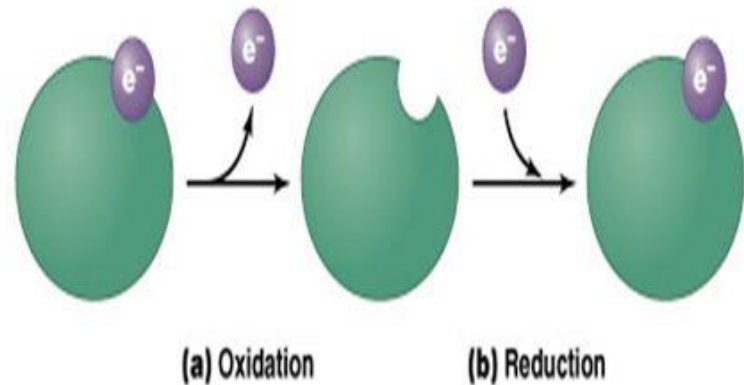


Oxidative stress and Antioxidants

Oxidative Stress in Malaria

Basics of Redox Chemistry

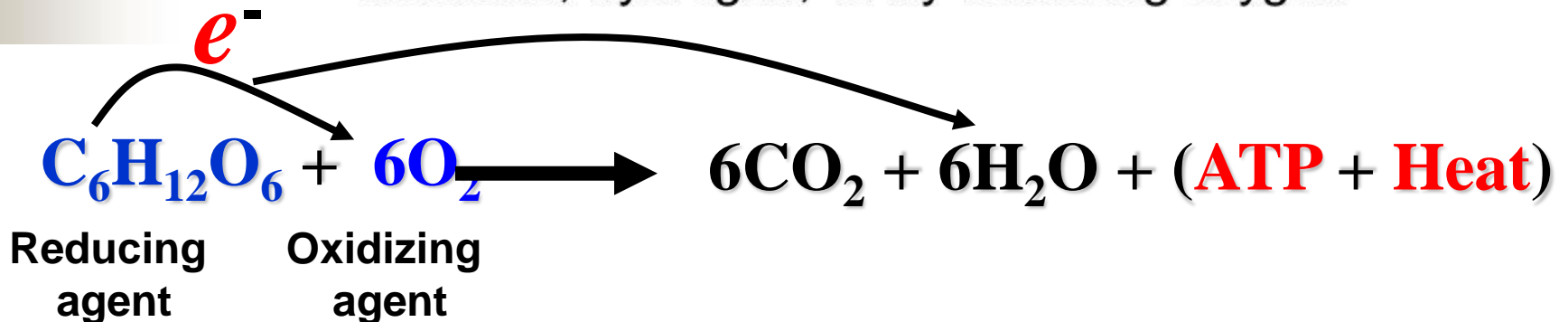
Term	Definition
Oxidation	Gain in oxygen Loss of hydrogen Loss of electrons



