

# Chapter 13

## Endogenous Antioxidants-II

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### ABSTRACT

Endogenous antioxidants are vital for protecting the body against oxidative stress and maintaining cellular health. Among these, glutathione peroxidase, glutathione, and vitamin C are key components of the body's antioxidant defense system. Glutathione peroxidase (GPx) is an essential enzyme that protects cells from oxidative damage by reducing hydrogen peroxide and lipid peroxides into harmless molecules like water and alcohol. This process is crucial in preventing the harmful effects of oxidative stress, particularly in the protection of cell membranes and DNA from free radical-induced damage. Glutathione, a tripeptide composed of glutamine, cysteine, and glycine, is one of the most important nonenzymatic antioxidants in the body. It plays a central role in neutralizing free radicals, regenerating other antioxidants like vitamin C and E, and detoxifying harmful substances. Glutathione is also involved in various cellular processes, including immune function and protein synthesis, making it indispensable for maintaining overall health. Vitamin C, or ascorbic acid, is a potent water-soluble antioxidant that works synergistically with glutathione and glutathione peroxidase. It scavenges free radicals, regenerates other antioxidants, and contributes to the stabilization of cellular components against oxidative damage. Vitamin C is also essential for collagen synthesis, immune function, and the absorption of iron from plant-based foods. Together, these antioxidants form a robust defense network that protects the body from the detrimental effects of oxidative stress, supports immune function, and contributes to the maintenance of overall health and well-being. Their roles in antioxidant defense highlight the importance of maintaining adequate levels of these compounds through diet and endogenous production.

### Glutathione

- 1. Overview:** Glutathione (GSH) is a crucial nonenzymatic antioxidant that plays a central role in the body's defense against oxidative stress. It is a tripeptide composed of three amino acids: glutamine, cysteine, and glycine. Glutathione is involved in various cellular processes, including detoxification, regulation of cellular redox state, and modulation of immune responses.
- 2. Function**
  - a. Antioxidant Defense:** Glutathione directly neutralizes reactive oxygen species (ROS) and free radicals, such as hydrogen peroxide ( $H_2O_2$ ) and hydroxyl radicals ( $\bullet OH$ ), by donating electrons.

- b. Detoxification:** It helps detoxify and neutralize various toxic substances, including heavy metals and xenobiotics, by conjugating with them through enzymatic reactions (e.g., glutathione S-transferases).
- c. Redox Regulation:** Glutathione maintains the redox balance within cells by participating in redox reactions and regenerating other antioxidants, such as vitamin C and E.
- d. Protein Function and Folding:** It influences protein function and stability by forming disulfide bonds and aiding in proper protein folding.

### 3. Forms of Glutathione

- a. Reduced Glutathione (GSH):** The active form that donates electrons to neutralize ROS and regenerate other antioxidants.
- b. Oxidized Glutathione (GSSG):** The disulfide-linked form resulting from the oxidation of GSH. GSSG is recycled back to GSH by glutathione reductase using NADPH.

### 4. Mechanism of Action

- a. Direct Scavenging:** GSH directly neutralizes ROS by donating electrons, thus preventing oxidative damage to cellular components.
- b. Regeneration of Other Antioxidants:** GSH helps regenerate oxidized antioxidants, such as vitamin C and E, restoring their antioxidant activity.
- c. Detoxification Reactions:** Through conjugation reactions catalyzed by glutathione S-transferases, GSH helps detoxify harmful substances and facilitate their excretion from the body.

### 5. Distribution and Localization

- a. Intracellular Concentration:** Glutathione is found predominantly in the cytoplasm, with high concentrations in the liver, kidneys, and other tissues. It is present in both reduced (GSH) and oxidized (GSSG) forms.
- b. Cellular Compartments:** It is also present in mitochondria and the nucleus, where it plays roles in mitochondrial function and regulation of nuclear processes.

### 6. Clinical Relevance

- a. Oxidative Stress and Disease:** Depletion of glutathione levels or impaired function can lead to increased oxidative stress and contribute to various diseases, including neurodegenerative disorders (e.g., Parkinson's and Alzheimer's diseases), cardiovascular diseases, and cancer.
- b. Aging:** Decreased levels of glutathione with age are associated with increased oxidative damage and age-related diseases.
- c. Therapeutic Potential:** Glutathione supplementation and strategies to boost its levels or enhance its recycling are being explored for their potential benefits in treating diseases related to oxidative stress and improving overall health.

## Vitamin C: Essential Nutrient and Potent Antioxidant

**Introduction:** Vitamin C, also known as ascorbic acid, is a vital water-soluble vitamin and a powerful antioxidant that plays a crucial role in maintaining overall health. As an essential nutrient, vitamin C cannot be synthesized by the human body and must be obtained through diet or supplementation.

