Small molecule antioxidants in action

Antioxidants

Macromolecule – enzymatic, non-enzymatic

Small molecule – natural, synthetic

Physical abundance – cytoplasmatic (hydrophilic), membrane (lipophilic)

When to use antioxidants

Therapy of disease (inflammation, ischemia)

Support therapy (diabetes mellitus)

Prevention (food supplements)

Food preservation (nontoxic, healthy)

Technical products stabilization (low toxicity)

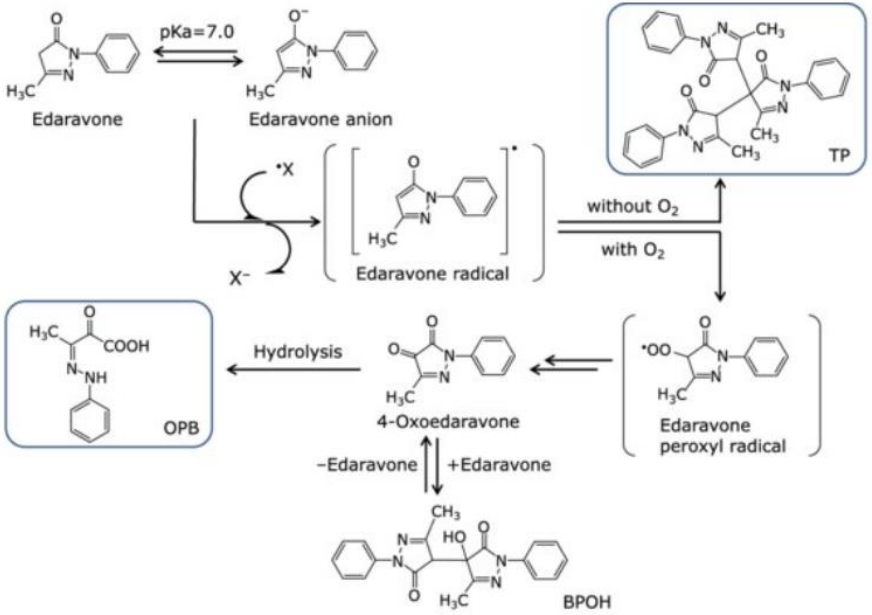
Mechanism of action

Prevention of forming RONS – chelating agents

Removing RONS – trapping, quenching

Decomposition of products of reactions with RONS – repairing mechanisms

EDARAVON - Therapy of neurodegenerative disease and stroke



Antioxidant efficiency

1. Highest possible reduction potentials between radical and antioxidant
2. Radicals formed from antioxidants must be relatively stable

ROS	E (mV)
Asc· –	282
TO·	480
O2 · –	940
RO·	1600
HO·	2310

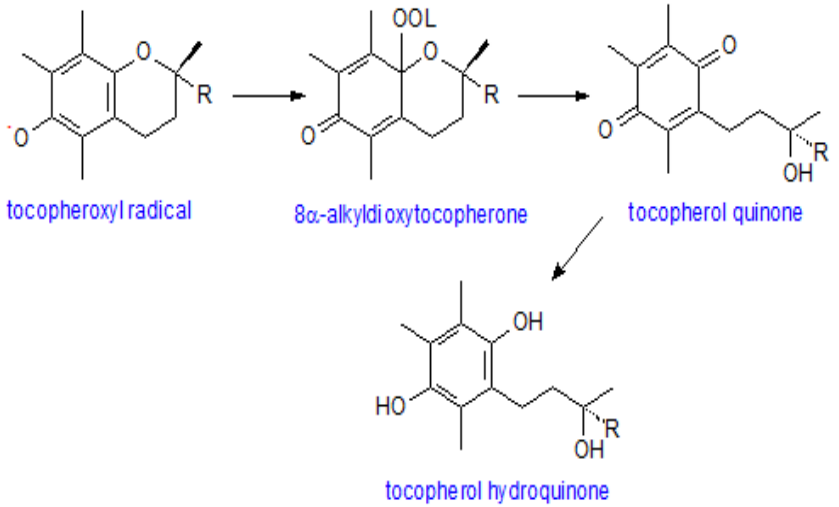
Antioxidants – hydrogen donors

Most commonly contains aromatic cycle with one or more hydroxyl groups

Radical is stabilized by electron delocalization

Radical can oxidize further

Antioxidants – hydrogen donors



Lipoperoxidation

Deterioration of sensorics properties

- Odor after "rancidity"
- Changes in color and texture
- Loss of consumer interest
- Economic losses

Deterioration of nutrition quality

- Essential fat acids

Health risks

- GIT, cardiovascular diseases

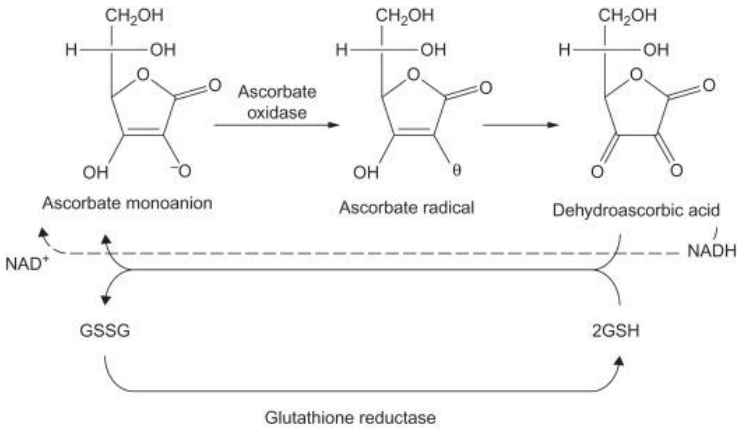
Dietary antioxidants

Ascorbic acid (vitamin C)