Reduction	Loss of oxygen Gain of hydrogen Gain of electrons
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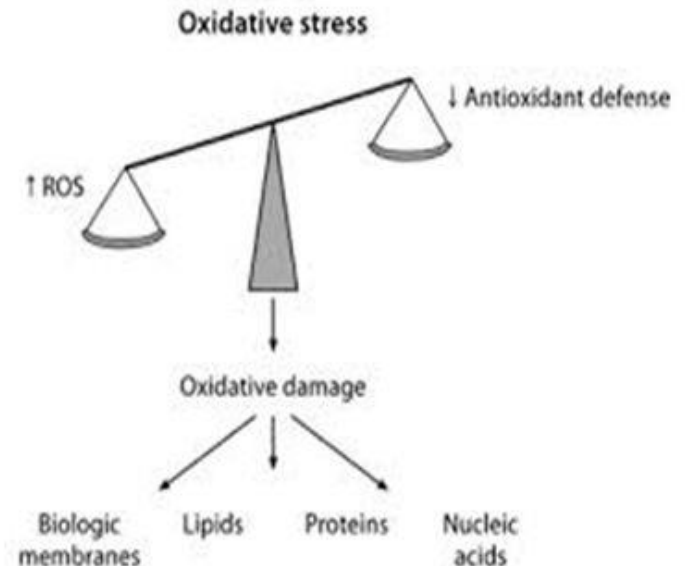
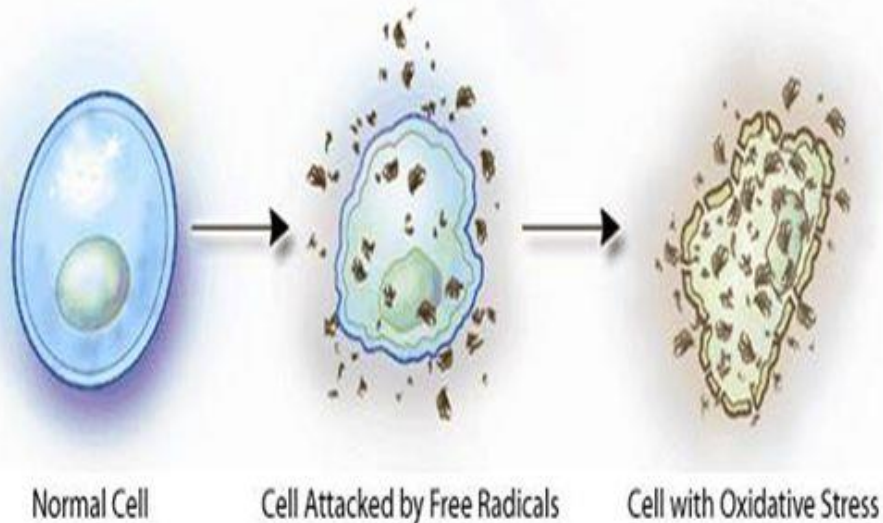
Oxidant	Oxidizes another chemical by taking electrons, hydrogen, or by adding oxygen
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Reductant	Reduces another chemical by supplying electrons, hydrogen, or by removing oxygen
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Oxidative stress

- It is an excess of free-radicals damages cells.
- **Oxidative stress has been identified as a causative factor in:**
 - Cognitive performance
 - Aging process
 - Development of diseases such as cancer, arthritis, cataracts, and heart disease



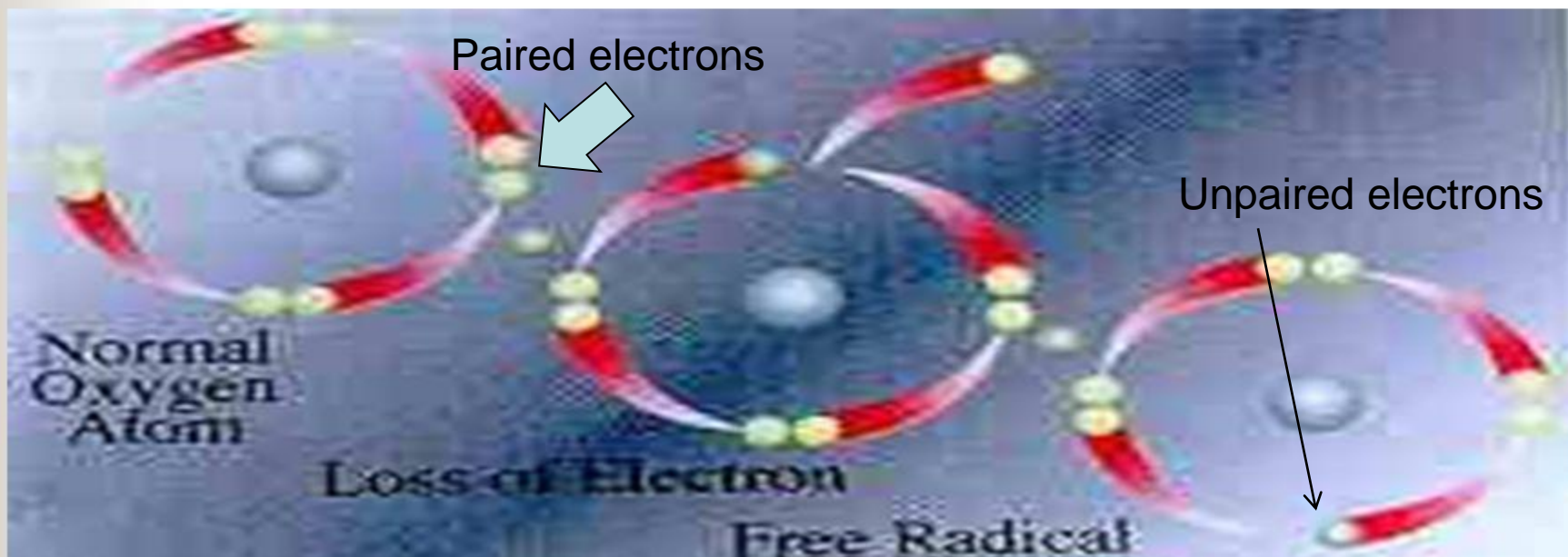
Research on Oxidative stress

- many research groups have driven efforts to assess the antioxidant properties of natural products.
- These properties have been investigated through either chemical (*in vitro*) or biological (*in vivo*) methods, **or both** .
- these researches have led some to suggest that the **long-term consumption** of food rich in antioxidants can retard or **avoid the occurrence** of such diseases .



