

**INFLUENCE OF MELATONIN ON
ARSENIC MEDIATED PANCREATIC
DAMAGE IN SWISS ALBINO MICE**

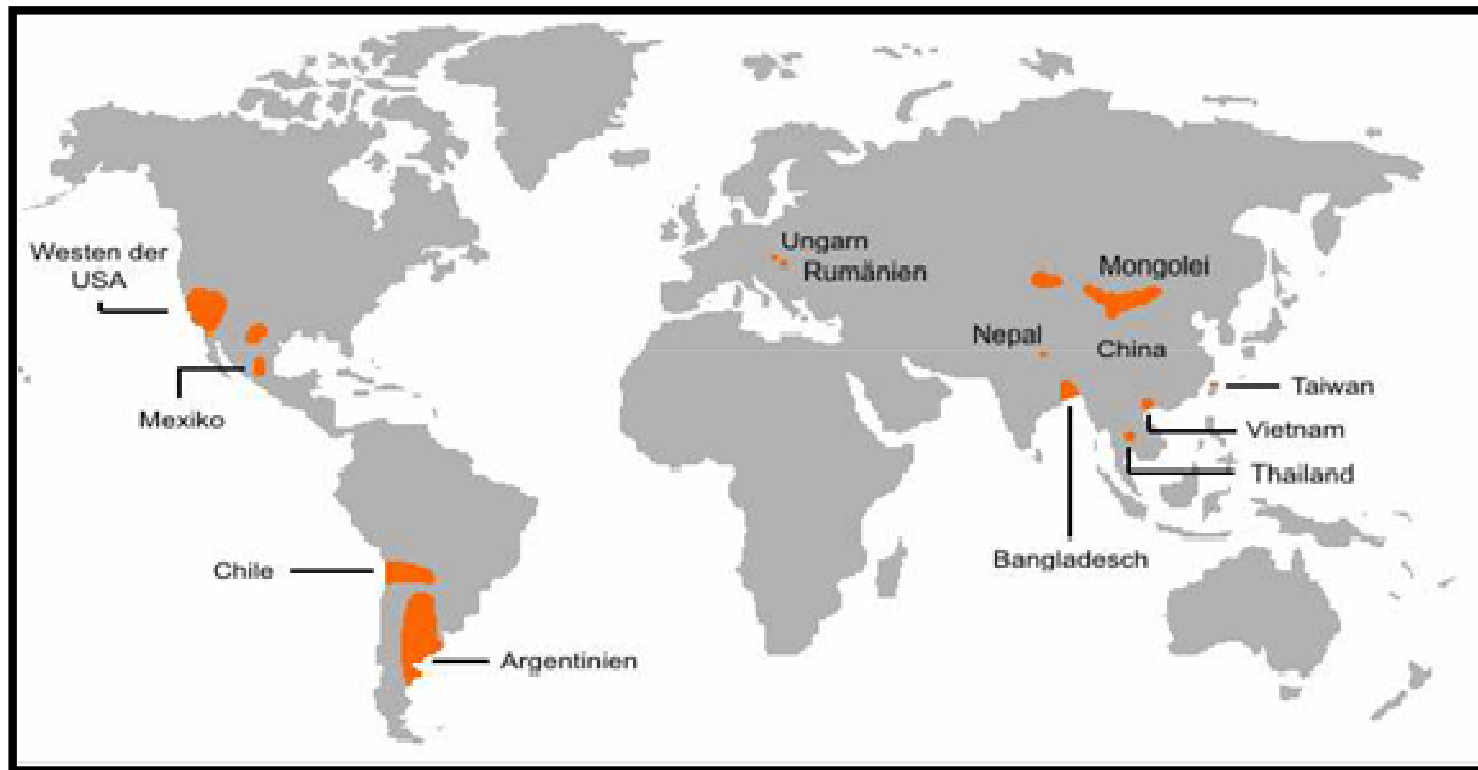
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INTRODUCTION

- **Arsenic** - 20th most abundant element
- **Arsenic toxicity** - global health problem affecting millions of people
- **Arsenic Contamination in the world** - US, Mexico, Chile, Bolivia, Argentina, Hungary, Romania, India, Bangladesh, Thailand, Vietnam, Taiwan, China Nepal
- **Asia** - Bangladesh, Taiwan and India (West Bengal)

ARSENIC CONTAMINATION IN THE WORLD



CONTAMINATION

- Natural geological sources

- Mining

- Industrial processes

- Commercial products

Pesticides, Herbicides, Fungicides

- Food - Seafood & Fish

- Absorption - predominantly from ingestion from the small intestine, though minimal absorption occurs from skin contact and inhalation
- Absorbed arsenic accumulates in the liver, pancreas, kidney, heart, and lungs and deposited in the keratin rich tissues: nails, hair, and skin.