Strong reducing agent

High intake – risk of Fenton reaction

Hydroxyl radical formation

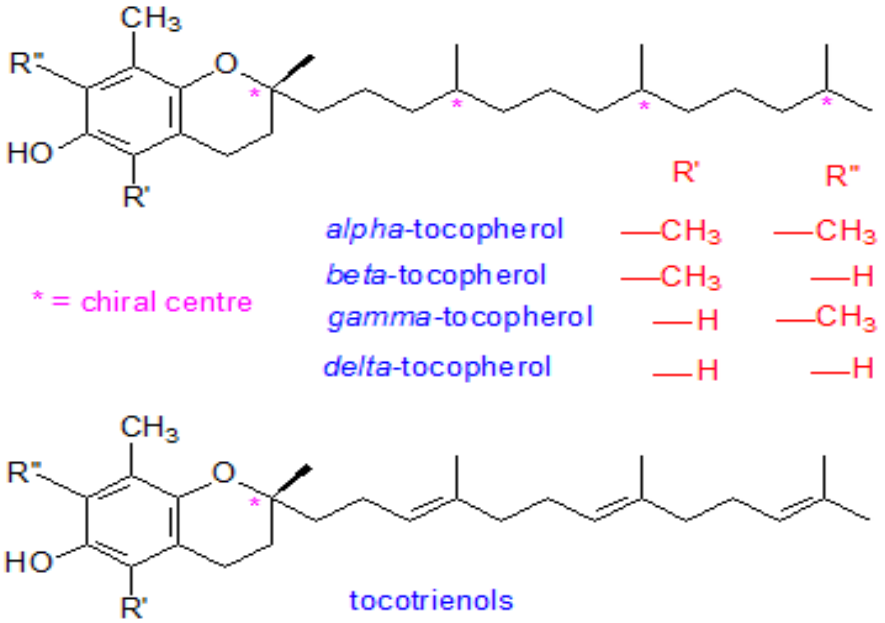


$Fe(III) + ascorbate \longrightarrow Fe(II) + ascorbate.$

$H2O2 + Fe(II) \longrightarrow HO\cdot + OH- + Fe(III)$

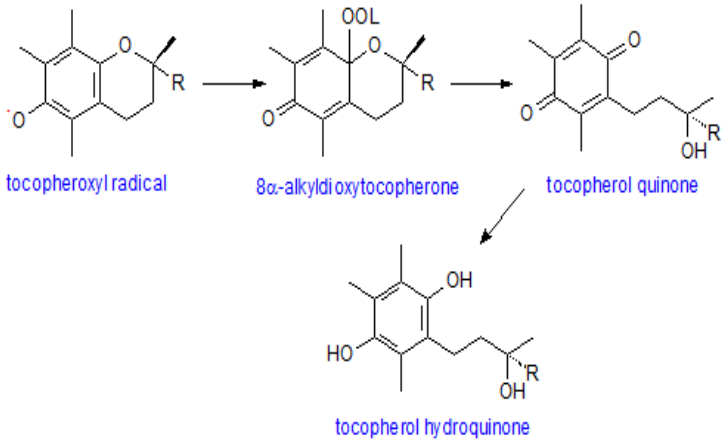
Dietary antioxidants

Tocopherols (vitamin E)



Dietary antioxidants

Tocopherols (vitamin E)



Flavonoids– example of action

Curcumin – neuroprotective, anti-inflammatory

Carnosol – lipoperoxidation reduction

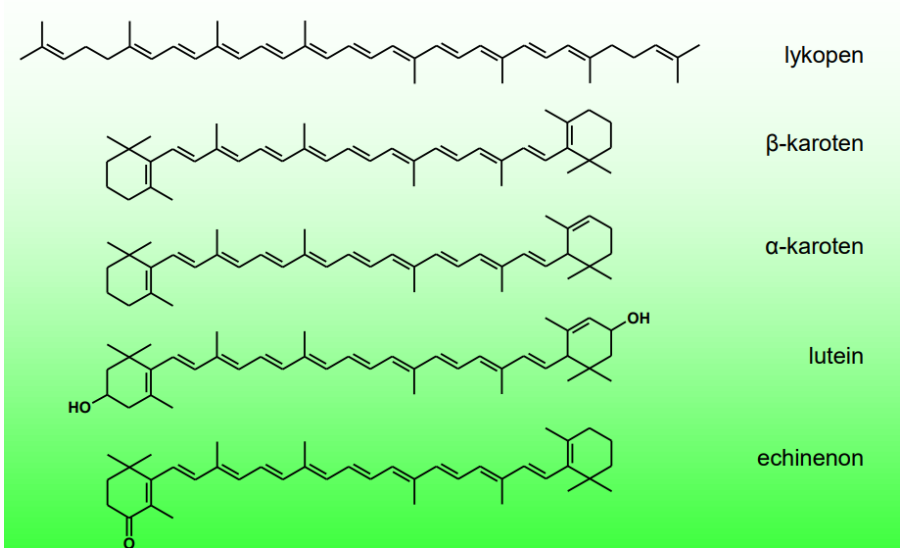
Quercetin – colorectal carcinom reduction