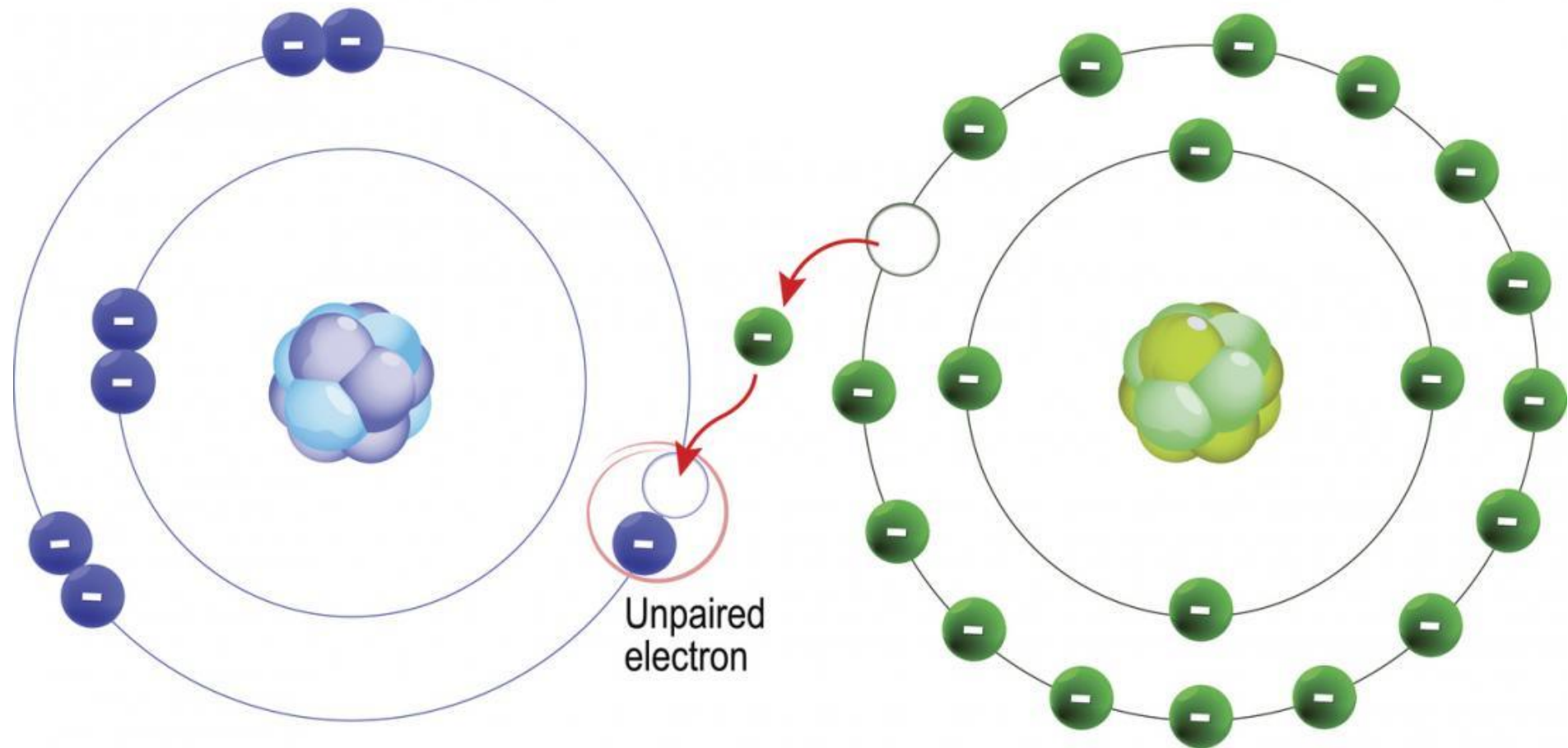
■ Free Radical:

