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 ($\mathbf{O_2}\bullet^-$)
- Hydroxyl radical ($\bullet\mathbf{OH}$) → *most dangerous*
- Hydrogen peroxide ($\mathbf{H_2O_2}$) → *not a free radical but forms radicals*

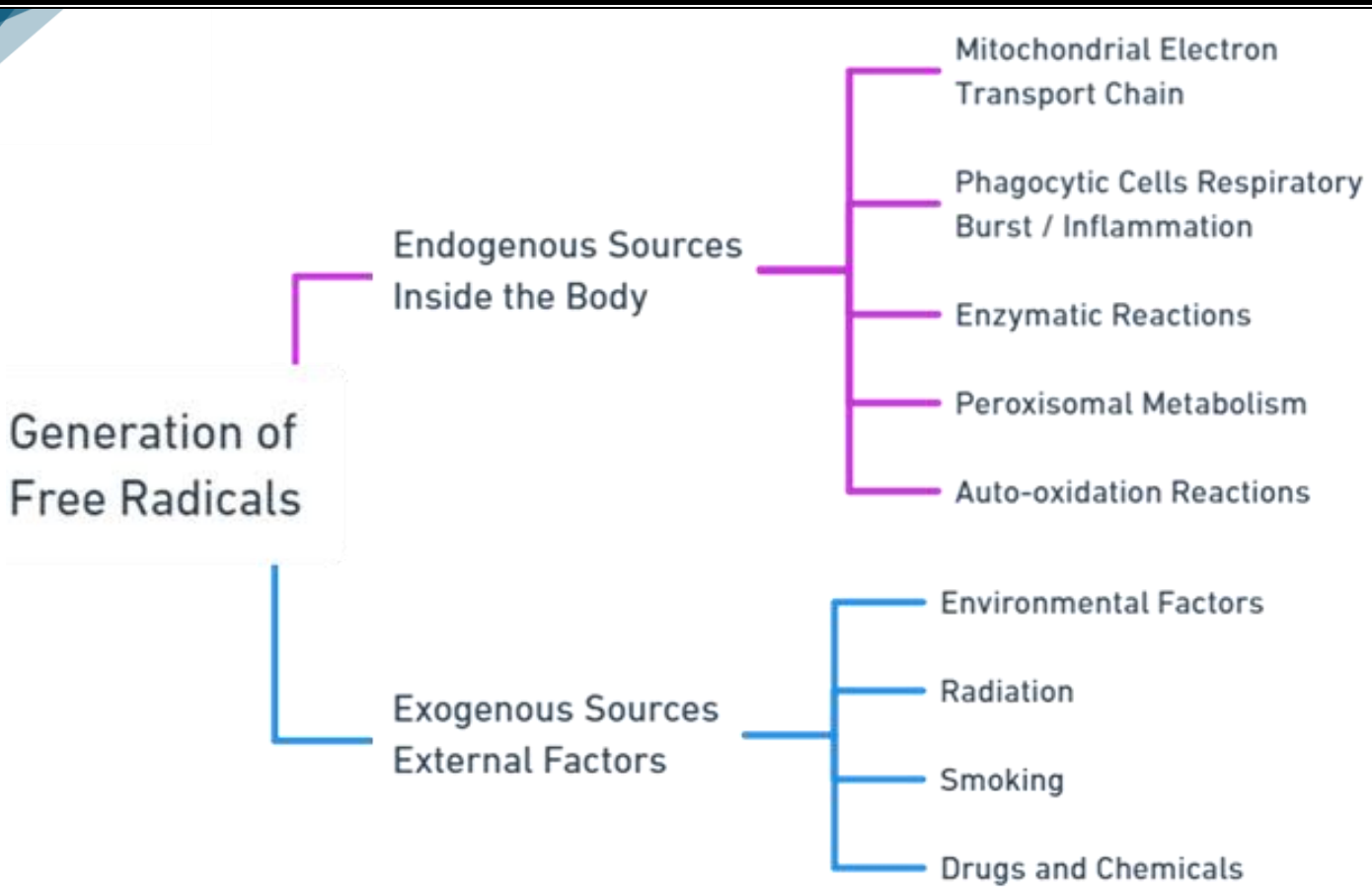
B. Reactive Nitrogen Species (RNS)

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

Generation of Free Radicals

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.



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)

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- 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 (•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:

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

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.

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- 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.

First Hope

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

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

First Hope

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

firsthope.co.in

Click here to visit >

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

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