Resveratrol – antiaging, CVS, CA, diabetes

Sofalcone - antiulcerosum, anti-inflammatory

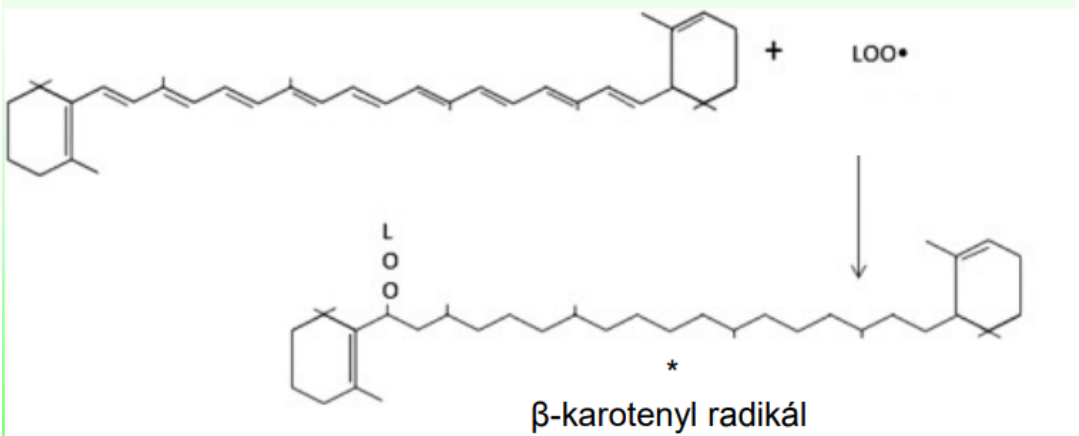
Dietary antioxidants

Carotenoids



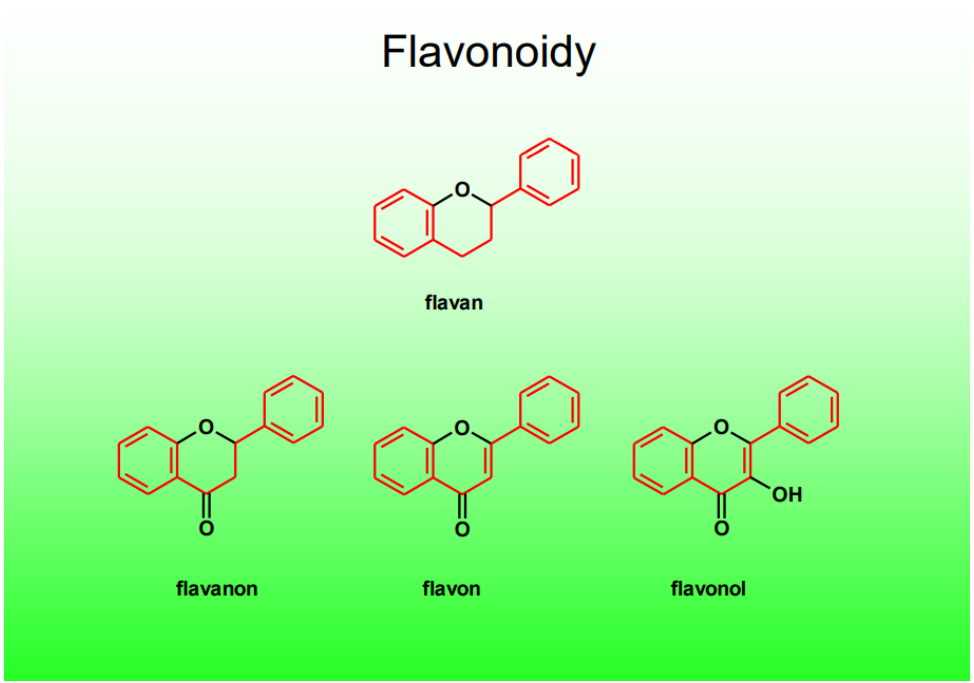
Dietary antioxidants

Carotenoids – mechanism of action

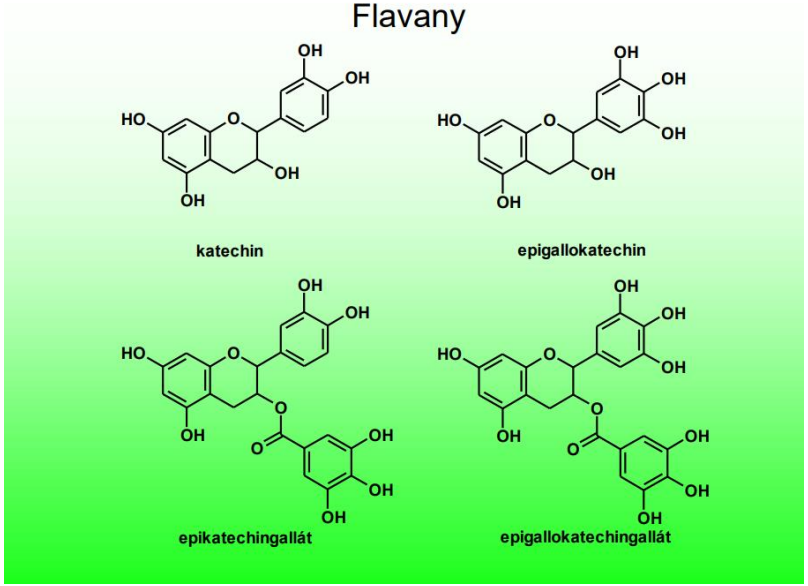


β-karotenyl radikál