- A free radical is an atom capable of independent existence (hence the term “free”) that contains one or more unpaired electrons in its outer orbital.
- It is an electron-deficient species.
- It is represented by a superscript dot to the right. (R^\bullet)



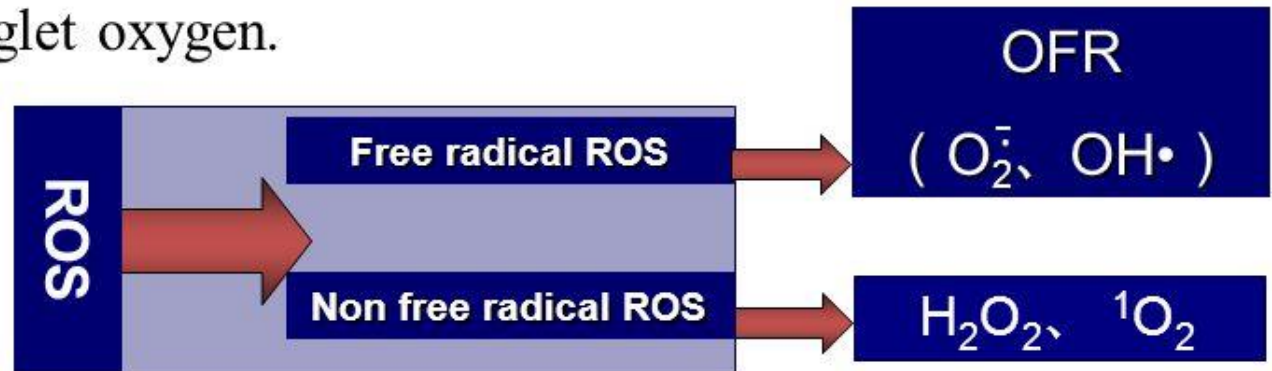
Free radical

Antioxidant



Reactive Oxygen Species (ROS)

ROS is a collective term that includes both oxygen free radicals (OFR), and non radicals that are oxidizing agents and / or are easily converted into radicals such as hydrogen peroxide and singlet oxygen.



Reactive species

Reactive Oxygen Species

Singlet oxygen $^1\text{O}_2$

Ozone O_3

Hydroperoxyl radical
 HO_2^{\bullet}

Hydroxyl peroxide H_2O_2

Hydroxyl radical $^{\bullet}\text{OH}$

Superoxide radical anion
 $\text{O}_2^{\bullet-}$

Lipid peroxy LOO^{\bullet}

Peroxide ROOH

Hypochlorous acid HOCl

Reactive Nitrogen Species

Nitrous oxide NO^{\bullet}

Peroxynitrate OONO^{\bullet}

Nitroxyl anion $\text{NO}^{\bullet-}$

Nitrogen dioxide NO_2^{\bullet}

Dinitrogen dioxide N_2O_3

Nitrous acid HNO_2

Nitryl chloride NO_2Cl

Reactive Oxygen Species (ROS)		Reactive Nitrogen Species (RNS)	
Free radical	Structural formula	Free radical	Free radical
Superoxide anion	O_{2^-}	Nitric oxide	NO
Hydrogen peroxide	H_2O_2	Nitrous oxide	N_2O
Hydroxyl radical	$OH\cdot$	Peroxynitrite	NO_{3^-}
Peroxyl radical	OH_{2^-}	Nitroxyl anion	HNO
Peroxynitrous acid	HNO_3		

