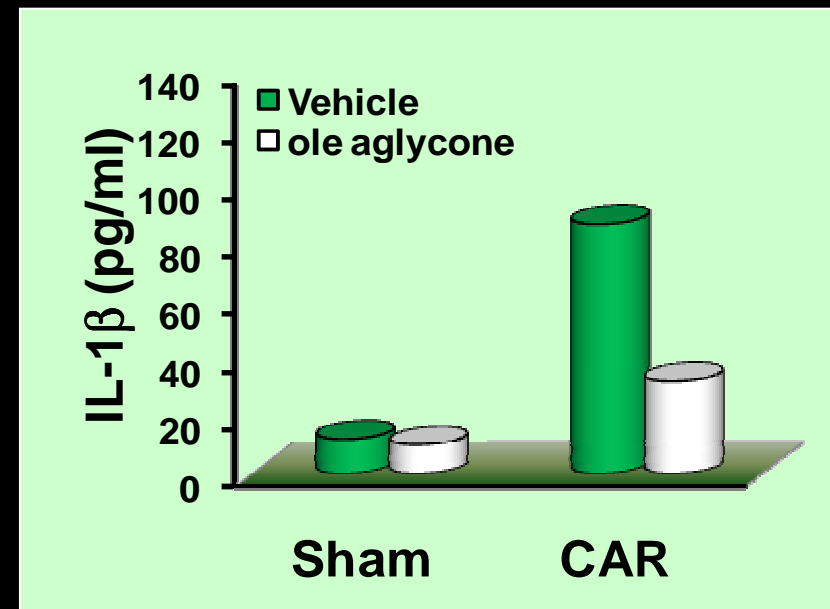


ACUTE INFLAMMATION-2

TNF- α ,

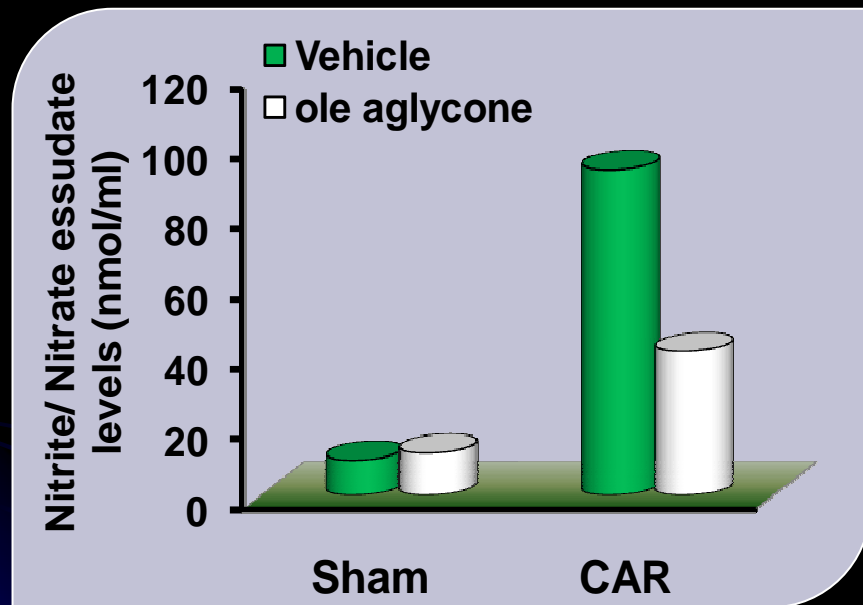


IL-1 β

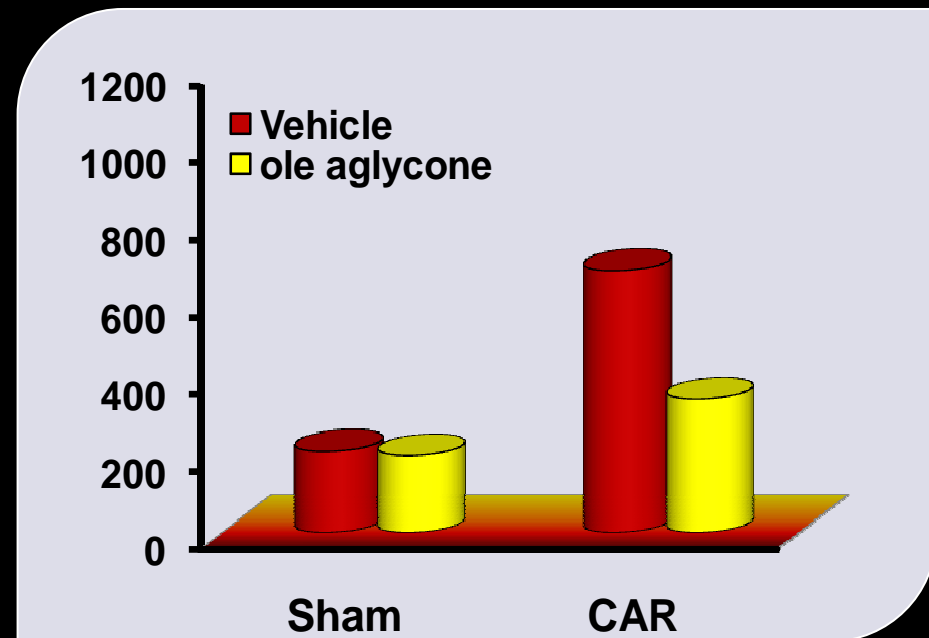


ACUTE INFLAMMATION-3

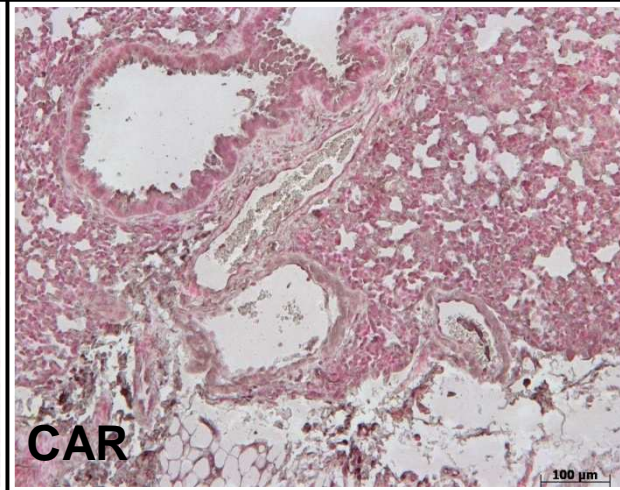
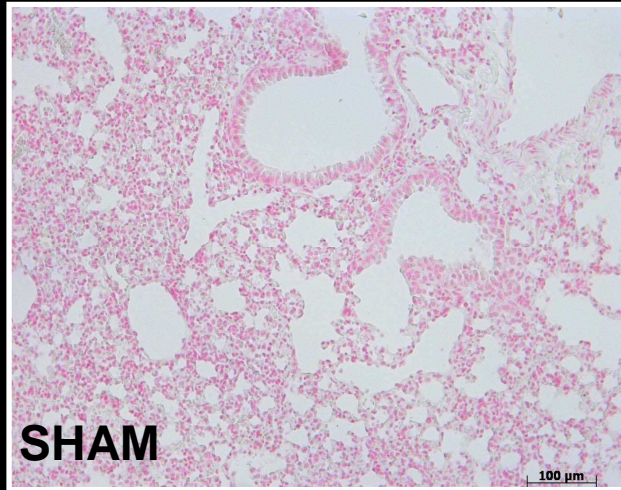
NO LEVELS



