

Toxicodynamics (Mechanism of Action)

- Cellular basis for toxic injury – Cellular damage is the basis for most toxicological injury.
- Toxic injury involves quantitative differences in the function of cells, tissues and organs.
- Cellular response of chemical toxicants occurs through both structural and metabolic mechanism of the cell, like altered membrane integrity, altered cell volume regulation, abnormal accumulation of lipids and pigments, altered protein synthesis and altered growth regulation.
- Mixed function oxidases play a role in biotransforming xenobiotics to electrophilic intermediates.

- Mixed function oxidases are a family of non specific enzymes that act primarily in the endoplasmic reticulum to promote phase I metabolism, which prepares xenobiotics for conjugation and excretion. These electrophilic intermediates are believed to bind covalently to important cellular macromolecules. These macromolecules may be denatured by binding.
- Electrophiles also bind to reduced glutathione which is considered to be a protective mechanism in the cell.
- Cellular macromolecules may also be damaged by free radicals.
- A free radical is a compound with an unpaired electron a result of an enzyme-catalyzed addition of electron to a carbon bond, with subsequent cleavage.

- Superoxide (active oxygen) is formed when some compounds are oxidised by mixed function oxidases to free radical, with electrons transferred to oxygen. This active oxygen reacts with polysaturated lipids, initiating an autocatalytic chain reaction, leading to lipid-free radicals and then lipid peroxidation.
- Glutathione can be depleted which enhances oxidative damage and leads to cell death. Agents that deplete glutathione, increase cell susceptibility to lipid peroxidation.
- Several major effects are initiated after free radical formation. Defenses against free radicals are built into cells as antioxidants like superoxide dismutase, catalase, glutathione peroxidase and vitamin E.

Toxicokinetics

- Toxicokinetics is the quantitation of the time course of toxicant in the body during the processes of absorption, distribution, metabolism, and excretion (ADME)
- Toxicokinetics describes how the body handles a toxicant, as a function of dose and time, in terms of ADME:
 - The rate of chemical absorption from the site of application into the blood stream (Absorption)
 - The rate and extent of chemical movement out of blood into the tissue (Distribution)
 - The rate and extent of chemical biotransformation into metabolites (i.e. Metabolism)
 - The rate of chemical removal from the body (Excretion).