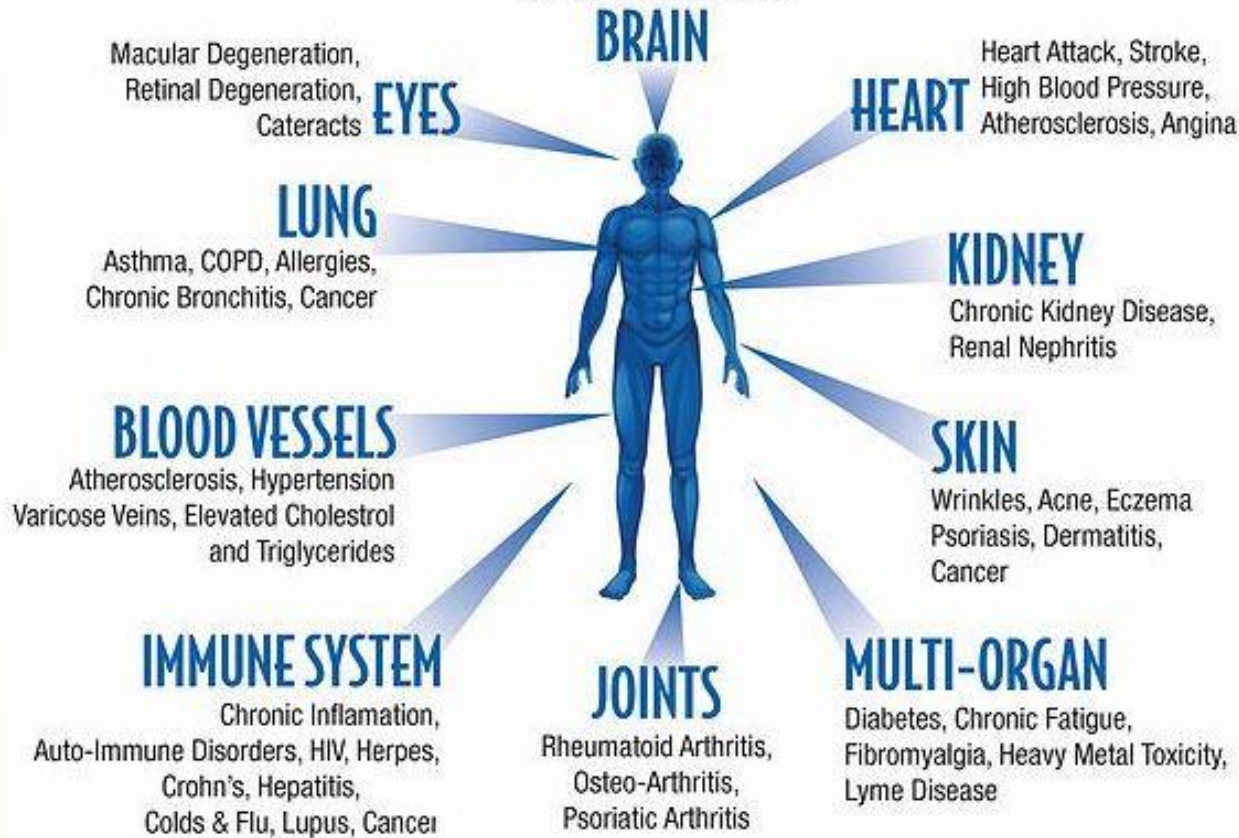
Sources of Free Radicals

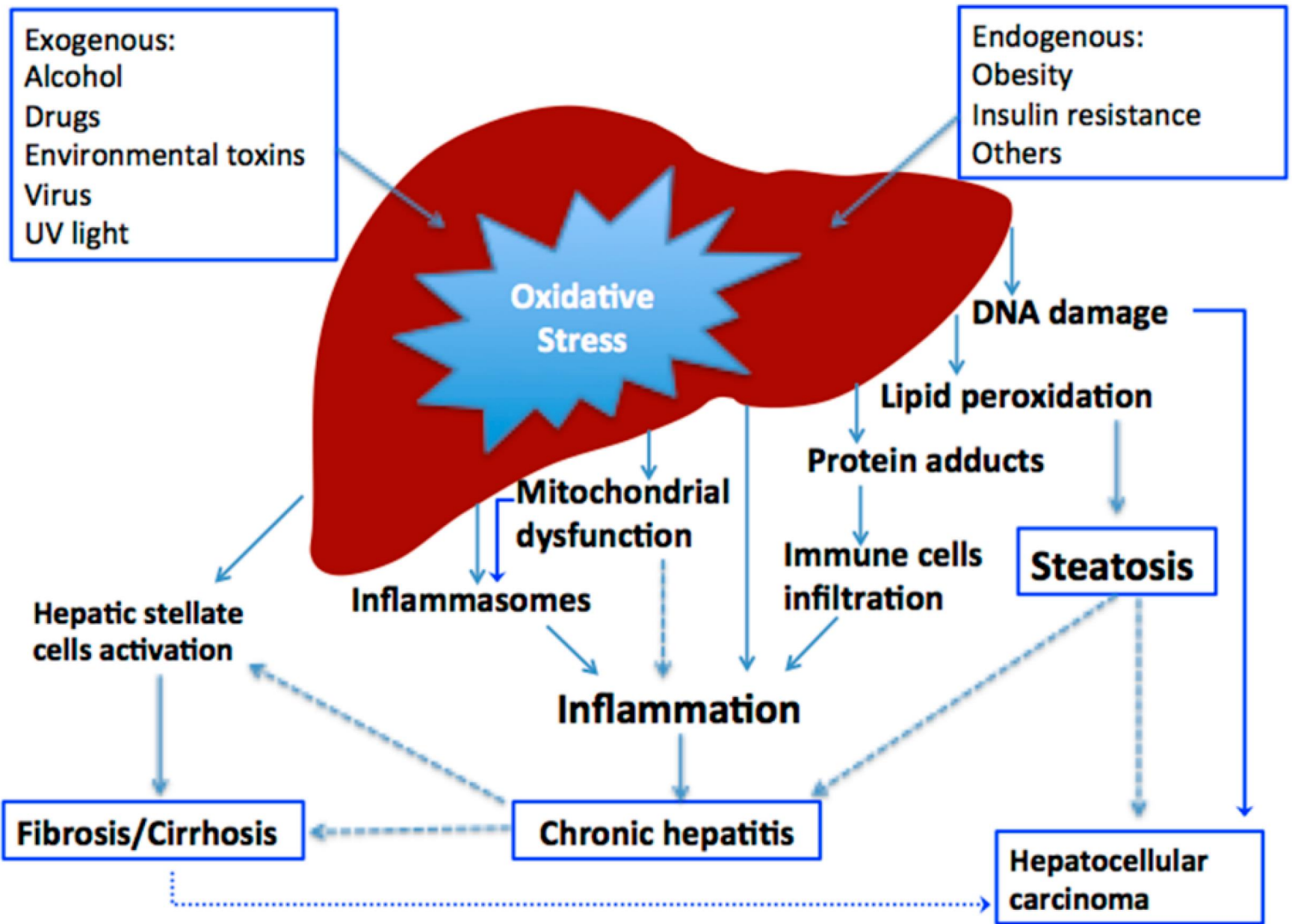


- **Exogenous sources of free radicals:**
 - Ionizing radiation
 - Ultraviolet radiation
 - Chemicals, smoking
 - Pollution
 - Diet
(fatty and processed foods)
- **Endogenous sources of free radicals:**
 - Respiration
 - Metabolism.
 - Inflammation
 - Phagocytosis

Free Radical Oxidative Stress

Alzheimer's, Parkinson's, MS, ALS, OCD, ADHD,
Autism, Migraine, Insomnia, Depression, Dementia,
Bi-Polar Disorder, Cancer





Antioxidant

- **Antioxidant** is a molecule that inhibits the oxidation of other molecules.
- **Oxidation reactions** can produce **free radicals**. In turn, these radicals can start **chain reactions**. When the chain reaction occurs in a cell, it can cause **damage** or **death** to the cell.