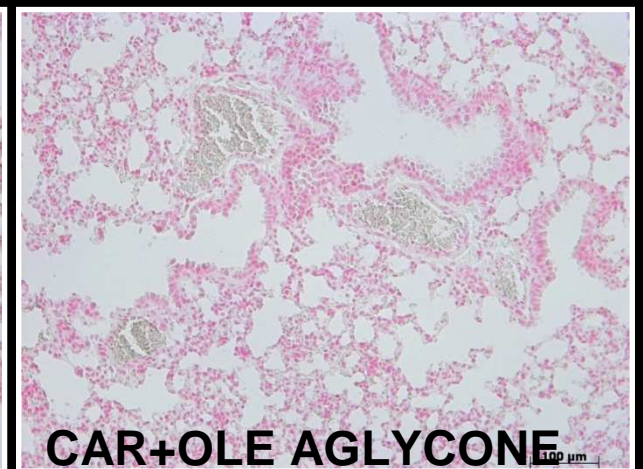
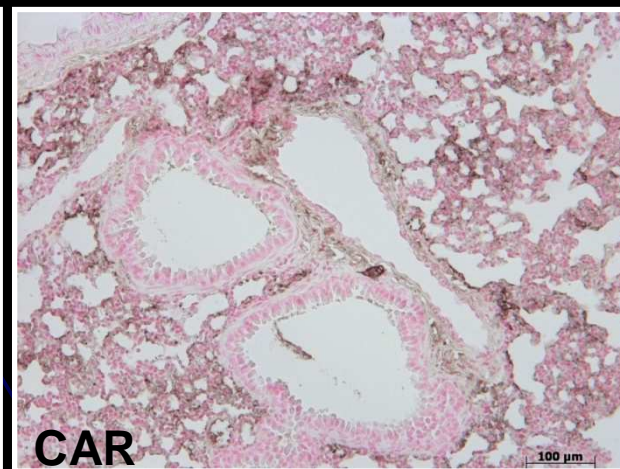
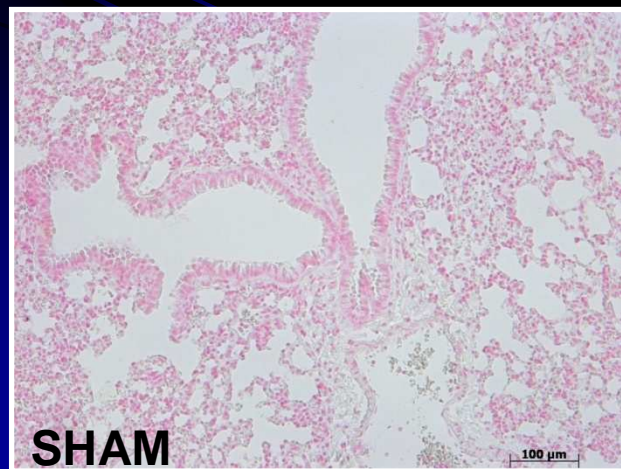
MPO ACTIVITY



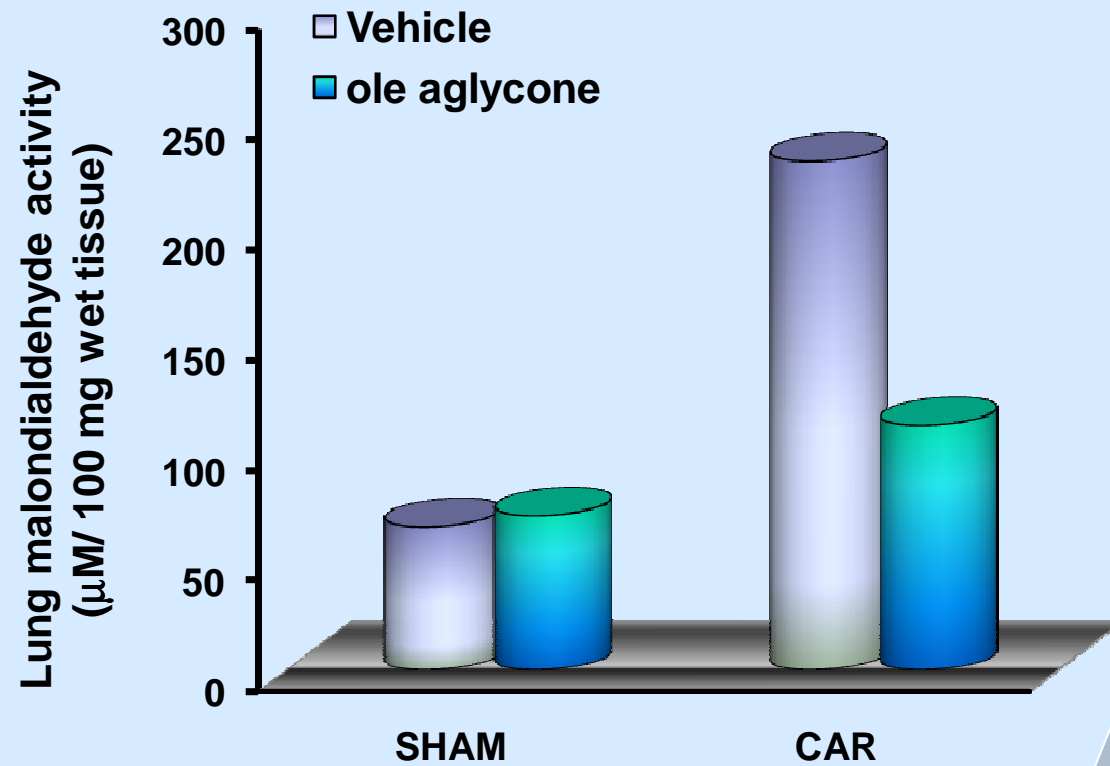
NITROTYROSINE EXPRESSION



PAR EXPRESSION

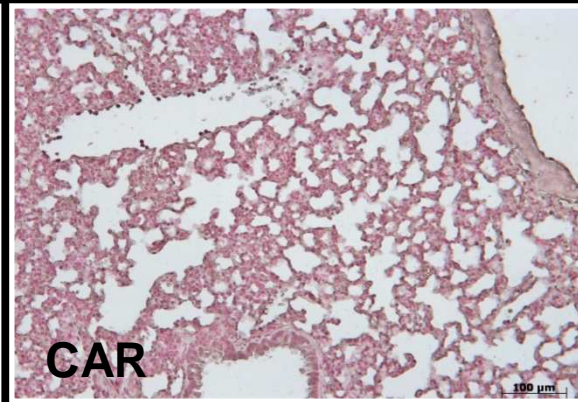
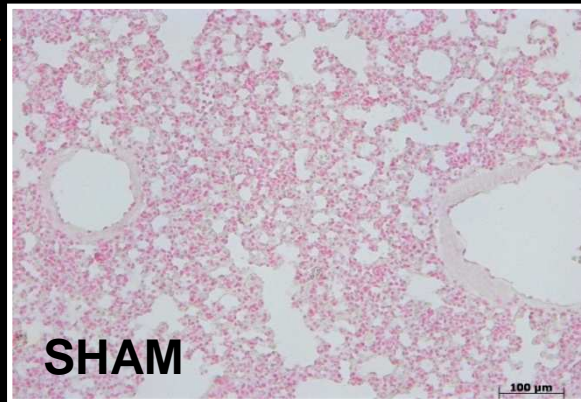


MDA LEVELS

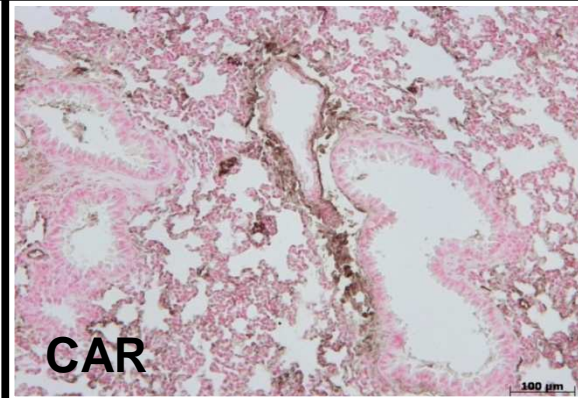
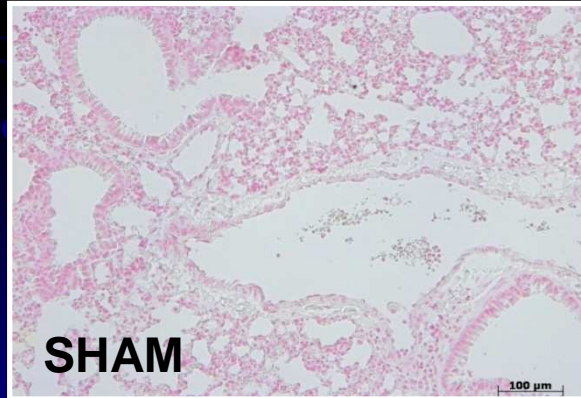


