Introduction to Free Radicals and ROS

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Definition

- Free radicals are highly reactive molecules with unpaired electrons.
- Due to their instability, they seek out other molecules to stabilize themselves, often causing cellular damage in the process.

Sources

- **Endogenous**: Produced naturally during normal metabolic processes (e.g., mitochondrial respiration).
- **Exogenous**: Result from external factors like pollution, UV radiation, smoking, and unhealthy lifestyle choices.

Health Impact

- Contribute to oxidative stress, a condition where free radicals outnumber antioxidants.
- Can lead to cellular damage, premature aging, and chronic diseases such as:
    - Cardiovascular diseases
    - Diabetes
    - Cancer

Common Examples of Free Radicals

- Superoxide anion ($O_2^{-}\cdot$)
- Hydroxyl radical (·OH)
- Nitric oxide (NO·)
- Peroxyl radicals (ROO·)
- Alkoxyl radicals (RO·)

Role of Nutraceuticals

- Many dietary supplements contain antioxidants that neutralize free radicals.
- Common antioxidant components:
    - Vitamins: Vitamin C, Vitamin E, beta-carotene
    - Coenzyme Q10
    - Phytochemicals: Flavonoids, polyphenols

Reactive Oxygen Species (ROS)

Definition

- ROS are a specific type of free radical that contains oxygen.
- They are common and impactful free radicals found in the human body.

Formation of ROS

- ROS are produced both endogenously and exogenously:

1. Endogenous Sources

- Mainly produced in the mitochondria during ATP (energy) production.

2. Exogenous Triggers

- Stress
- Environmental pollutants
- Smoking
- Excessive alcohol consumption
- UV exposure

Types of ROS and Their Effects

ROS Type	Characteristics	Damage Potential
Superoxide Anion (O2•–)	Generated in mitochondria during respiration	Precursor to other ROS
Hydrogen Peroxide (H2O2)	Not a radical but a ROS; more stable and membrane-permeable	Can form hydroxyl radicals in presence of metal ions
Hydroxyl Radical (•OH)	Highly reactive, formed via Fenton reaction	Causes severe DNA, protein, and lipid damage
Singlet Oxygen ($^1O_2$)	High-energy form of oxygen	Damages lipids and sensitive biomolecules

Impact of ROS (When in Excess)

Cellular Damage

- Lipid peroxidation
- Protein degradation
- DNA damage (mutations, strand breaks)

Associated Diseases

- Aging
- Cancer
- Cardiovascular disease
- Neurodegenerative disorders
  - Alzheimer's Disease
  - Parkinson's Disease
- Inflammatory and autoimmune conditions

Production of Free Radicals in Cells

- Free radicals are highly reactive molecules with unpaired electrons.
- In cells, they are produced through both endogenous (internal) and exogenous (external) sources.
- While they play certain roles in the body, excessive free radicals can cause cellular damage unless neutralized by antioxidants.

Endogenous Sources (Internal)

1. Mitochondrial Electron Transport Chain

- This is the primary site for energy production during aerobic respiration.
- As electrons are transferred through the mitochondrial electron transport chain, some may leak and prematurely react with oxygen, forming superoxide radicals (O_2^-)—a type of Reactive Oxygen Species (ROS).

2. Enzymatic Reactions

- Certain enzymes naturally generate ROS as by-products of their normal activity.
- Examples include:
  - NADPH oxidase
  - Xanthine oxidase
  - Lipoxygenases
- These enzymes participate in various metabolic processes but may release free radicals during their actions.

3. Immune Response (Respiratory Burst)

- During infection or inflammation, immune cells like phagocytes (e.g., neutrophils and macrophages) produce ROS to destroy invading pathogens.
- This deliberate release of free radicals, known as the respiratory burst, helps in pathogen killing but also contributes to oxidative stress.

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