EFFECTS

Gastrointestinal

Dermal

Developmental

Reproductive

Respiratory

Cardiovascular

Renal

Haematological

Musculoskeletal

Endocrine

Neurological

Hepatic

HALLMARK SIGNS OF ARSENIC TOXICITY

skin lesions on palm , blackfoot disease



ARSENIC TOXICITY

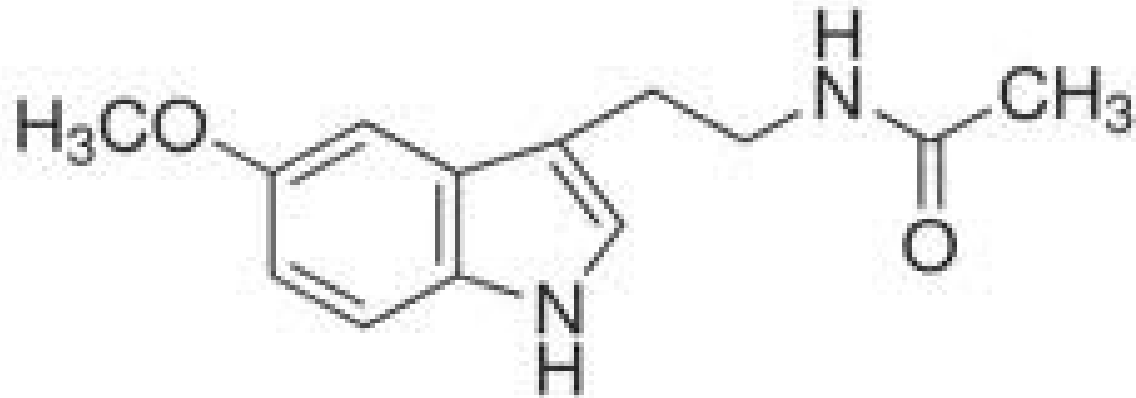
- Formation of ROS/RNS,
- Alter sulfhydryl homeostasis
- Lipid peroxidation
- Conformational changes to biomolecules
- DNA damage
- Depletion of glutathione
- Carcinogenicity of Lung, Skin, Kidney, Liver, Bladder, GI tract

Antioxidants used to combact Arsenic toxicity

- Vitamins A, C, D & E
- Calcium Supplementation
- Protein Supplementation
- Combination of Vitamins and Calcium
- Selenium
- Antioxidants like SOD, GSH, Catalase
- Amino acids (Methionine, Cystine & Cysteine
- Plant Extracts (Curcumin & Kalmegh-Andrographis paniculata)
- Antioxidant Used in this study - Melatonin

MELATONIN

(5-methoxy-N-acetyl tryptamine)



MELATONIN (MLT)

- Regulation of retinal function, Circadian rhythm, Reproduction
- Oncostatic effects
- Anti inflammatory functions
- Immune system stimulations
- Powerful antioxidant

MELATONIN (MLT)

- Direct free radical scavenger
- Detoxifies ROS/RNS
- Stimulation of antioxidant enzymes
- Augmenting the efficiency of other antioxidants
- Increasing the efficiency of mitochondrial oxidative phosphorylation and reduces electron leakage there by lowers free radical generation

OBJECTIVES : IN VIVO STUDIES

- To study the effect of arsenic trioxide (As_2O_3) on biochemical parameters, serum indices & histological analysis of Pancreas
- To investigate the ameliorative effect of melatonin (MLT) on arsenic induced pancreatitis

EXPERIMENTAL PROTOCOL

Animals : Adult Swiss Female Mice.
(*Mus musculus*) (30-35g)

Experimental Groups :

Control

As₂O₃ treated (LD - 0.5mg/kg bw)

As₂O₃ treated (HD - 1.0mg/kg bw)

Melatonin (MLT) alone

As₂O₃ (HD) + MLT

Mode of administration :

As₂O₃ (*po*) and MLT (*ip*)

Duration of Treatment : 30 days

PARAMETERS STUDIED

- **Gravimetric :**
Body weight & organ weight
- **Biochemical :**
Protein (Lowry *et al.*, 1951)
Total -SH (Sedlak & Lindsay., 1968)
Blood Glucose (Nelson & Somogyi., 1945)
Serum Amylase (Schwiara., 1972)
Serum Lipase (Moss & Henderson., 1999)
- **Arsenic Retention Estimation**
- **STATISTICAL ANALYSIS**

