

The logo of Galgotias University is a stylized circular emblem composed of several overlapping, curved segments in shades of yellow, orange, and blue, resembling a sun or a flower.

Antioxidants

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Antioxidants

- Antioxidants are man-made or natural substances that may prevent or delay some types of cell damage.
- Antioxidants are found in many foods, including fruits and vegetables.
- Although oxidation reactions are crucial for life, they can also be damaging; plants and animals maintain complex systems of multiple types of antioxidants, such as glutathione, vitamin C, vitamin A, and vitamin E as well as enzymes such as catalase, superoxide dismutase and various peroxides.
- Antioxidants are widely used in dietary supplements and have been investigated for the prevention of diseases such as cancer, coronary heart disease and even altitude sickness

Function of antioxidants

- The Food and Drug Administration (FDA) defines antioxidants only as dietary supplements to be taken in addition to normal food consumption in an effort to prevent these diseases ([Ohlsson and Bengston, 2002](#)).
- Antioxidants are known to play a key role in the protective influence exerted by plant foods ([Gey KF, 1990](#); [Gey KF et al., 1991](#); [Willett WC \(1991\)](#); [Liyana et al., 2006](#)).
- Regular consumption of vegetables and fruits has been recognized as reducing the risk of chronic diseases ([Dembinska et al. \(2008\)](#)).
- Studies demonstrate that an antioxidant-rich diet has a very positive health impact in the long run ([Sin et al., 2013](#); [Wills et al., 2009](#)).

- Recently, antioxidants have attracted considerable attention in relation to radicals and oxidative stress, cancer prophylaxis and therapy, and longevity ([Kalcher et al.,2009](#)).
- All antioxidants are working in concert as a team, the (antioxidant system), responsible for prevention of the damaging effects of free radicals and toxic products of their metabolism.
- However, the antioxidant (team) acts to control levels of free radical formation as a coordinated system where deficiencies in one component impact the efficiency of others ([Peter, 2007](#)).

- **Tirilazad** is an antioxidant steroid derivative inhibits the lipid peroxidation and neuronal death in stroke and head injury
- Animal models: Activity shown
- Human model
- **NXY-059** has efficacy in animal models,
- Human clinical trial: failed
- **Eugenol** (Nonpolar antioxidants) major component of oil of cloves—
- have toxicity limits that can be exceeded with the misuse of undiluted essential oils.

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Adverse effects

- The beta-carotene and Retinol Efficacy Trial (CARET) study of lung cancer patients.
- Smokers given supplements containing beta-carotene and vitamin A had increased rates of [lung cancer](#).
- Vitamin E supplementation [increased mortality](#), increased the risk of [colon cancer](#).
- Beta-carotene may also increase [lung cancer](#).
- Overall, the large number of clinical trials carried out on antioxidant supplements suggest that either these products have no effect on health, or that they cause a small increase in mortality in elderly or vulnerable populations.

Bioactive Antioxidant Classification

- **Hydrophilic**- Water soluble
React with cell cytosol and blood plasma oxidants
- **Lipophilic**- Lipid soluble
Protect cell membrane from lipid peroxidation

Transferrin, ferritin bind Fe act as antioxidant

Antioxidants	solubility
Ascorbic acid	Water
Glutathione	Water
Lipoic acid	Water
Uric acid	Water
Carotenes	Lipid
α -Tocopherols	Lipid
Ubiquinol (Coenzyme Q)	Lipid

Uric acid

- Antioxidants present on highest concentration in human blood

Xanthine oxidase enzyme

- Xanthine- ----- Uric acid

Urate oxidase enzyme

- Uric acid----- Allantoin

- Reduce oxidative stress produce in hypoxia at high altitude

- Allantoin is excreted in most mammals except human and ape
- In fish, allantoin is broken down further (into ammonia) before excretion.
- Allantoin has been shown to improve insulin resistance when administered to rats and increased lifespan when administered to the nematode worm *Caenorhabditis elegans*.

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- In bacteria, purines and their derivatives (such as allantoin) are used as secondary sources of nitrogen under nutrient-limiting conditions.
- Their degradation yields ammonia, which can then be utilized.
- For instance, *Bacillus subtilis* is able to utilize allantoin as its sole nitrogen source

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Vitamin C

- Monosaccharide redox catalyst
- Availability: Animals and plants
- Human : Diet
- Plants-Production chloroplast
- Function
- Procollagen----- Collagen
Proline amino acid ----- Hydroxyproline AA

Vitamin C antioxidant property

- $2 \text{Fe}^{3+} + \text{Ascorbate} \rightarrow 2 \text{Fe}^{2+} + \text{Dehydroascorbate}$
- **Fenton's reagent (Fe^{++} and Hydrogen peroxide)**
- $2 \text{Fe}^{2+} + 2 \text{H}_2\text{O}_2 \rightarrow 2 \text{Fe}^{3+} + 2 \text{OH}\cdot + 2 \text{OH}^-$

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Glutathione

1. Glutathione is a cysteine-containing peptide found in most forms of **aerobic life**.
2. Synthesized in cells from its constituent amino acids **glycine, glutamate, cysteine**
3. Glutathione has antioxidant properties since the **thiol group** in its cysteine moiety is a reducing agent and can be reversibly oxidized and reduced
4. In cells, glutathione is maintained in the reduced form by the enzyme **glutathione reductase**

- Due to its **high concentration** and its central role in **maintaining the cell's redox state**, glutathione is one of the most important cellular antioxidants
- **Mycothiol** in the Actinomycetes
- **Bacillithiol** in some Gram-positive bacteria