ICAM-1 (A), P-SELECTIN (B) EXPRESSION

A

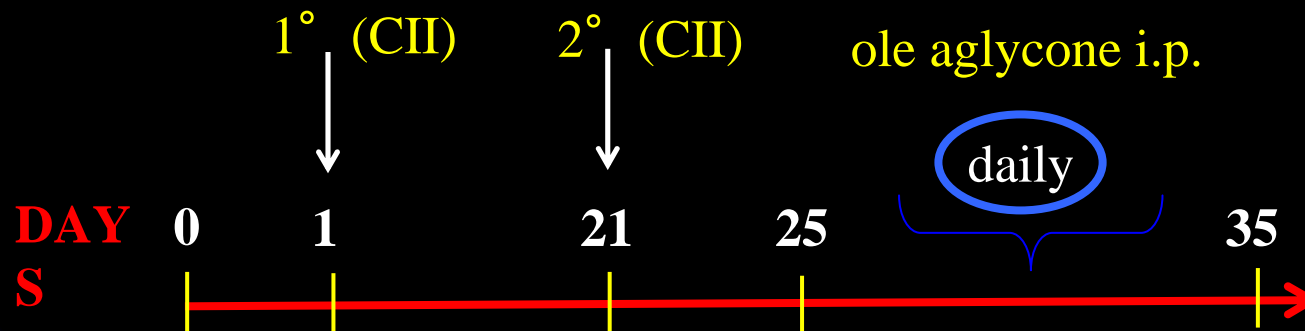


B



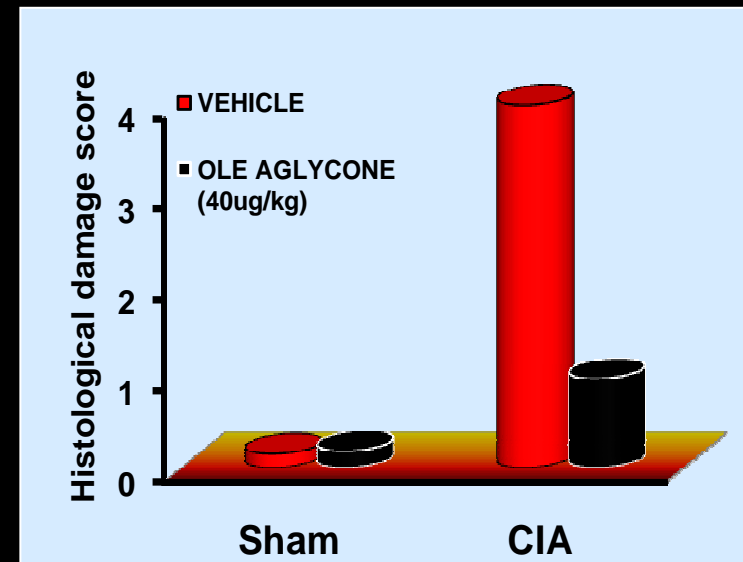
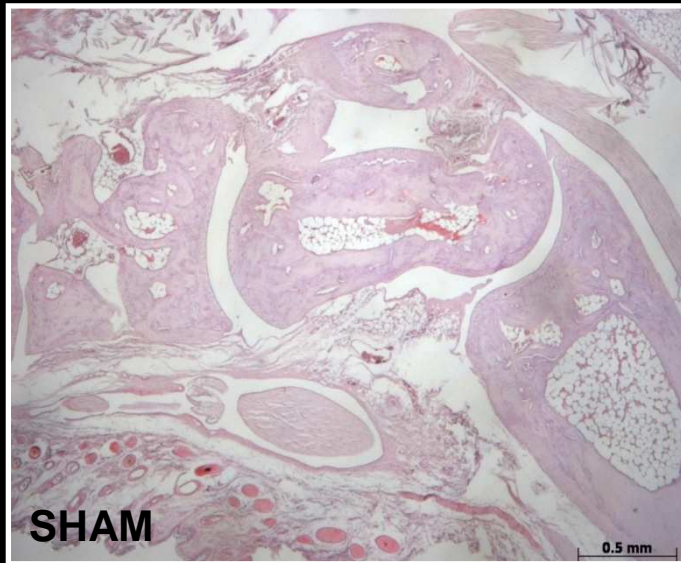
Experimental design – “CIA” Model

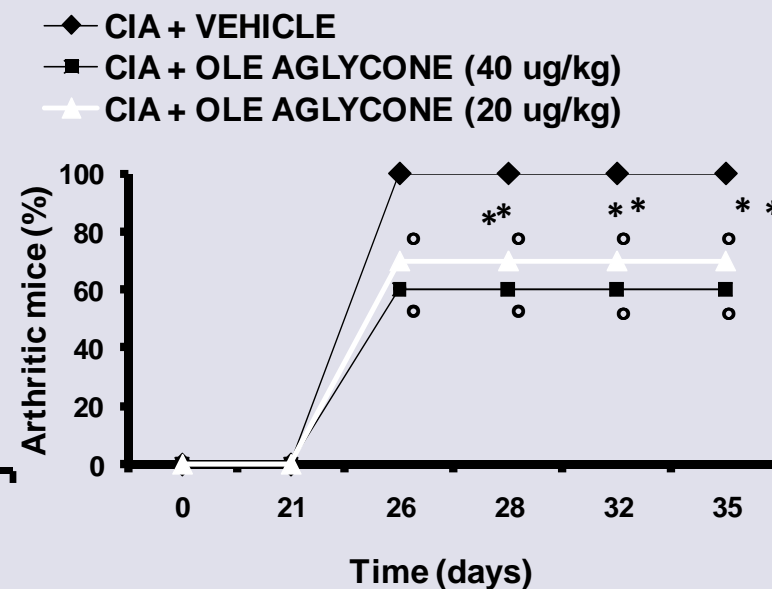
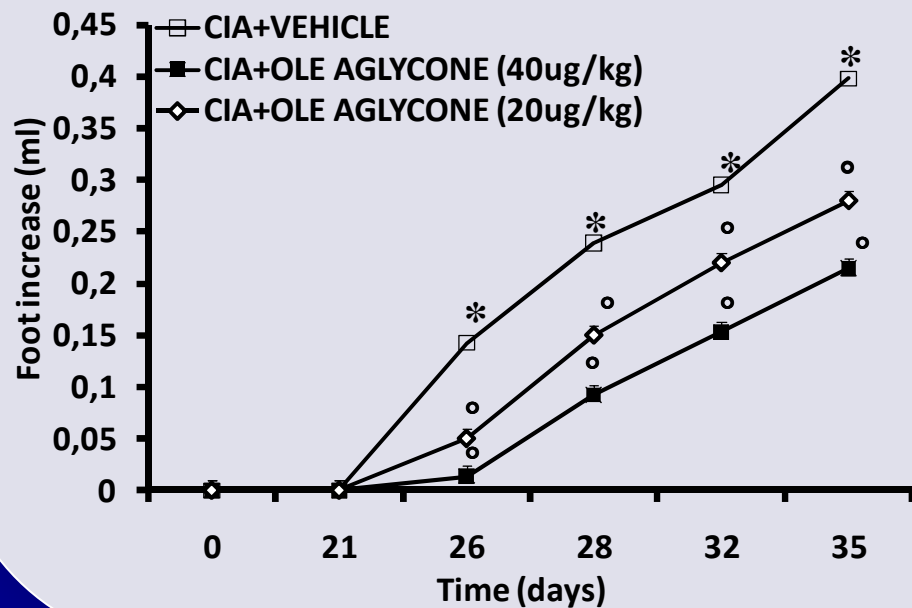
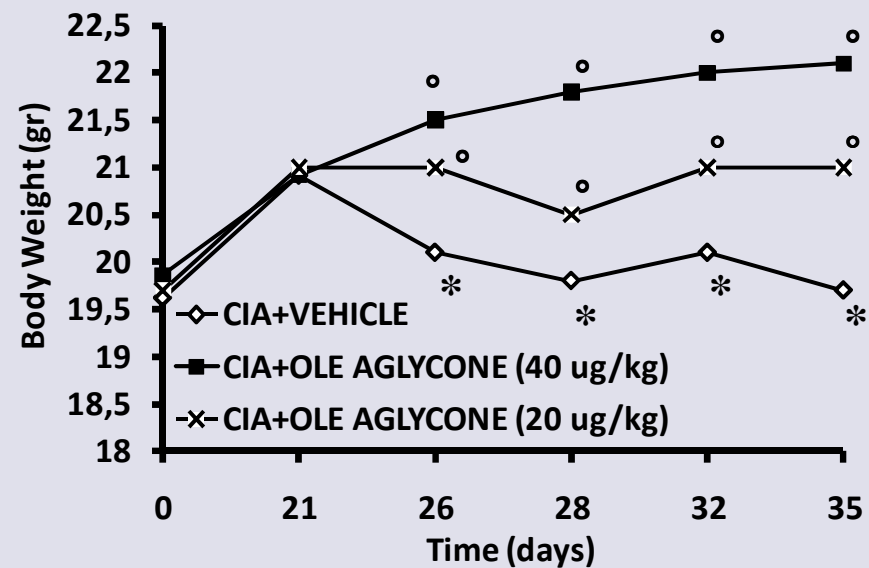
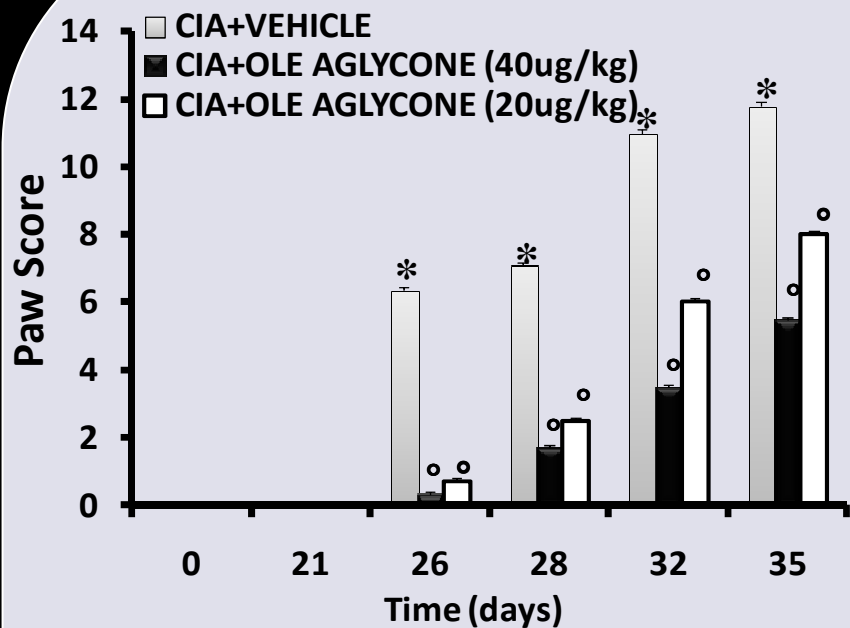
On day 1, CIA was induced in mice by an intradermal injection of 100 μ l of an emulsion containing 100 μ g of bovine type II collagen (CII) and complete Freund's adjuvant (CFA) at the base of the tail.