- Antioxidants terminate these chain reactions by **removing free radical** intermediates, and inhibit other oxidation reactions.
- **The lichens** have played an important role as a source for new antioxidant agents.



Antioxidant

- Antioxidants are **classified** into two broad divisions, depending on whether they are soluble In water (**hydrophilic**) or in lipids (**lipophilic**).

Hydrophilic



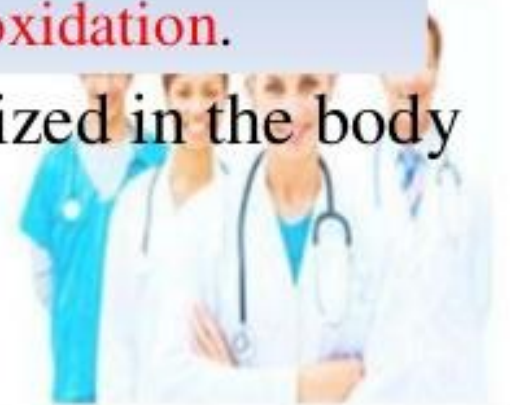
antioxidants react with oxidants in the cell **cytosol** and the **blood plasma**

Lipophilic



antioxidants protect **cell membranes** from **lipid peroxidation**.

- These compounds may be synthesized in the body or obtained from the diet.