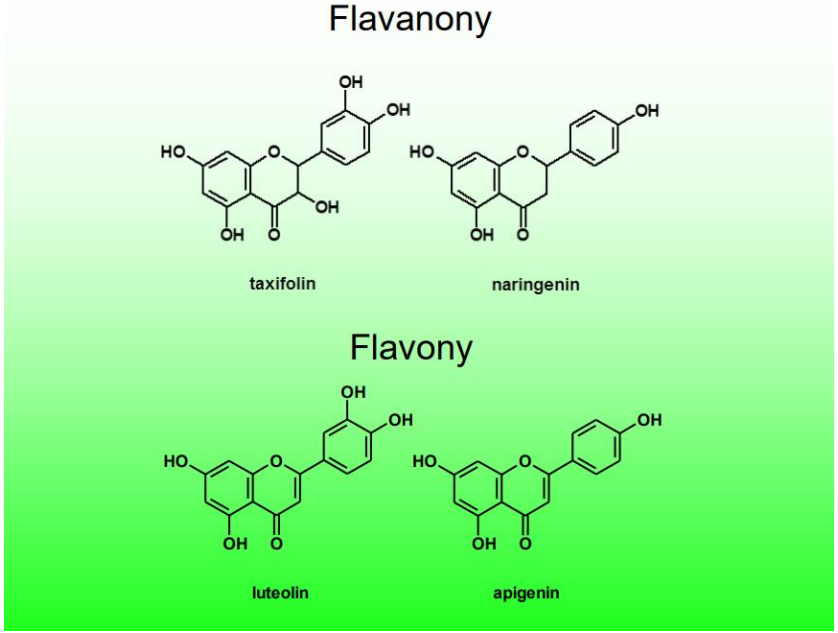
Dietary antioxidants - Flavonoids



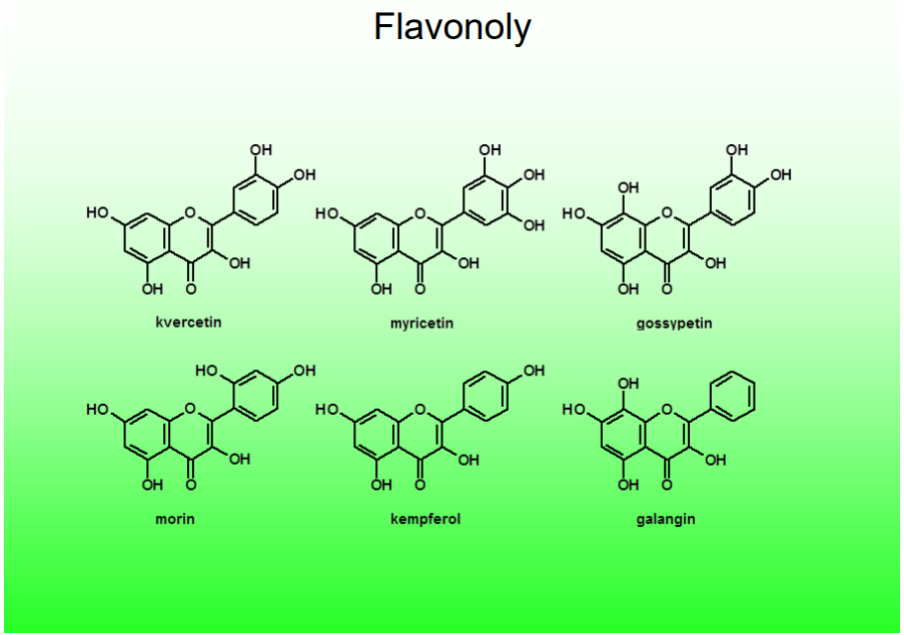
Dietary antioxidants - Flavonoids



Dietary antioxidants - Flavonoids

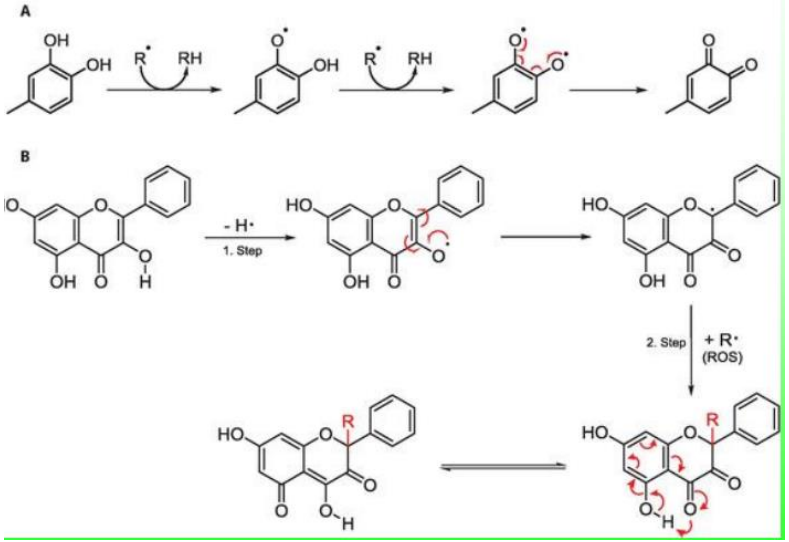


Dietary antioxidants - Flavonoids

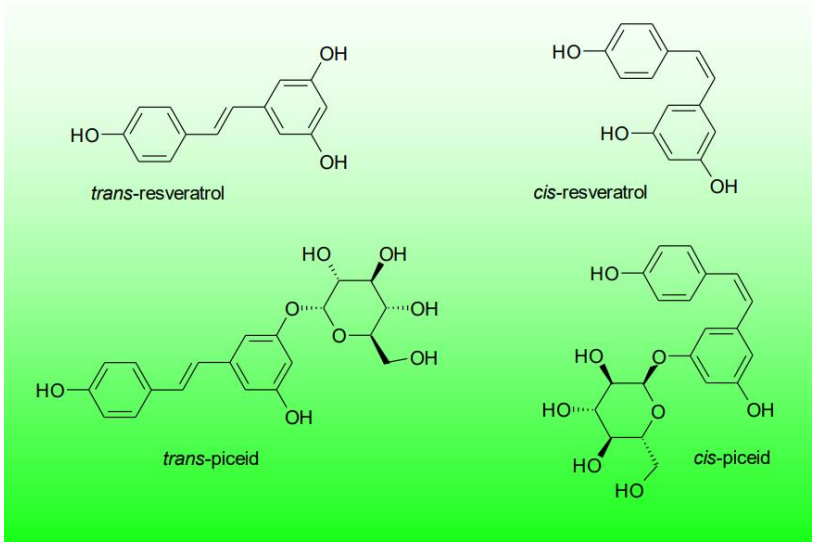


Dietary antioxidants – Flavonoids

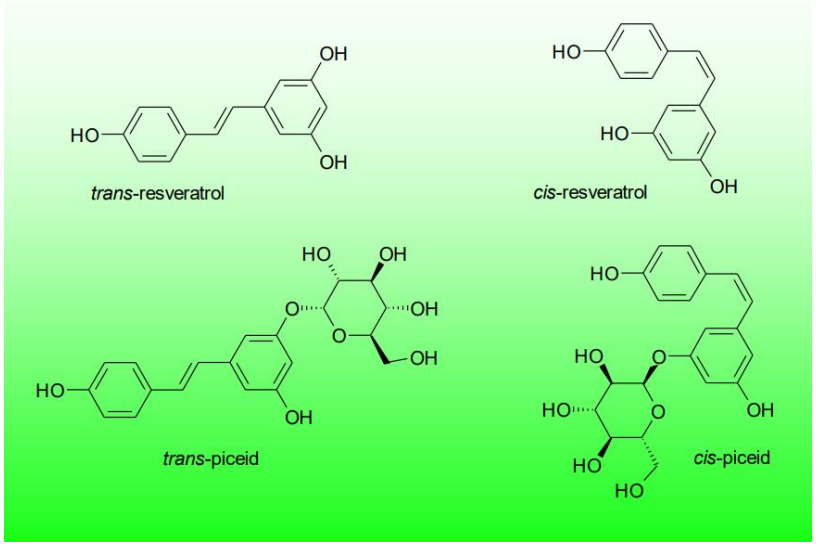