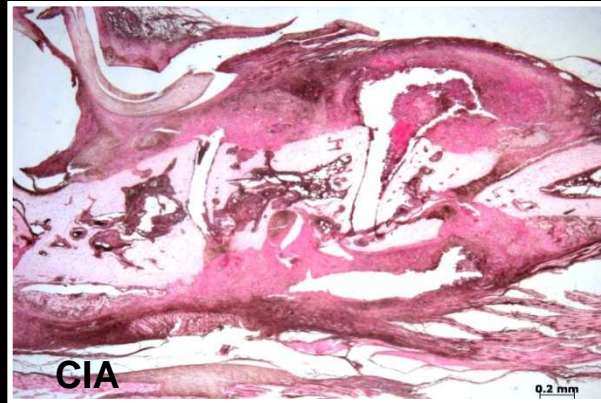
- CIA Control
- CIA + Ole Aglycone (20 μ g/Kg)
- CIA + Ole Aglycone (40 μ g/Kg)
- Sham Control
- Sham + Ole Aglycone

HISTOLOGICAL EVALUATION

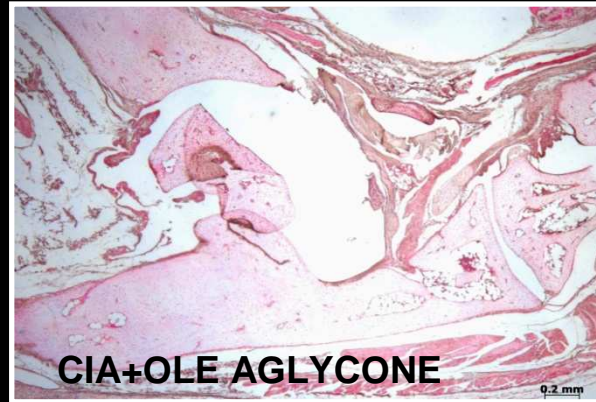
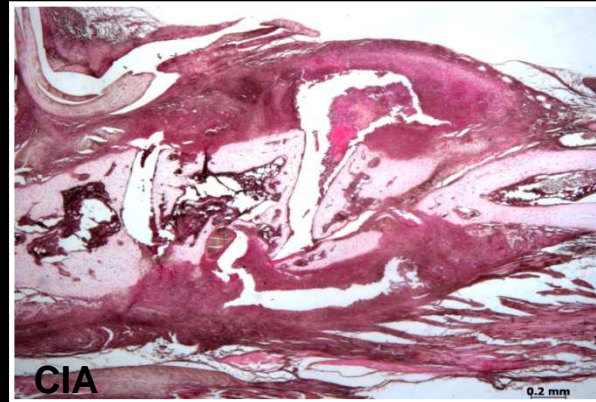




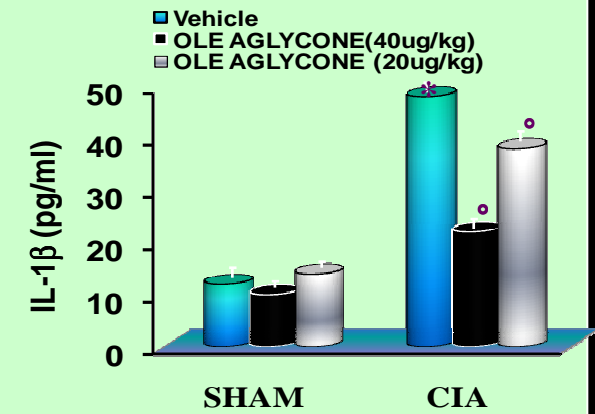
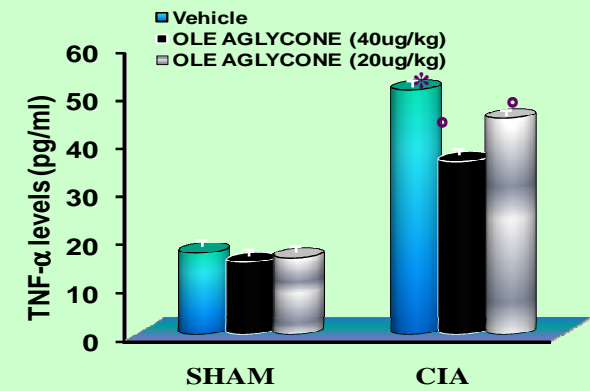
COX-2 EXPRESSION