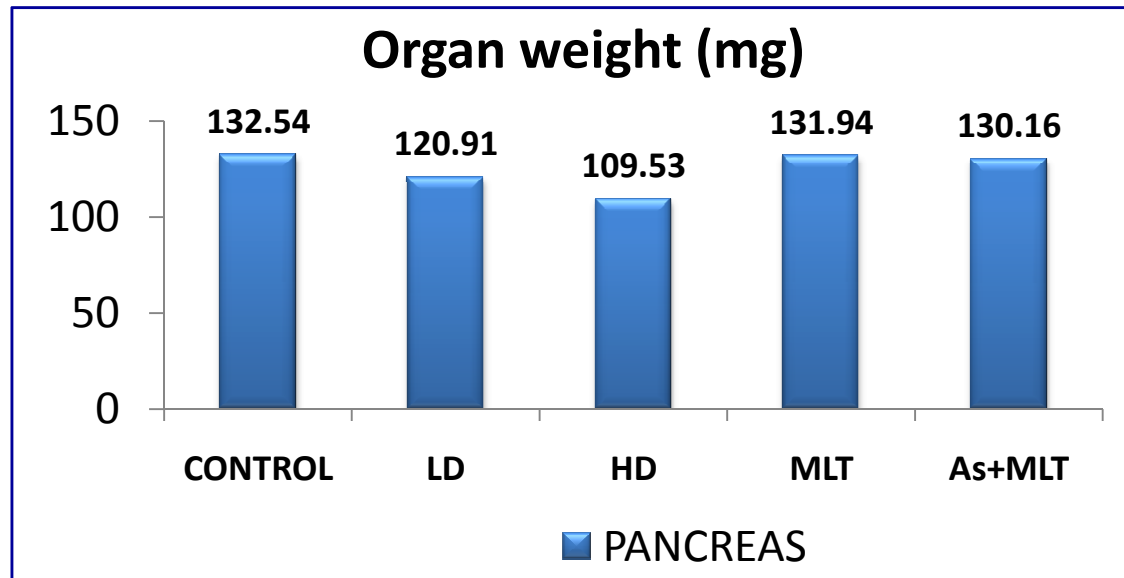
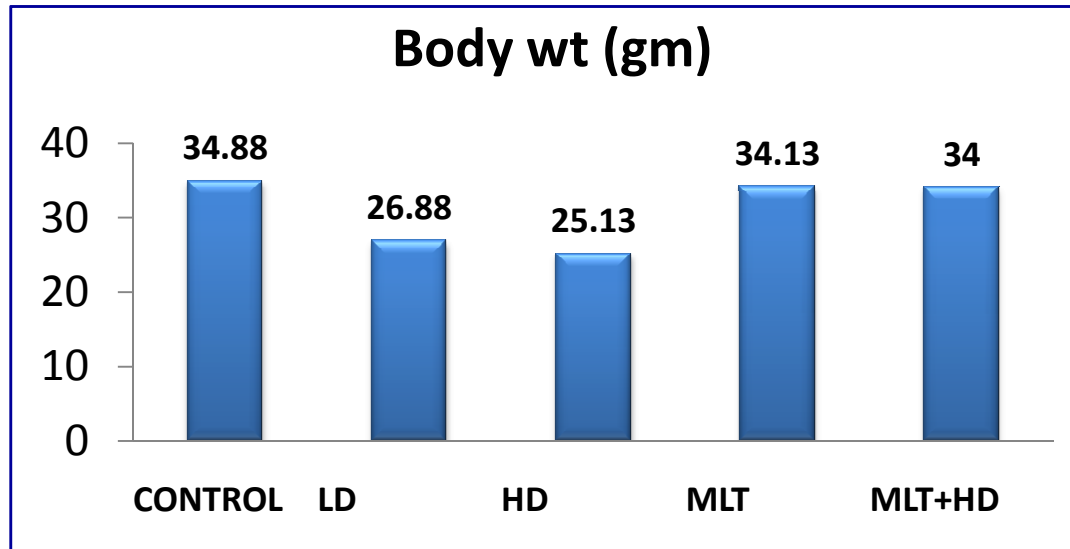
General Mechanism of Arsenic Induced Toxicity

As - High affinity for -SH groups -Protein degradation
↓ Carbohydrate metabolism ↓ Enzymes

