

Free Radicals Pharmacology

Generation of Free Radicals

Definition

- Free radicals are **atoms or molecules with one or more unpaired electrons** in their outer orbit.
- Because electrons prefer to exist in pairs, these molecules are **highly unstable and reactive**.
- To gain stability, they **steal electrons from nearby molecules**, leading to cellular damage.

Key Characteristics

- Highly reactive and short-lived
- Can initiate chain reactions
- Damage important biomolecules:**
 - Lipids
 - Proteins
 - DNA
- Cause oxidative stress when their production exceeds antioxidant defenses

Types of Free Radicals

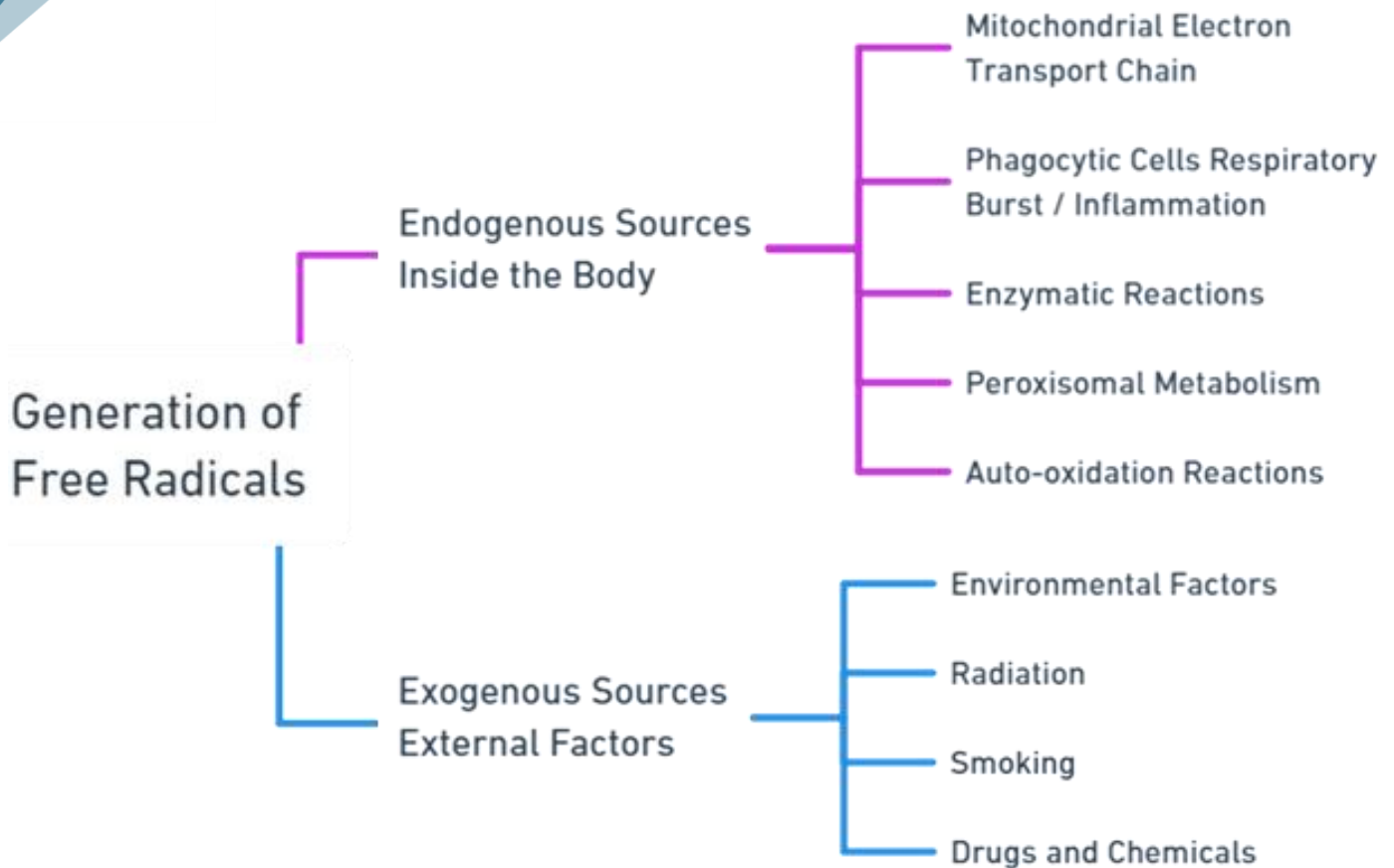
A. Reactive Oxygen Species (ROS)

- Superoxide radical ($\text{O}_2\bullet^-$)
- Hydroxyl radical ($\bullet\text{OH}$) → *most dangerous*
- Hydrogen peroxide (H_2O_2) → *not a free radical but forms radicals*

