Effects of Dapagliflozin against Cyclophosphamide-induced Hepatotoxicity in Male Rats in Comparison to Silymarin

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This presentation explores the mechanisms of cyclophosphamide-induced liver toxicity and investigates the potential of dapagliflozin and milk thistle as protective agents.

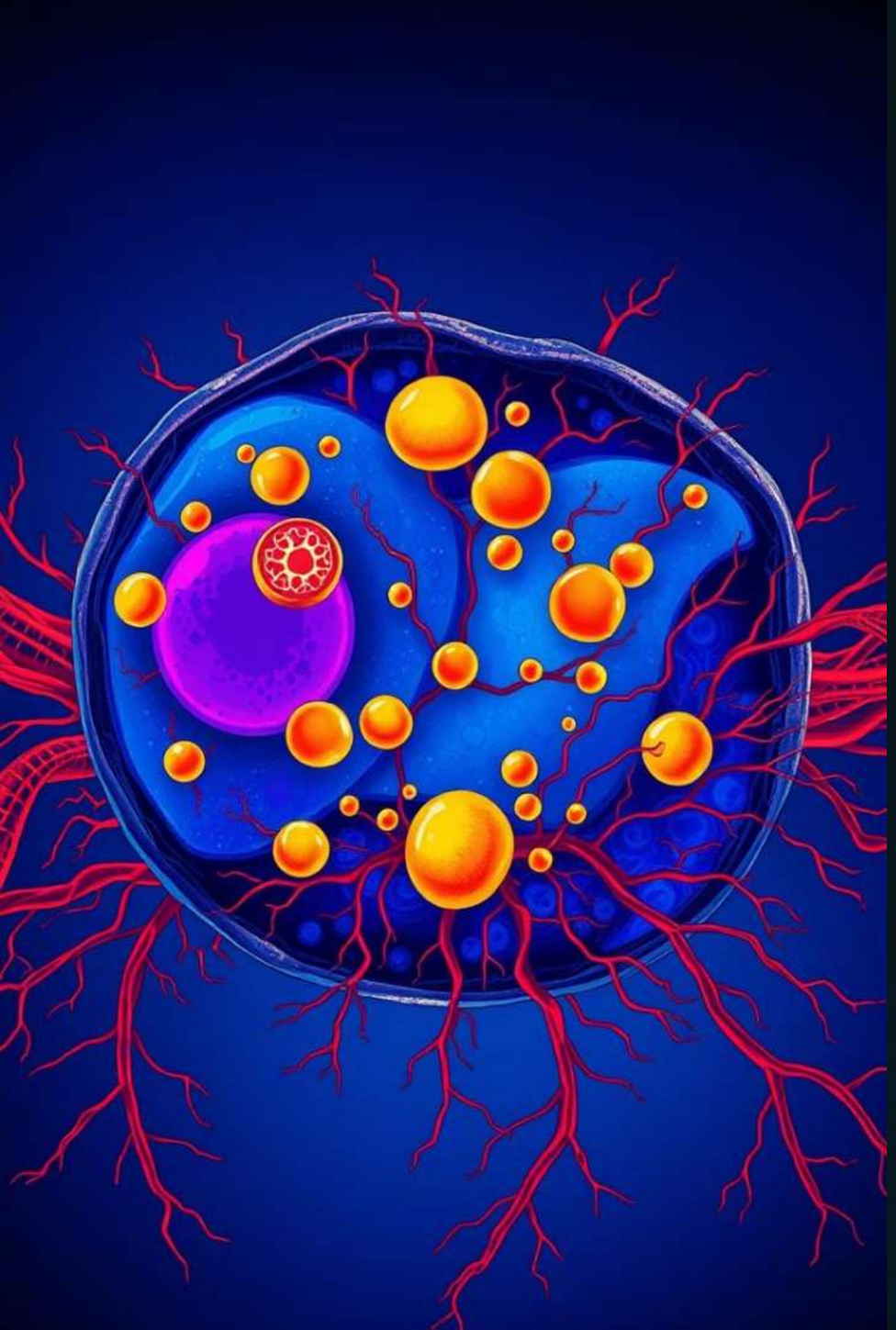
Cyclophosphamide: A Powerful Drug with Limitations

Cyclophosphamide (CPA)

A widely used drug for cancer and autoimmune diseases.

Challenge

Therapeutic doses cause liver toxicity, limiting its clinical use.



Mechanisms of CPA-Induced Hepatotoxicity

Oxidative Stress

Imbalance in oxidant/antioxidant systems.