ANTIOXIDANTS

Enzymatic antioxidants

Non-enzymatic Antioxidants

Primary Enzymes

*SOD, catalase,
glutathione peroxidase*

Secondary Enzymes

*glutathione reductase,
glucose 6-phosphate
dehydrogenase*

Minerals

Zinc, Selenium

Vitamins

*Vitamin A, Vitamin C,
Vitamin E, Vitamin K*

Carotenoids

*β -carotene, lycopene,
lutein, zeaxanthin*

Organosulfur compounds

allium, allyl sulfide, indoles

Low Molecular Weight Antioxidants

glutathione, uric acid

Antioxidant cofactors

Coenzyme Q₁₀

Polyphenols

Flavonoids

Phenolic acids

Flavonols

*quercetin
kaempferol*

Flavanols

*catechin
EGCG*

Flavanones

hesperitin

Isoflavanoids

genistein

Anthocyanidins

*cyanidin,
pelargonidin*

Flavones

chrysin

Hydroxy-cinnamic acids

*ferulic,
p-Coumaric*

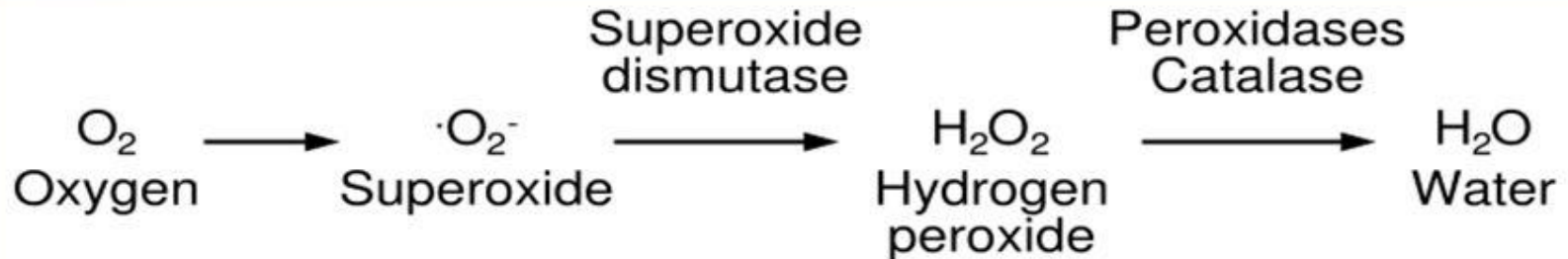
Hydroxy-benzoic acids

*gallic acid
ellagic acid*

Antioxidant System in our body

The enzymatic antioxidants:

- **Superoxide dismutase (SOD)** eliminates the superoxide ($O_2^{\cdot-}$).
- **Catalase and the glutathione peroxidase** eliminate hydrogen peroxide (H_2O_2).



The non enzymatic antioxidants:

Vitamins E, C, A or Pro vitamin A(beta-carotene).

Table 1. Reactive Oxygen Species and Antioxidants that Reduce Them

Reactive Species	Antioxidant
Singlet oxygen $^1\text{O}_2$	Vitamin A, vitamin E
Superoxide radical ($\text{O}_2^{\bullet-}$)	superoxide dismutase, vitamin C
Hydrogen peroxide (H_2O_2)	Catalase; glutathione peroxidase
Peroxyl radical (ROO^{\bullet})	Vitamin C, vitamin E
Lipid peroxyl radical (LOO^{\bullet})	Vitamin E
Hydroxyl radical (OH^{\bullet})	Vitamin C

Counteracting free radical damage

- ❑ The human body has several mechanisms to counteract damage by free radicals and other reactive oxygen species.
- ❑ One important line of defense against free radical damage is the presence of antioxidants.
- ❑ Some such antioxidants, are produced during normal metabolism in the body.
- ❑ Other lighter antioxidants are found in the diet.