Mechanism of action



Dietary antioxidants - Stilbens

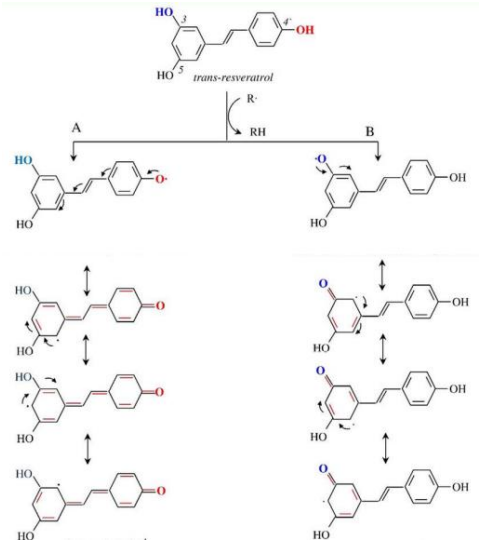


Dietary antioxidants - Stilbens



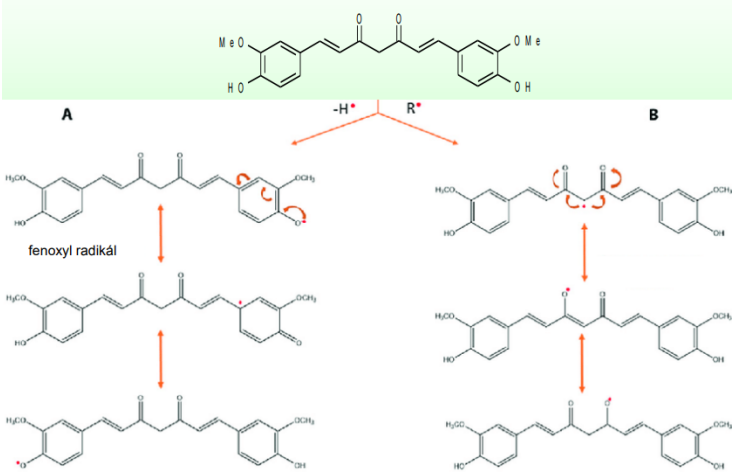
Dietary antioxidants - Stilbens

Resveratrol



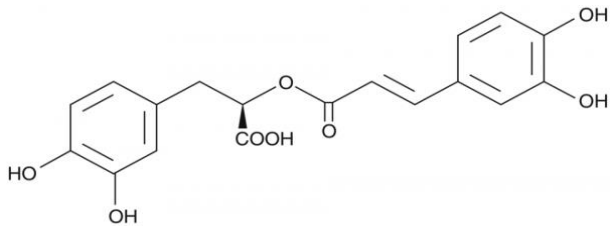
Dietary antioxidants - Curcumin

Curcuma longa L. (Zingiberaceae)