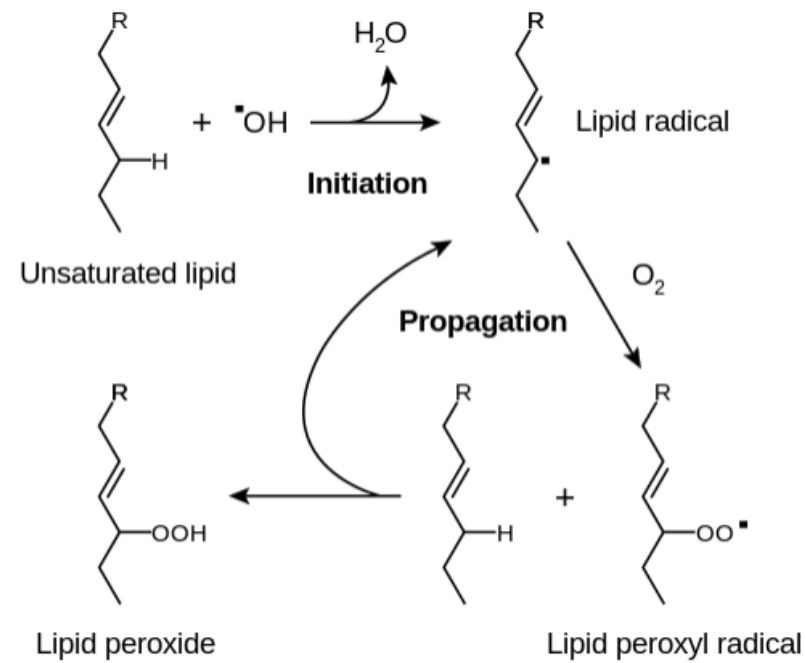
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Vitamin E

- Vitamin E is the collective name for a set of eight related **tocopherols and tocotrienols**
- α -tocopherol has been most studied as it has the **highest bioavailability**
- α -tocopherol form is the most important lipid-soluble antioxidant because it protects membranes from oxidation by **reacting with lipid radicals** produced in the lipid peroxidation chain reaction

- Vitamins E and C inhibit oxidation of LDL in a synergistic manner
- The unequivocal biological action of vitamin E as an antioxidant was first demonstrated against carbon tetrachloride toxicity in liver damage
- As mentioned above, carbon tetrachloride induces lipid peroxidation mediated by free radicals and leads to liver damage, which is inhibited by prior administration of vitamin E.
- Numerous studies have confirmed the antioxidant effects of vitamin E and other antioxidants against carbon tetrachloride toxicity in cell culture and animal experiments.

Lipid radicals



Lipid peroxidation chain reaction

- Vitamin E efficiently protects **glutathione peroxidase 4 (GPX4)**-deficient cells from cell death
- **GPx4** is the only known enzyme that efficiently reduces **lipid-hydroperoxides** within biological membranes.
- Most important function of α -tocopherol is as a **signaling molecule**
- γ -tocopherol is a **nucleophile** that may react **with electrophilic mutagens**
- **Tocotrienols** protecting neurons from damage

Pro-oxidants

Chemical that induce oxidative stress either by generating reactive oxygen species or by inhibiting antioxidant system

- Vitamin C, oxidizing polypeptides

Conditional pro-oxidants

Some substances can serve as either antioxidants or pro-oxidants, depending on conditions include the higher concentration of the chemical and if oxygen or transition metals are present

- Uric acid
- Homocysteine (Sulfhydryl amino acids)
- Melatonin

Melatonin as Conditional pro-oxidants

1. Melatonin promoted the generation of ROS at pharmacological concentrations (μm to mm range) in several tumor and nontumor cells
2. Melatonin may stimulate ROS production through its interaction with calmodulin
3. Melatonin may interact with mitochondrial complex III or mitochondrial transition pore to promote ROS production.

Paracetamol as Conditional pro-oxidants:

- **Paracetamol** (acetaminophen) can fatally damage the liver, partly through its production of reactive oxygen species (ROS)

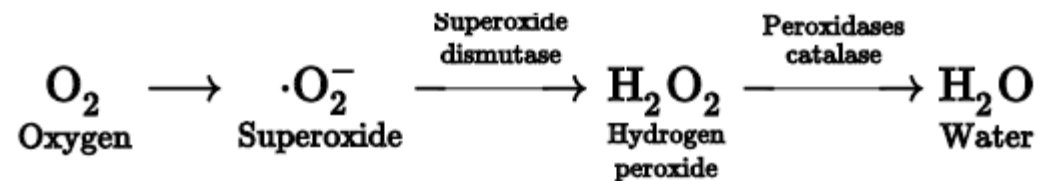
Transition metals as Conditional pro-oxidants:

Transition metals can serve as pro-oxidants.

1. **Chronic manganism**
2. **Hemochromatosis** elevated iron tissue levels
3. **Wilson's disease** elevated tissue levels of copper.

Enzyme systems (prevent lipid peroxidation)

- With the chemical antioxidants, cells are protected against oxidative stress by an interacting network of antioxidant enzymes



Enzymatic pathway for detoxification of reactive oxygen species

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J Clin Pathol 2001;54:176–186;

Biomed Res.Int. 2014; 2014: 761264

- Superoxide dismutase enzymes contain metal ion cofactors
 - copper, zinc, manganese or iron
1. Extracellular SOD----- copper/zinc
 2. Cytosolic SOD----- copper/zinc
 3. Mitochondria-----Mn
- Mitochondrial SOD **most biologically important** mice lacking this enzyme die soon after birth
 - The mice lacking cytosolic copper/zinc less pathologies and a **reduced lifespan** (see article on superoxide)
 - Mice without the extracellular SOD **hyperoxia**)

Thanks

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