

Oxygen Toxicity: Radicals, Damage & Defense

The Radical Nature of O₂

Superoxide Anion

Highly reactive free radical with limited lipid solubility; cannot diffuse far from formation site.

Hydrogen Peroxide

Weak oxidizing agent that generates hydroxyl radicals. Lipid soluble, diffuses through membranes to mitochondria.

Hydroxyl Radical

Most powerful ROS. Initiates chain reactions forming lipid peroxides and organic radicals.

Major Sources of ROS

O1

Coenzyme Q

Electron transporter in mitochondria. Not protein-bound, diffuses through inner mitochondrial membrane. Major site for toxic oxygen free radical generation when accidentally transferring electrons to O₂.

O2

Oxidases, Oxygenases & Peroxidases

Found in mitochondria, peroxisomes, lysosomes. Manage oxygen and ROS. May accidentally release free radical intermediates during single-electron transfers to O₂.

O3

Ionizing Radiation

Alpha particles, beta particles, gamma rays, X-rays split water into hydrogen and hydroxyl radicals, causing skin damage, mutations, cancer, and cell death.

ROS Damage to Cellular Components

Membrane Attack

Hydroxyl radicals extract hydrogen from lipids, forming lipid peroxy radicals and peroxides. Lipid degradation produces malondialdehyde (blood/urine indicator of free radical damage).

Proteins & Peptides

Radicals cause protein fragmentation and amino acid cross-linking. Attack on cysteine residues forms aggregates preventing degradation. Increases susceptibility to enzymatic digestion.

DNA

Hydroxyl radicals cause base alterations and strand breaks. ROS extract hydrogen from C-4 of deoxyribose sugar, leading to single strand breaks.

Cellular Defenses Against Oxygen Toxicity

Antioxidant Enzymes

Mechanism	Location	Function	Enzyme
Converts superoxide anion to H ₂ O ₂ and O ₂ using metal ions (Cu, Zn, Mn)	Nucleus, mitochondria, extracellular	Primary defense against oxidative stress	Superoxide Dismutase (SOD)
Prevents hydroxyl radical formation	Peroxisomes, cytosol (kidney, liver)	Reduces H ₂ O ₂ to water	Catalase
Reduces H ₂ O ₂ to water, oxidizes glutathione to GSSG	Throughout cell	Major H ₂ O ₂ removal outside peroxisomes	Glutathione Peroxidase
Transfers electrons from NADPH to GSSG disulfide bond	Throughout cell	Regenerates reduced glutathione	Glutathione Reductase

Dietary Antioxidants

Food Sources	Properties	Function	Antioxidant
Olive oil, margarine, almonds, peanuts, meats, dairy, leafy greens	Lipid-soluble, widely distributed in nature	Protects against lipid peroxidation in membranes; reacts with lipid radicals to stop chain reactions	Vitamin E (α-tocopherol)
Citrus fruits, vegetables	Water-soluble, circulates unbound in blood and extracellular fluid	Regenerates reduced vitamin E by donating electrons to oxidized vitamin E	Ascorbic Acid (Vitamin C)
Fruits and vegetables	Vitamin A precursor	Chain-breaking antioxidants; may slow cancer and degenerative disease progression	Carotenoids (β-carotene)