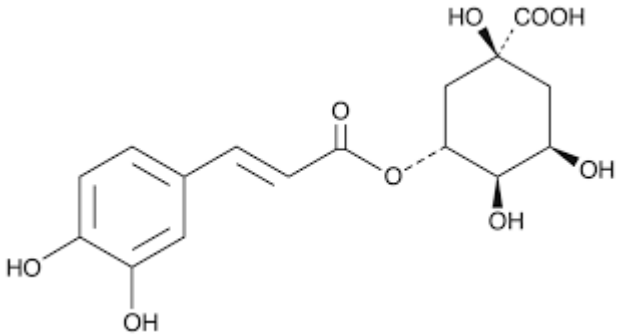


Dietary antioxidants – Aromatic acids

Rosmarinic acid

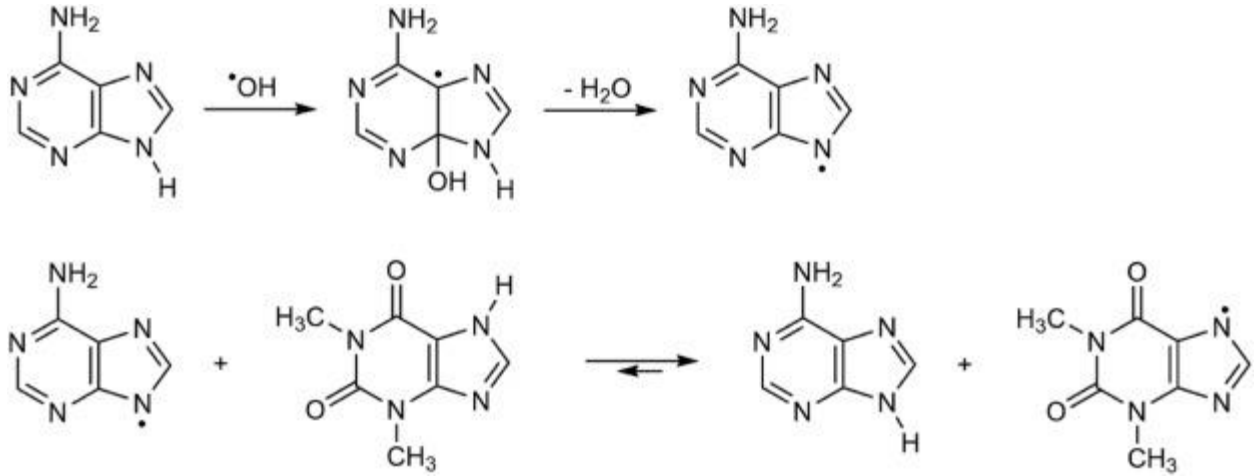


Chlorogenic acid



Dietary antioxidants – Nitrogen based antioxidants

Caffeine



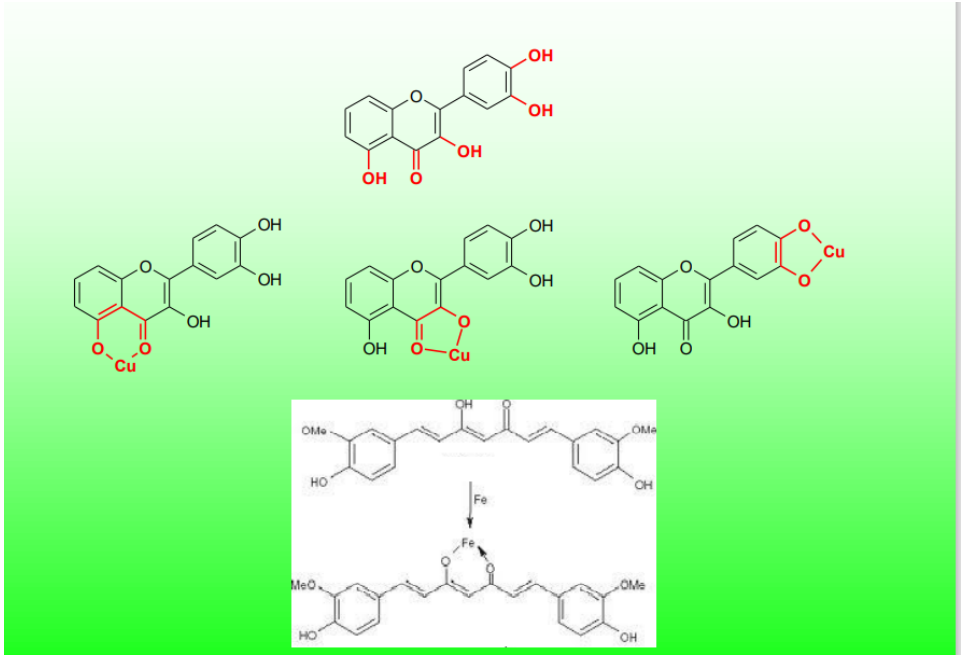
Dietary antioxidants – Chelating agens

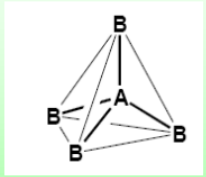
Formation complexes with metallic ions

Prevention of oxidative state changes of metallic ion