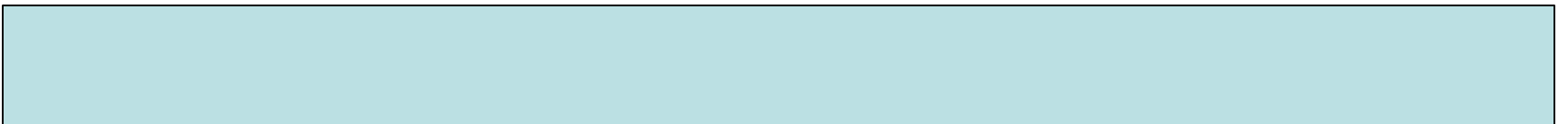
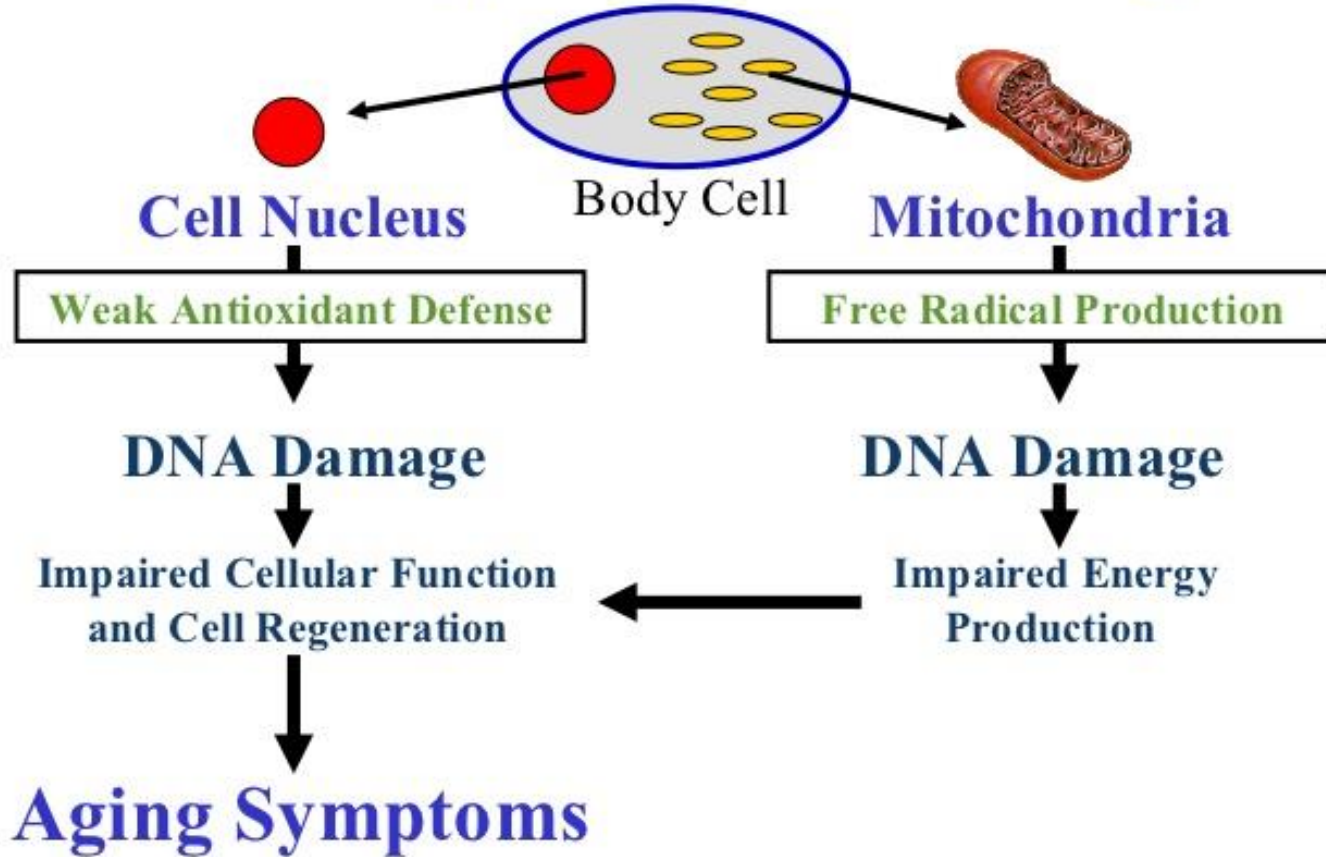




What do antioxidants do?

- ❑ Provides key nutrients needed by the body to neutralize free radicals.**
- ❑ Aid the human body's natural defenses.**
- ❑ Repair oxidative damage.**
- ❑ Slow or prevent damage to body cells.**
- ❑ May exhibit anti-aging benefits.**
- ❑ May improve immune function and lower risk for infection and cancer.**

Summary: How Do We Age?



- Many of the changes associated with aging are actually due to the effects of free-radicals.
- As we age, the antioxidant enzyme systems work less efficiently.

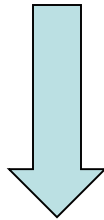


Scientific Support for Antioxidants

- Animals with longer life spans have higher antioxidant levels
- Dietary increase in antioxidants increase life span
- Caloric restriction (reduces ROS formation) leads to significantly increased life span

Oxidative Stress in Malaria

We should know first



**Apical complex structure and
parasite invasion**