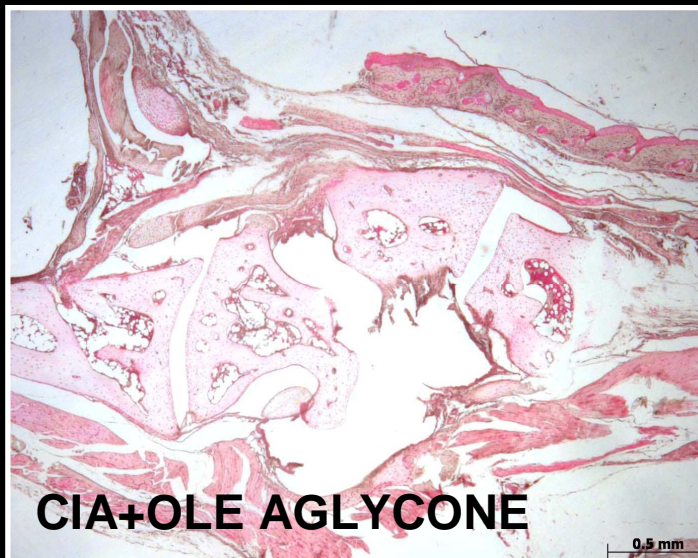
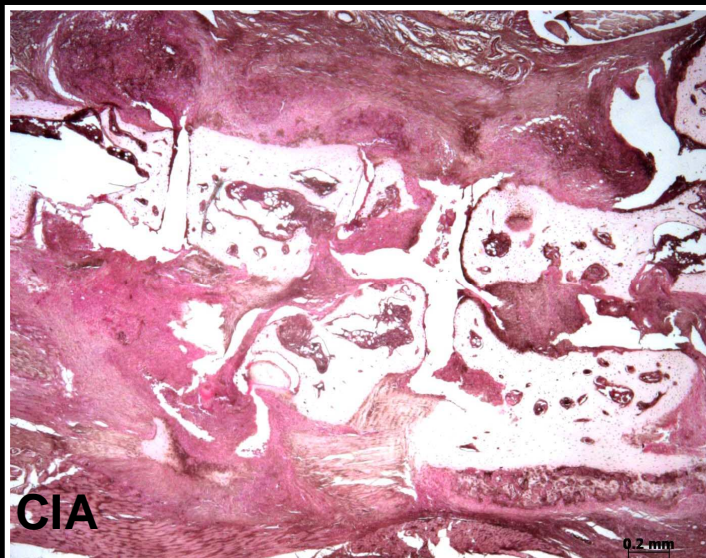
iNOS EXPRESSION



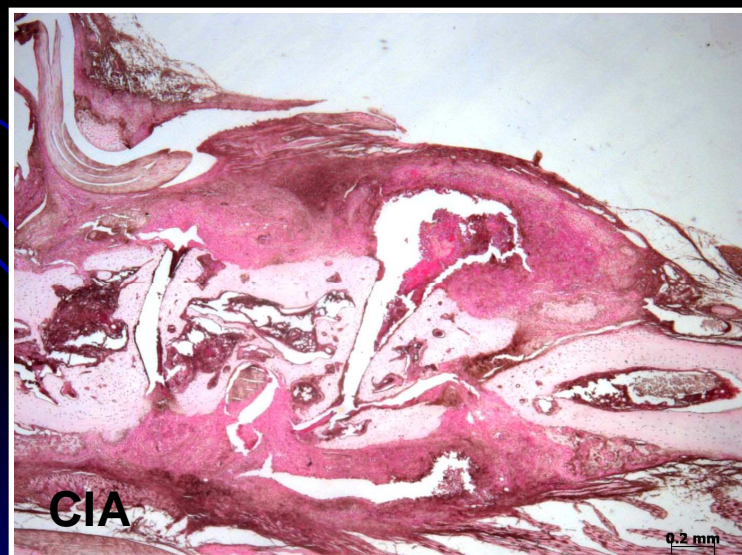
CYTOKINES LEVELS



NITROTYROSINE EXPRESSION



PAR EXPRESSION



Oleuropein Aglycone, an Olive Oil Compound, Ameliorates Development of Arthritis Caused by Injection of Collagen Type II in Mice

Daniela Impellizzeri, Emanuela Esposito, Emanuela Mazzon, Irene Paterniti, Rosanna Di Paola, Valeria Maria Morittu, Antonio Procopio, Domenico Britti, and Salvatore Cuzzocrea

Department of Clinical and Experimental Medicine and Pharmacology, School of Medicine, University of Messina, Messina, Italy (D.I., E.E., I.P., S.C.); Istituto Di Ricovero e Cura a Carattere Scientifico Centro Neurolesi "Bonino-Pulejo," Messina, Italy (E.M., R.D., S.C.); and Departments of Pharmacobiological Sciences (V.M.M., D.B.) and Clinical and Experimental Medicine (A.P.), University of Catanzaro Magna Graecia, Catanzaro, Italy

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Original Article

The effects of oleuropein aglycone, an olive oil compound, in a mouse model of carrageenan-induced pleurisy

Daniela Impellizzeri^{a,e}, Emanuela Esposito^{a,b,e}, Emanuela Mazzon^b, Irene Paterniti^a, Rosanna Di Paola^a, Placido Bramanti^b, Valeria Maria Morittu^c, Antonio Procopio^d, Domenico Britti^c, Salvatore Cuzzocrea^{a,b,*}

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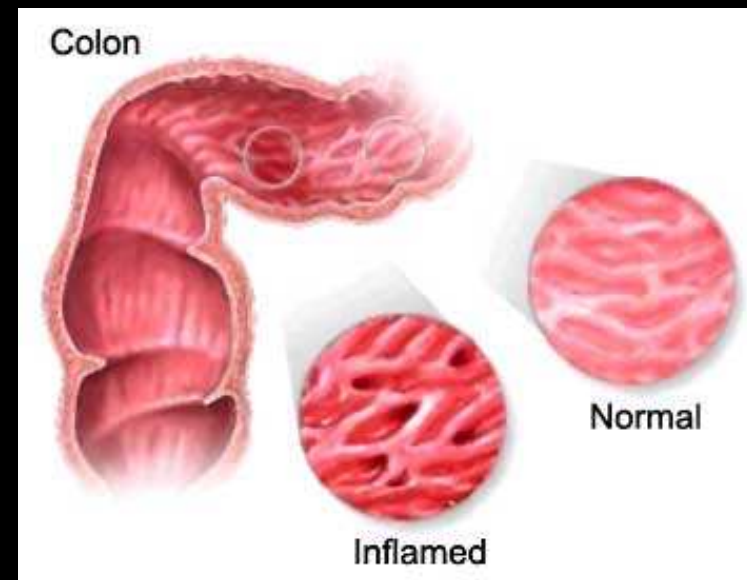
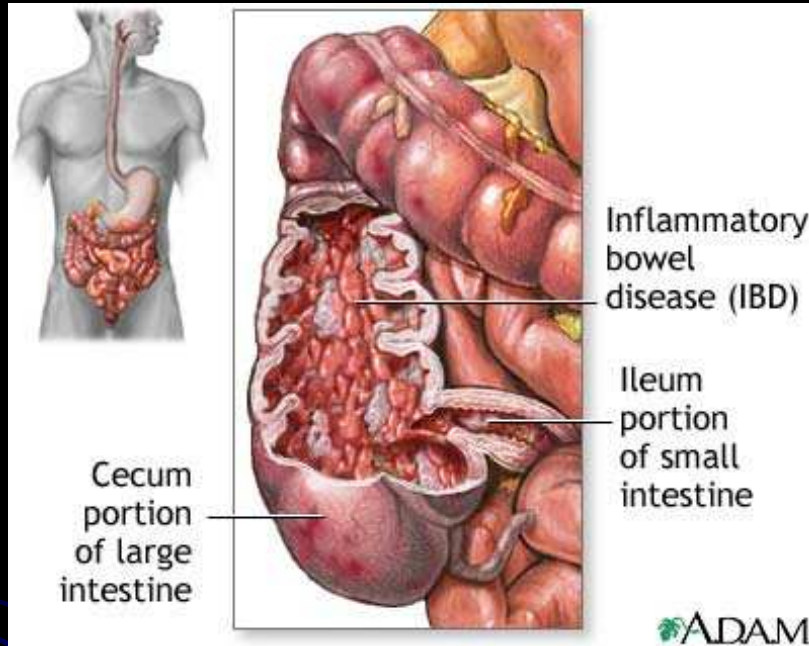
^d Department of Clinical and Experimental Medicine, University of Catanzaro Magna Graecia, Catanzaro, Italy

Why almond skins???