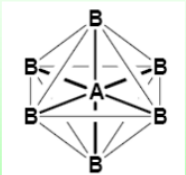
Sterically shielding metallic ion and lipid radical

Dietary antioxidants – Chelating agents





Cu(I)
Fe(III)



Cu(II)
Fe(II)

Endogenous antioxidants

Ubiquinone (coenzyme Q10)

Bilirubin

Melatonin

Lipoic acid

Uric acid

Melanine

Retarders vs. antioxidants

Retarders – just slowing oxidation and requires high concentration

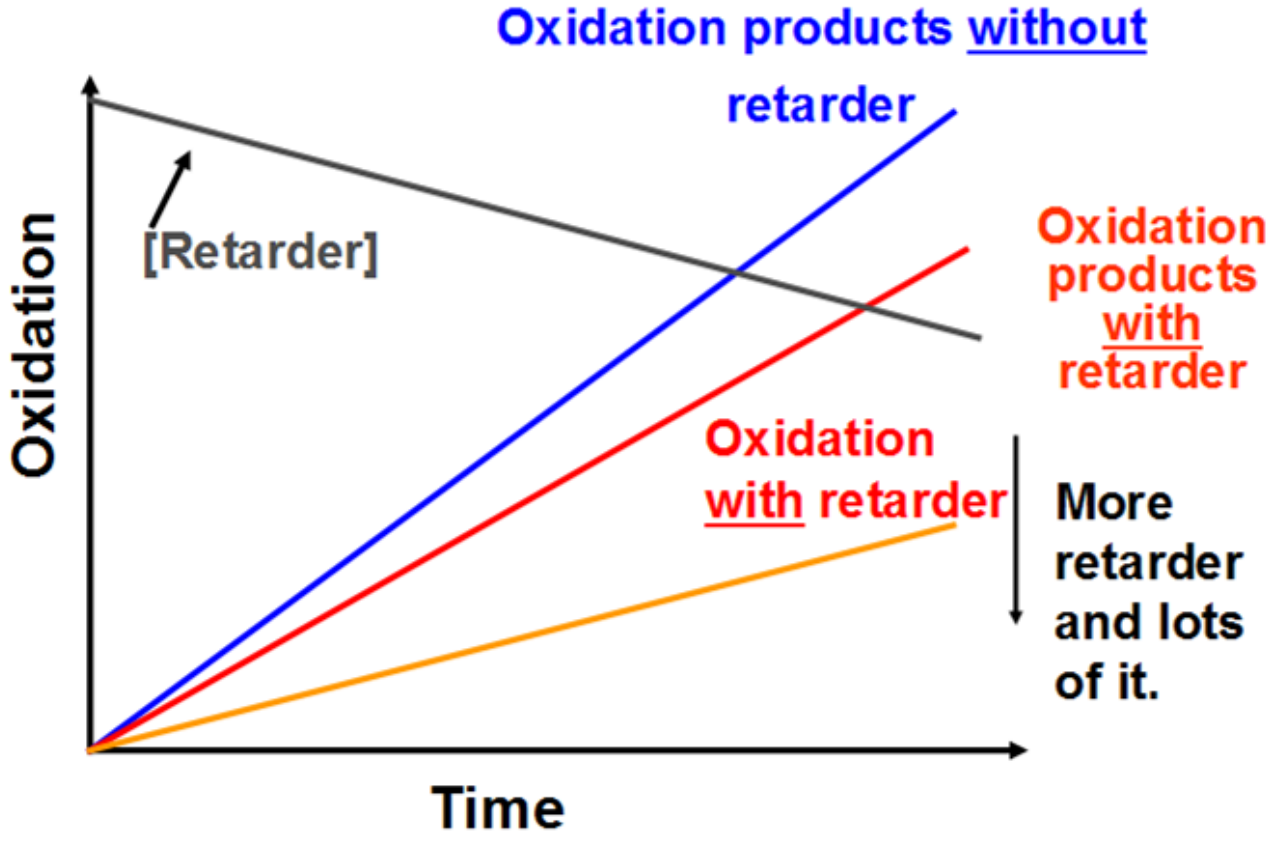
HO* - reaction rate constant - 10^{9} – 10^{10} $M^{-1} * s^{-1}$