**Nutritional Sources:** Vitamin C is abundant in various fruits and vegetables, particularly citrus fruits (like oranges, lemons, and grapefruits), strawberries, kiwi, bell peppers, broccoli, and spinach. Due to its water-soluble nature, vitamin C is easily lost during cooking, so consuming raw or lightly cooked foods is often recommended to maximize intake.

**Biological Functions:** Vitamin C is essential for several vital bodily functions. It is a critical cofactor in the synthesis of collagen, a protein necessary for the maintenance of skin, blood vessels, bones, and cartilage. Vitamin C also plays a role in wound healing, repair of tissues, and the formation of neurotransmitters. Additionally, it enhances the absorption of non-heme iron from plant-based foods, helping prevent iron deficiency anemia.

**Antioxidant Properties:** As a potent antioxidant, vitamin C helps neutralize free radicals, which are unstable molecules that can cause oxidative stress and damage to cells. By reducing oxidative stress, vitamin C helps protect against chronic diseases, such as cardiovascular disease, certain cancers, and age-related eye conditions like cataracts and macular degeneration. Its antioxidant activity also supports immune function by protecting immune cells from oxidative damage and enhancing the body's overall defense against infections.

**Therapeutic Uses:** Vitamin C is commonly used to support the immune system, especially during cold and flu seasons. High doses of vitamin C have been studied for their potential role in reducing the duration and severity of the common cold, although results are mixed. Beyond immune support, vitamin C is also explored for its potential in improving skin health and reducing the appearance of wrinkles due to its role in collagen synthesis.

**Overview:** Vitamin C, also known as ascorbic acid, is a water-soluble vitamin that functions as a powerful antioxidant. It plays a crucial role in protecting cells from oxidative damage, supporting immune function, and aiding in various physiological processes.

### Function

- a. **Antioxidant Defense:** Vitamin C acts as a potent scavenger of reactive oxygen species (ROS) and free radicals, such as superoxide radicals ( $O_2^-$ ) and hydroxyl radicals ( $\bullet OH$ ). It neutralizes these harmful molecules by donating electrons, thereby preventing oxidative damage to cellular components like lipids, proteins, and DNA.
- b. **Regeneration of Other Antioxidants:** Vitamin C helps regenerate other antioxidants, such as Vitamin E, by converting the oxidized form of Vitamin E back to its active form. This synergistic action enhances the overall antioxidant defense system.
- c. **Collagen Synthesis:** It is essential for the synthesis and stabilization of collagen, a key structural protein in connective tissues, skin, blood vessels, and bones. Vitamin C acts as a cofactor for prolyl and lysyl hydroxylases, enzymes required for collagen formation.

- d. **Immune Function:** Vitamin C supports the immune system by enhancing the function of immune cells, such as leukocytes, and promoting the production of antibodies. It also helps protect immune cells from oxidative damage.

### Mechanism of Action

- a. **Direct Scavenging:** Vitamin C neutralizes ROS directly by donating electrons, which helps reduce oxidative stress and prevent cellular damage.
- b. **Regeneration of Vitamin E:** By reducing the oxidized form of Vitamin E (tocopherol), Vitamin C enhances Vitamin E's ability to protect cell membranes from oxidative damage.
- c. **Collagen Biosynthesis:** It stabilizes collagen by facilitating the hydroxylation of proline and lysine residues in collagen molecules, which is critical for maintaining the strength and integrity of connective tissues.

### Absorption and Distribution

- a. **Absorption:** Vitamin C is absorbed in the small intestine through active transport mechanisms. It can also be taken up by cells via specific transporters (e.g., sodium-dependent vitamin C transporters).
- b. **Distribution:** Once absorbed, Vitamin C is distributed throughout the body, with higher concentrations found in the adrenal glands, pituitary gland, brain, and eyes. It is also present in extracellular fluids and tissues.

### Clinical Relevance

- a. **Deficiency Diseases:** Vitamin C deficiency can lead to scurvy, a condition characterized by bleeding gums, joint pain, and poor wound healing due to impaired collagen synthesis.
- b. **Oxidative Stress and Disease:** Adequate Vitamin C levels are associated with reduced risk of chronic diseases related to oxidative stress, such as cardiovascular diseases, cancer, and neurodegenerative disorders.
- c. **Supplementation:** Vitamin C supplementation is often used to enhance antioxidant defense, support immune function, and manage conditions associated with oxidative stress. However, excessive intake can cause gastrointestinal issues and other side effects.