The polyphenols localized in almond skins include a variety of flavonols, flavanones and simple phenolic acids which have a role in reducing risk factors against chronic inflammatory diseases and ageing disorders

Chronic disease: Colitis



Experimental design- colitis induction



DNBS

0

15'
(observation time)



Start treatment
3 hr



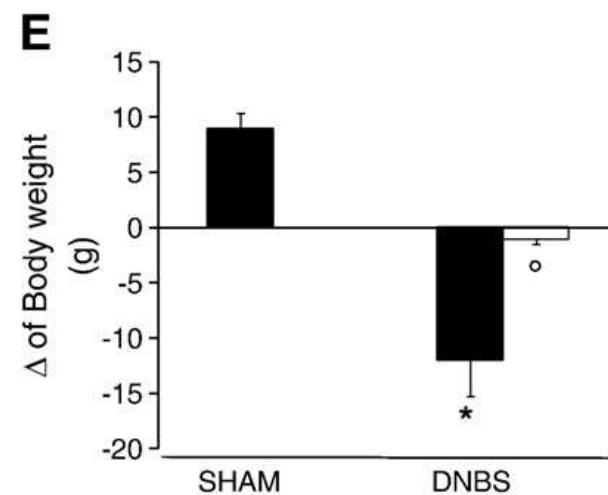
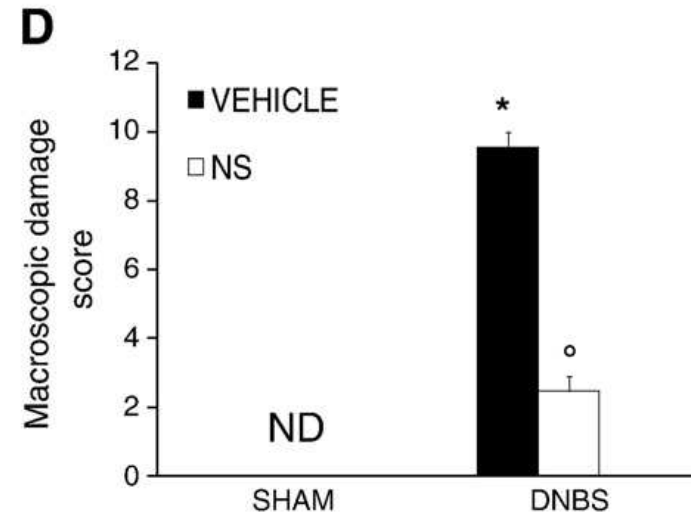
4 days

Sacrifice

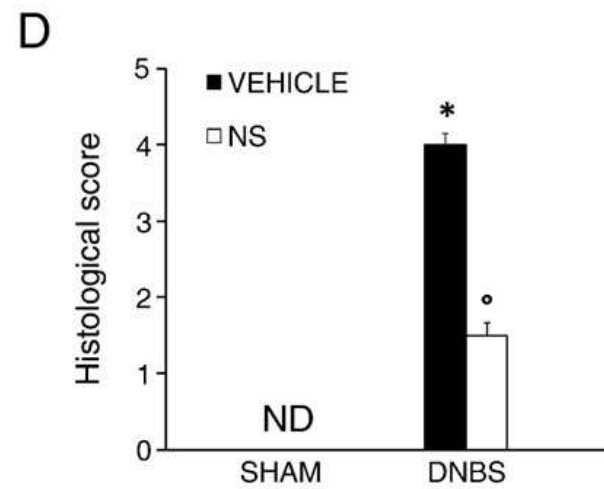
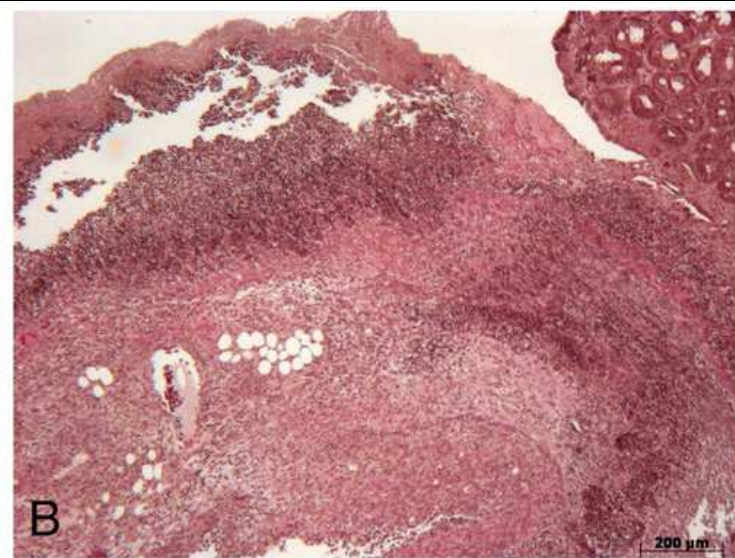
Histological and
immunoistochemical
studies

1. Sham + Vehicle group: saline was administered daily orally.
2. Sham + NS powder (30 mg/kg): was administered daily orally.
3. DNBS+Vehicle: administration of DNBS.
4. DNBS + NS powder (30 mg/kg): administered daily starting from 3 h after the administration of DNBS.

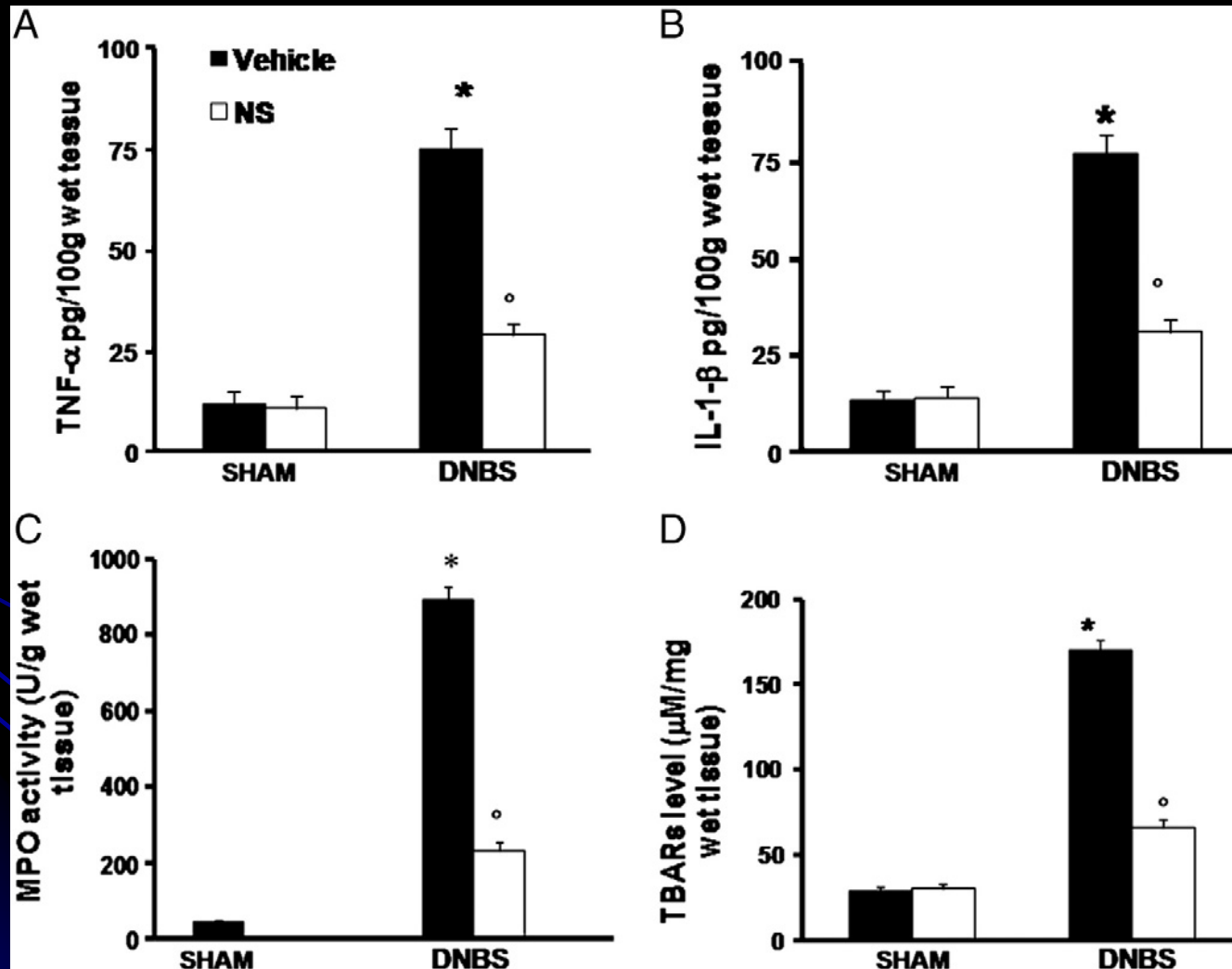
Effect of NS powder treatment on clinical expression of DNBS-induced colitis-macroscopic damage score and body weight changes