Effective antioxidant $1 * 10^{13}$ $M^{-1} * s^{-1}$

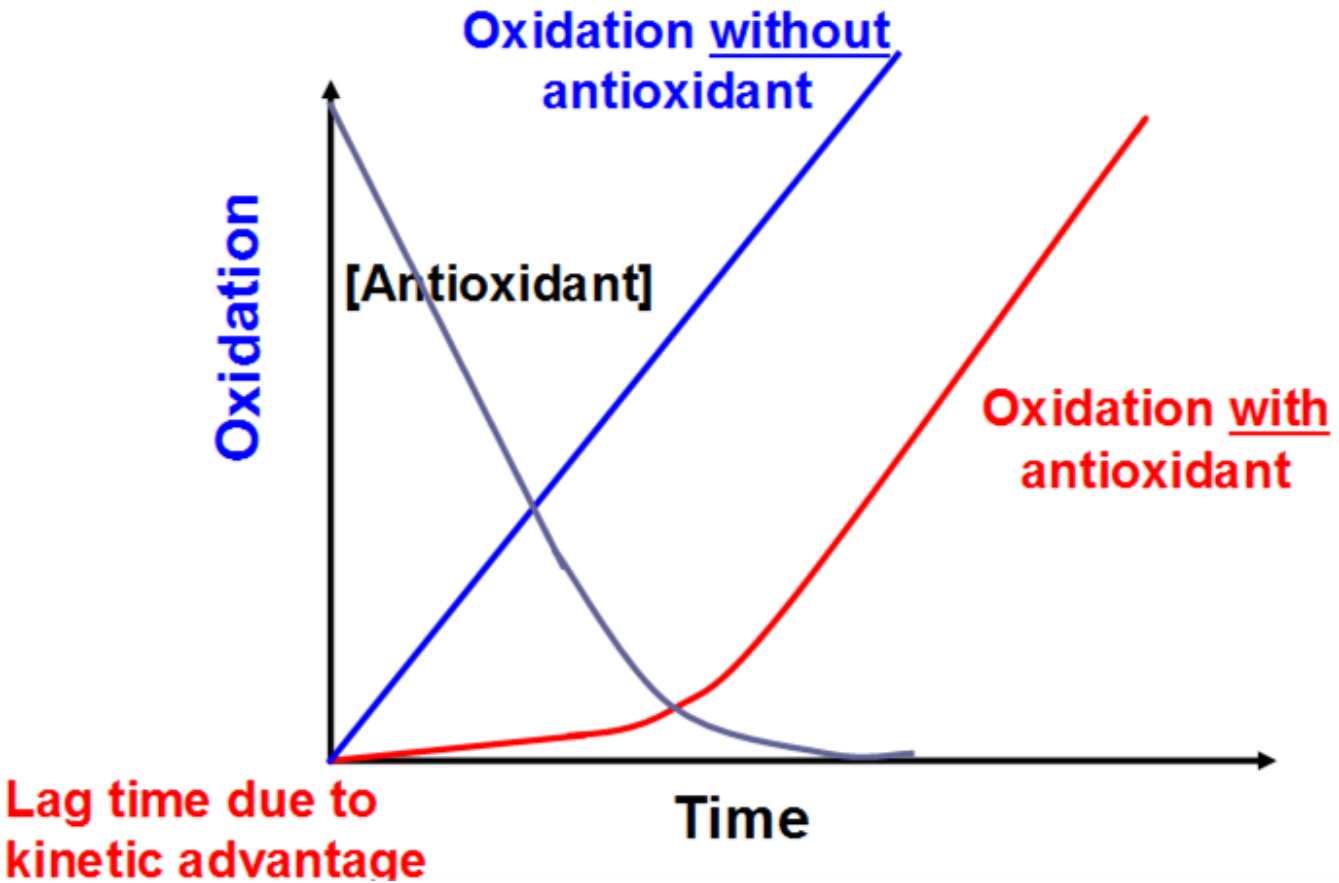
Impossible in water $1 * 10^{11}$ $M^{-1} * s^{-1}$

HO· no antioxidants just retarders

Retarder


Oxidation products without retarder
[Retarder]
Oxidation products with retarder
Oxidation with retarder
More retarder and lots of it.
Oxidation
Time

Antioxidant - no recycling



Reaction rate constants

SOD	$7 \times 10^{9}\ M^{-1}s^{-1}$
HO·	$1.1 \times 10^{10}\ M^{-1}s^{-1}$
RO· (tert-butyl alkoxyl radical)	$1.6 \times 10^{9}\ M^{-1}s^{-1}$
ROO· (alkyl peroxyl radical, e.g. CH3OO·)	$1\text{-}2 \times 10^{6}\ M^{-1}s^{-1}$
Cl3COO·	$1.8 \times 10^{8}\ M^{-1}s^{-1}$
GS· (glutathiyl radical)	$6 \times 10^{8}\ M^{-1}s^{-1}$
UH·- (Urate radical)	$1 \times 10^{6}\ M^{-1}s^{-1}$
TO· (Tocopheroxyl radical)	$2 \times 10^{5}\ M^{-1}s^{-1}$
Asc·- (dismutation)	$2 \times 10^{5}\ M^{-1}s^{-1}$
CPZ·+ (Clorpromazine radical radical)	$1.4 \times 10^{9}\ M^{-1}s^{-1}$
Fe(III)EDTA/ Fe(II)EDTA »	$1 \times 10^{2}\ M^{-1}s^{-1}$
O_2·-/HO_2·	$2.7 \times 10^{5}\ M^{-1}s^{-1}$

Thank you