Inflammatory Pathways

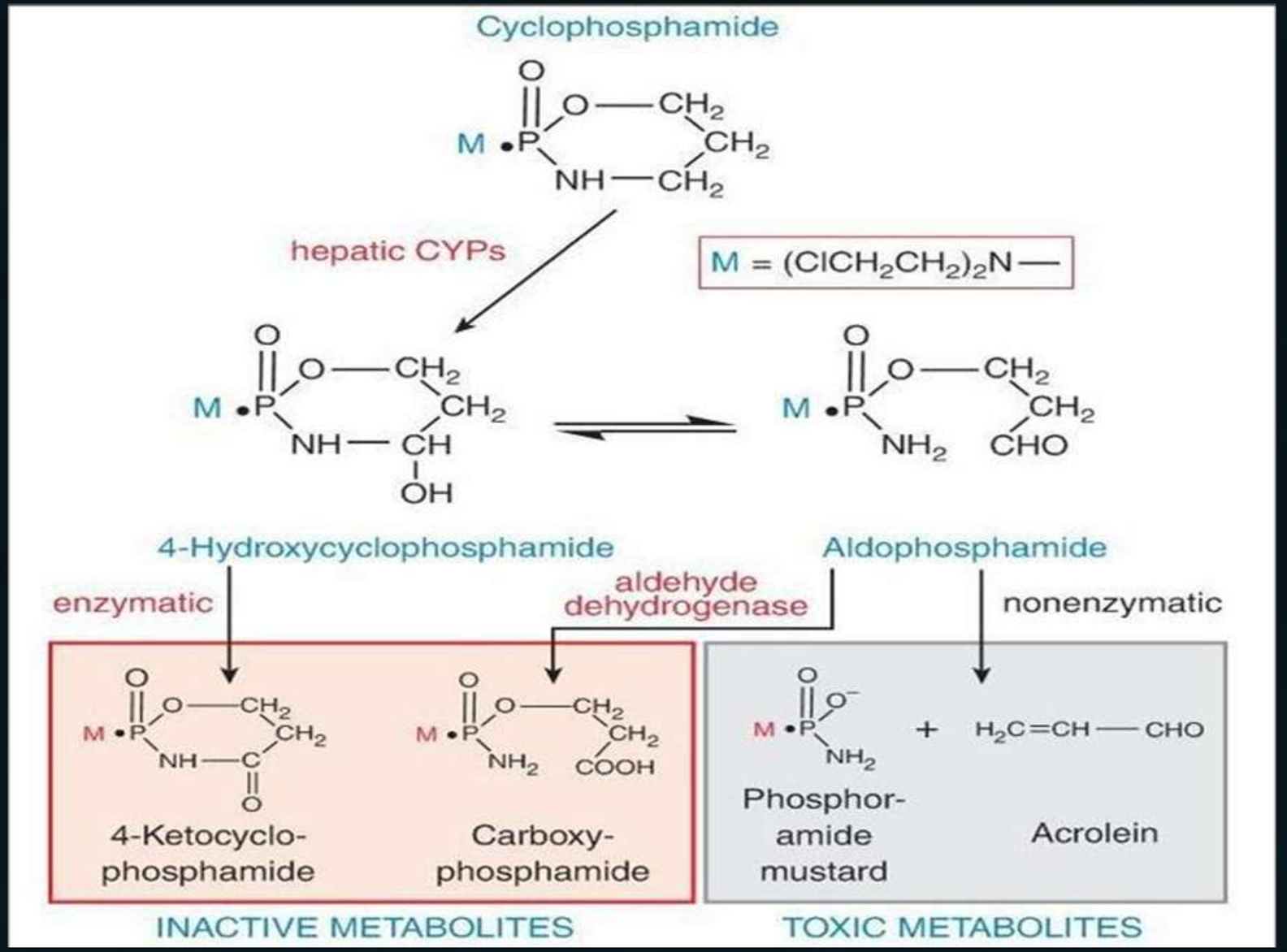
Lipid peroxidation activates signaling pathways.

Mitochondrial Damage

Impairs cellular respiration and disrupts balance.

Apoptosis

Reactive Oxygen Species induce apoptosis.


Cyclophosphamide
hepatic CYPs
M = (ClCH2CH2)2N—
4-Hydroxycyclophosphamide
Aldophosphamide
enzymatic
aldehyde dehydrogenase
nonenzymatic
4-Ketocyclo-phosphamide
Carboxy-phosphamide
Phosphor-amide mustard
Acrolein
INACTIVE METABOLITES
TOXIC METABOLITES

Parameters of CPA-Induced Liver Toxicity

1 Biochemical Indicators

Increased hepatic enzyme activity: AST, LDH, ALP.

2 Inflammatory Markers

TNF-α, IL-1β, anti-inflammatory marker IL-10.

3 Molecular Indicators

Apoptotic markers: Caspase-3, Bcl-2, HNF4α.

Dapagliflozin: A Potential Hepatoprotective Agent

Overview

SGLT2 inhibitor approved for type 2 diabetes management.

Hepatoprotective Effects

Attenuates hepatic steatosis and reduces glucose uptake.

Milk Thistle: (Silymarin)
A NaturalHepatoprotective Agent

Anti-oxidative

Anti-inflammatory

Regenerative

Study Objectives

1

Understand CPA-Induced Liver Toxicity

Molecular mechanisms, biochemical, molecular, and histological parameters.

2

Evaluate Protective Effects of Dapagliflozin

Assess parameters like MDA, GSH, SOD, inflammatory markers, and apoptotic markers.

Methodology

1

Animal Model

Rats treated with CPA (30 mg/kg/day for 10 days).

2

Experimental Groups

Control, CPA-only, CPA + dapagliflozin and CPA +Silymarin

3

Analytical Techniques

Biochemical assays, qRT-PCR, Western blot, ELISA and histological analysis.

Key Findings (Expected Results)

Oxidative Stress

Inflammatory Markers

Apoptosis

Conclusion and Future Directions

1

CPA-induced hepatotoxicity

Mediated through oxidative stress, inflammation, and apoptosis.

2

Dapagliflozin

Shows promise as a protective agent.

3

Future Directions

Explore combined effects, investigate long-term outcomes, study molecular pathways.


Thank yor listening!
Hepatopotective
LIVER
LIVER
Thank you listening!