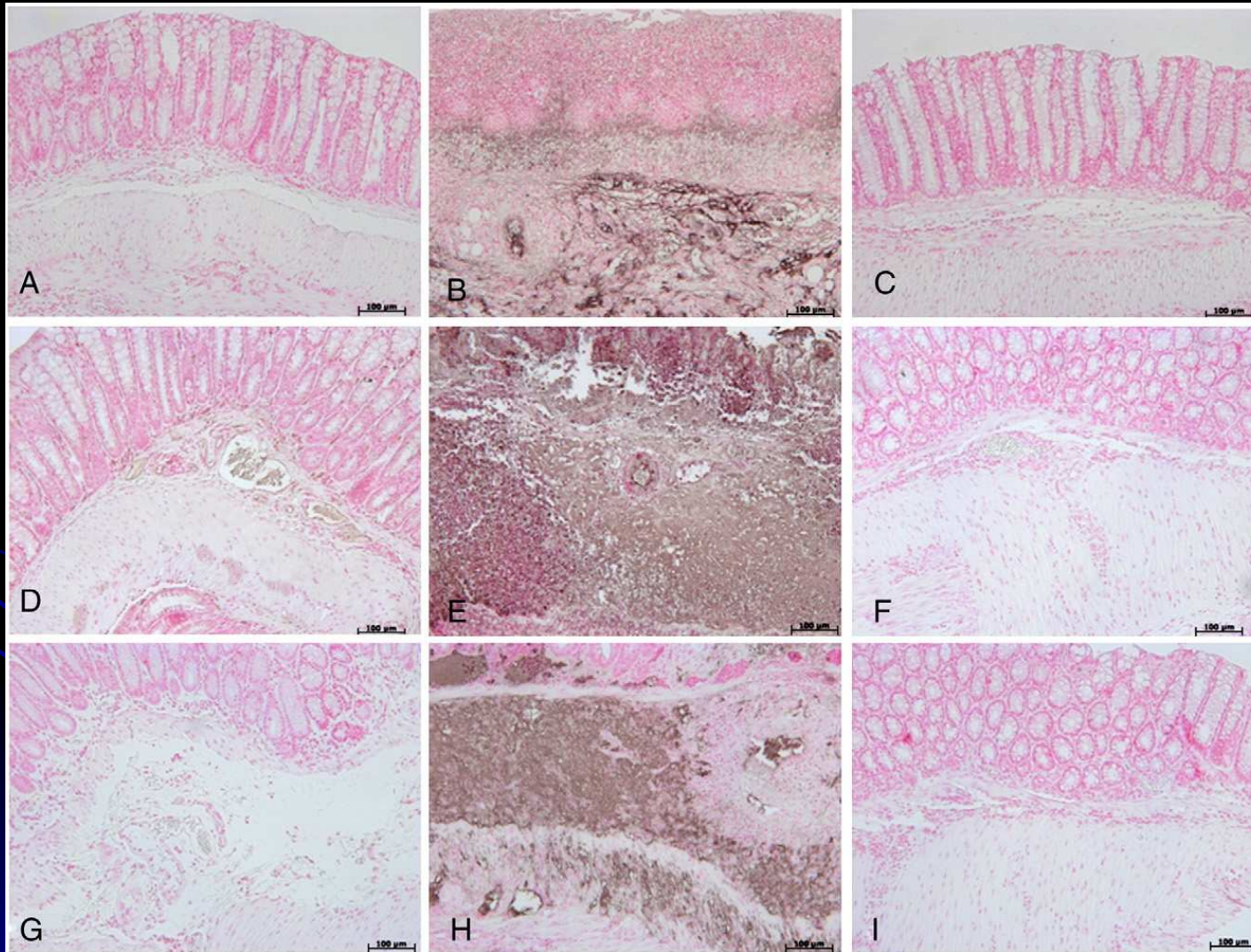
Effect of NS powder treatment on colon injury and histological score



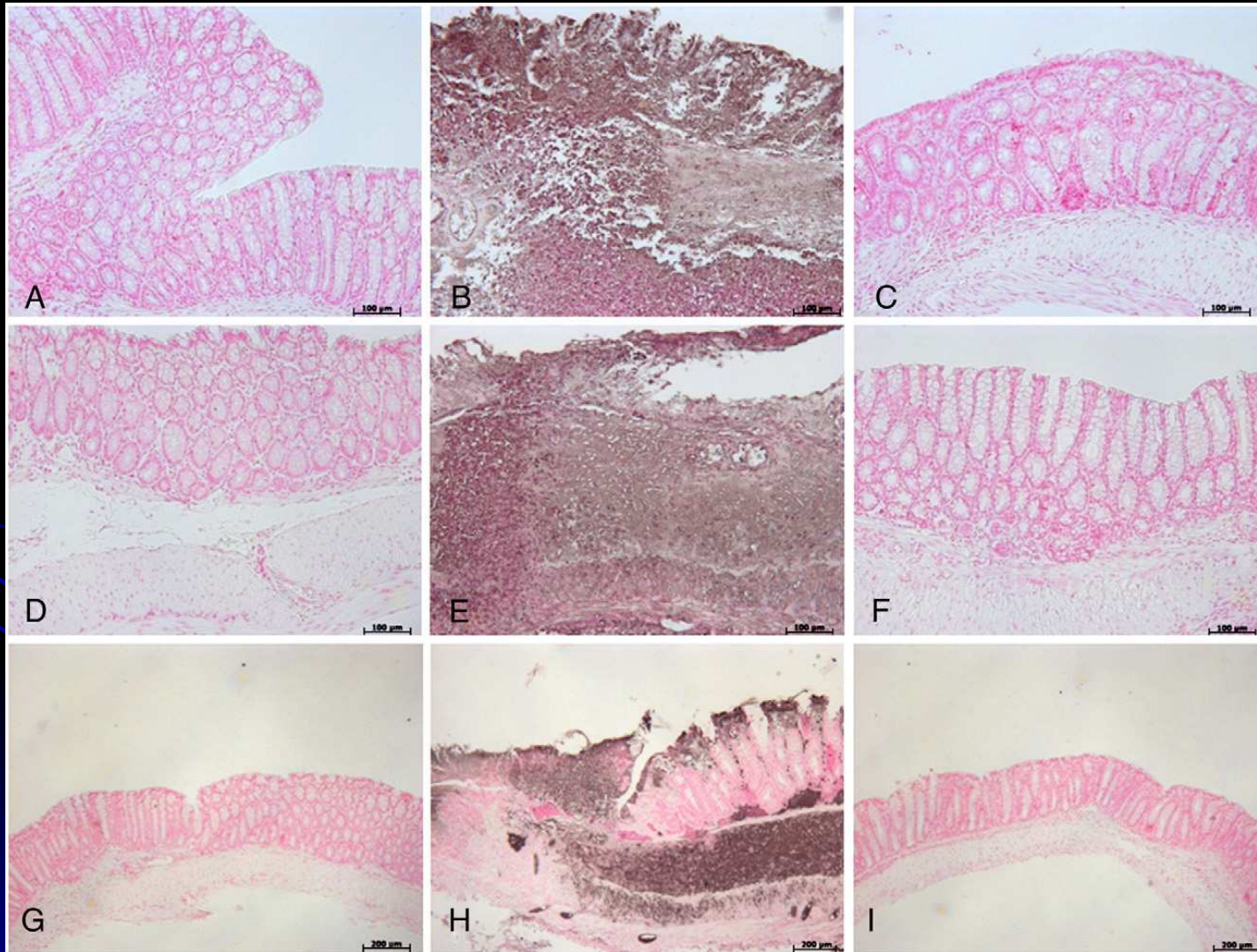
Effect of NS powder treatment on colon levels of cytokine and MPO activity and lipid peroxidation