B. Reactive Nitrogen Species (RNS)

- Nitric oxide ($\text{NO}\bullet$)
- Peroxynitrite (ONOO^-)

Generation of Free Radicals



A. Endogenous Sources (Inside the Body)

1. Mitochondrial Electron Transport Chain

- Main source of free radicals
- **During ATP production:**
 - Oxygen is partially reduced
 - Forms superoxide radicals ($O_2\bullet^-$)

2. Phagocytic Cells (Respiratory Burst / Inflammation)

- Neutrophils and macrophages generate radicals to kill pathogens
- **Enzyme:** NADPH oxidase
- **Products:**
 - Superoxide
 - Hydrogen peroxide
 - Hypochlorous acid

3. Enzymatic Reactions

- **Certain enzymes produce free radicals during metabolism:**
 - Xanthine oxidase
 - Cyclooxygenase (COX)

- Lipoxygenase
- Cytochrome P450 system

4. Peroxisomal Metabolism

- Fatty acid oxidation produces:
- **Hydrogen peroxide (H_2O_2)**

5. Auto-oxidation Reactions

- Some molecules undergo oxidation:
- Dopamine
- Hemoglobin
- Leads to free radical formation

B. Exogenous Sources (External Factors)

1. Environmental Factors

- Air pollution
- Ozone
- Industrial chemicals

2. Radiation

- Ultraviolet (UV) rays
- X-rays
- Gamma rays
- Cause breakdown of water → **hydroxyl radicals ($\bullet OH$)**

3. Smoking

- Cigarette smoke contains large amounts of free radicals
- Causes direct lung tissue damage

4. Drugs and Chemicals

- Alcohol
- Pesticides
- Heavy metals (iron, copper)
- Certain drugs (e.g., **paracetamol overdose**)

Chain Reaction Mechanism

Free radicals can start chain reactions:

1. Initiation

- Free radicals are formed

2. Propagation

- Radical reacts with stable molecule → new radical formed

3. Termination

- Two radicals combine → stable product

How Free Radicals Cause Damage

Free radicals damage cells by reacting with major **cell components**.

1. Lipid Peroxidation

- Cell membranes are rich in lipids.
- Free radicals attack these lipids, especially polyunsaturated fatty acids.
- This damages membrane structure.
- The membrane becomes weak and leaky.
- Cell function becomes abnormal.

Effects:

- Loss of membrane fluidity
- Disturbed transport of ions and nutrients
- Cell swelling and cell death

2. Protein Oxidation

- Free radicals change the structure of proteins.
- Enzymes lose activity.
- Receptors and transport proteins stop functioning properly.
- Structural proteins become weak.

Effects:

- Reduced enzyme activity
- Abnormal signaling
- Tissue damage

3. DNA Damage

- Free radicals can break DNA strands or alter DNA bases.

- Mutations may occur.
- If repair fails, the cell may die or become cancerous.

Effects:

- Mutation
- Abnormal cell growth
- Carcinogenesis

4. Mitochondrial Injury

- Mitochondria are highly sensitive to oxidative damage.
- Their membrane and DNA can be injured.
- Energy production decreases.
- More radicals are generated, creating a harmful cycle.

5. Cell Death

- **Severe oxidative stress can cause:**
 - Apoptosis (programmed cell death)
 - Necrosis (uncontrolled cell death)

6. Oxidative Stress

- **Oxidative stress happens when:**
 - Free radical production increases, or
 - Antioxidant defense decreases, or
 - Both happen together
- This imbalance results in damage to tissues and contributes to many diseases.

Role of Free Radicals In Etiopathology of Diabetes Mellitus

Basic Concept

- In diabetes mellitus, **chronic hyperglycemia** leads to excessive production of **reactive oxygen species (ROS)**
- This causes oxidative stress, resulting in cellular damage
- Contributes to disease progression and complications

Mechanisms of Free Radical Generation

A. Hyperglycemia-Induced ROS Production

- High glucose → increased ROS formation



FREE PREVIEW

[Click here to visit our website](#)

PHARMACY PREMIUM NOTES

Complete subject
and semesters are
available on
FirstHope app only.



[Scan or click here](#)

Click here to get the app



Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram



[Scan or click here](#)

@FirstHopeNotes

Instagram

@firsthope.official

[Click here to follow >](#)

YouTube channel

FirstHope-Pharmacy / Live streams

[Click here to watch >](#)

WhatsApp channel

Follow FirstHope on WhatsApp

[Click here to join >](#)

FirstHope website

firsthopenotes.com

[Click here to visit >](#)

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.