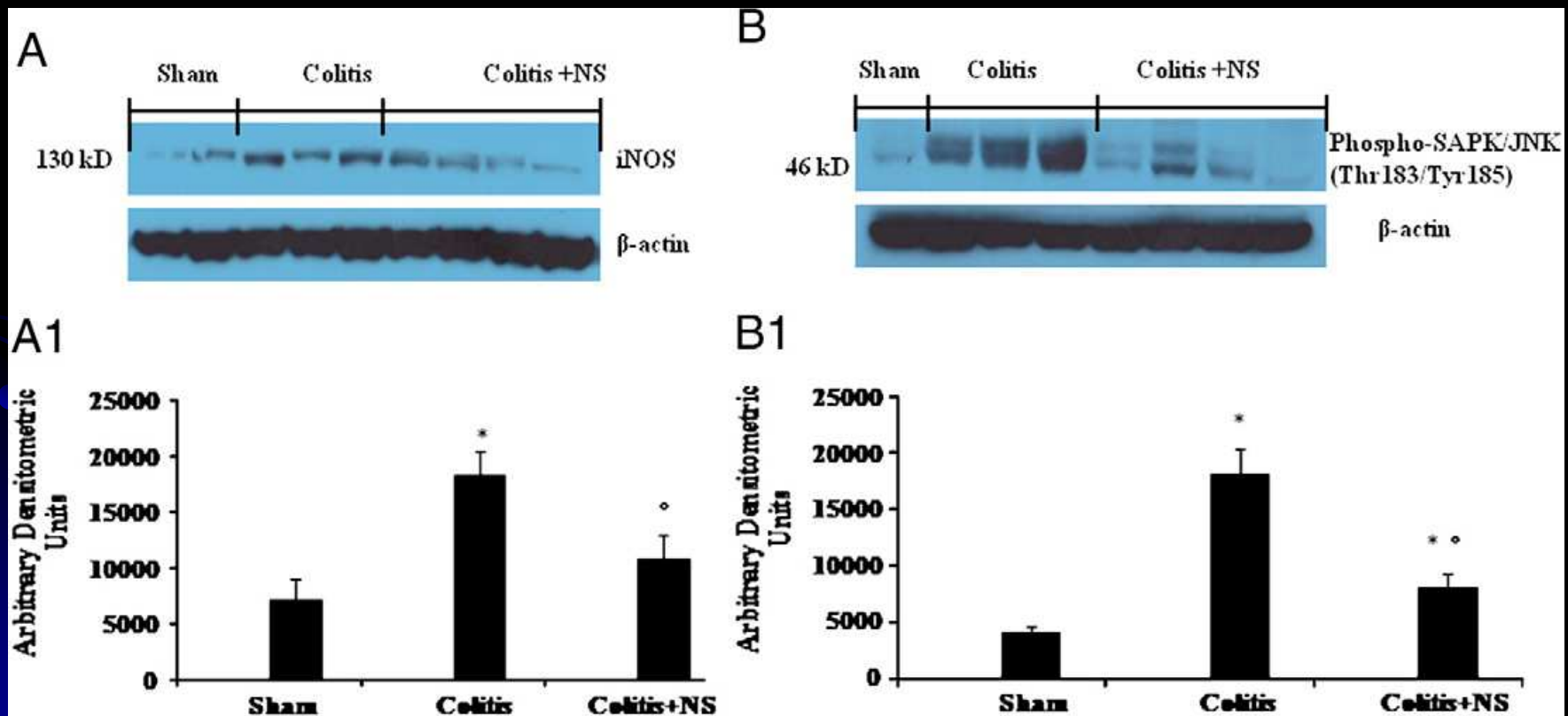
Effect of NS powder treatment on immunohistochemical localization of TNF α , ICAM-1 and P-selectin



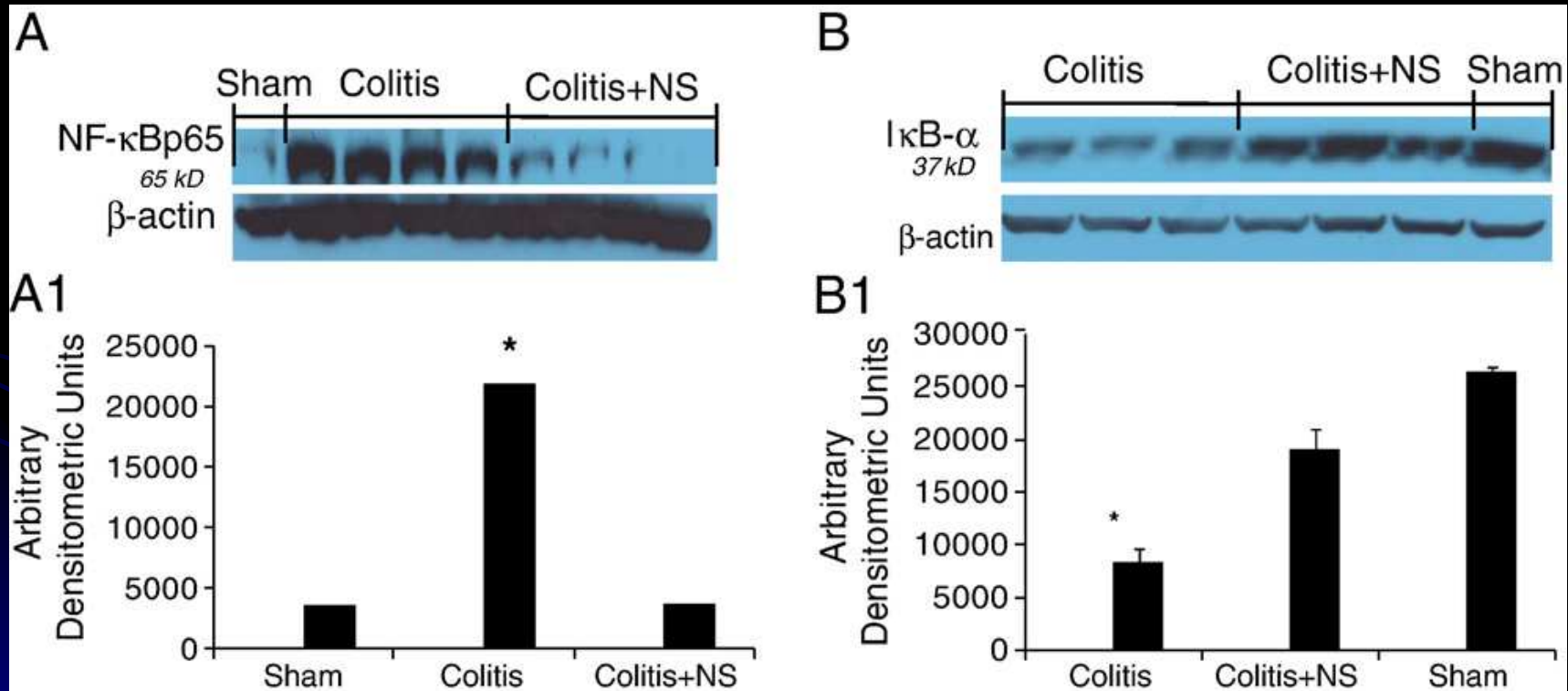
Effect of NS powder treatment on immunohistochemical localization of iNOS, pJNK and FAS-L in the colon



Effect of NS powder treatment on iNOS and pJNK



Effect of NS powder treatment on NF- κ Bp65 and I κ B- α





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Natural almond skin reduced oxidative stress and inflammation in an experimental model of inflammatory bowel disease

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Conclusion

The data presented in these studies demonstrate that oleuropein aglycone and natural almond skin reduce the development of acute and chronic inflammation.

Moreover, future studies using different models are needed in order to better clarify the possible use of oleuropein aglycone and natural almond skin powder for the treatment of inflammatory diseases in patients.