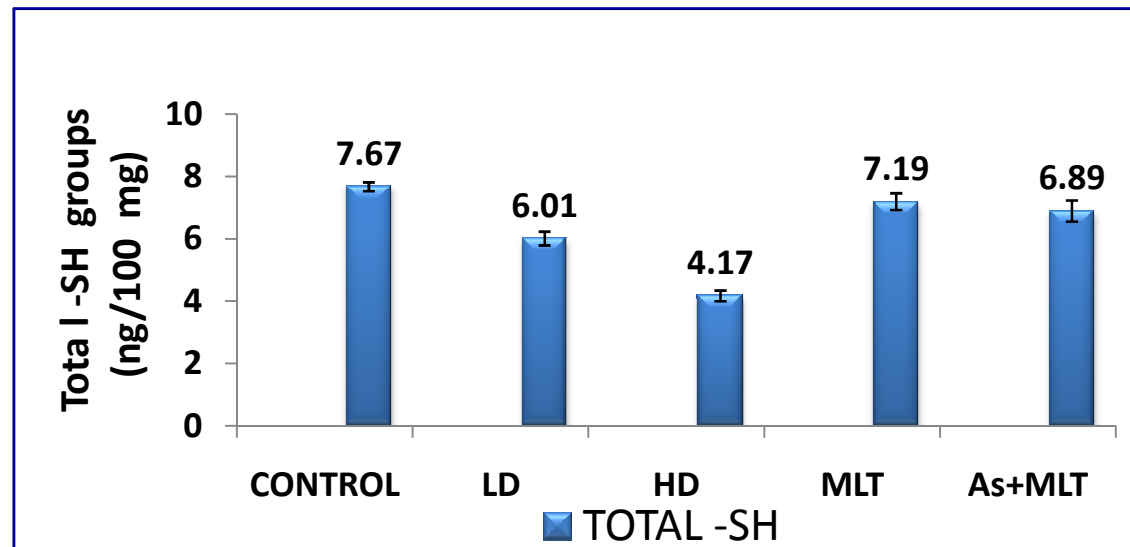
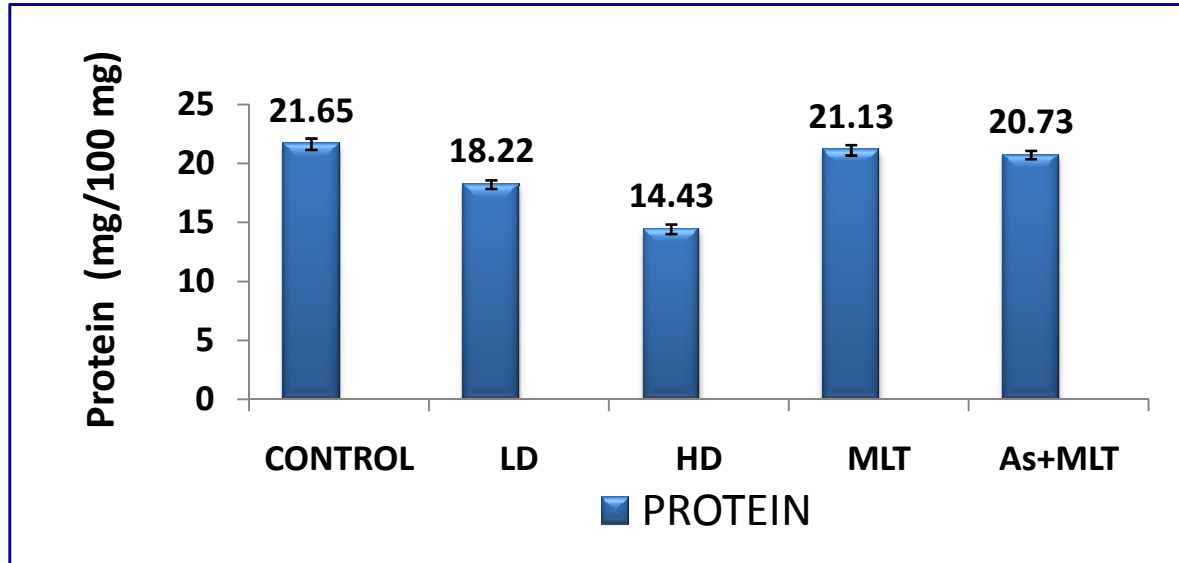
- ROS/Radicals/H₂O₂ - ↓ Antioxidant system - ↑ LPO
Oxidative Stress - Protein degradation

- Accumulation in mitochondria - ↓ Carbohydrate
metabolism ↓ Enzymes - Metabolic Insult -
Pancreatitis

GRAVIMETRIC

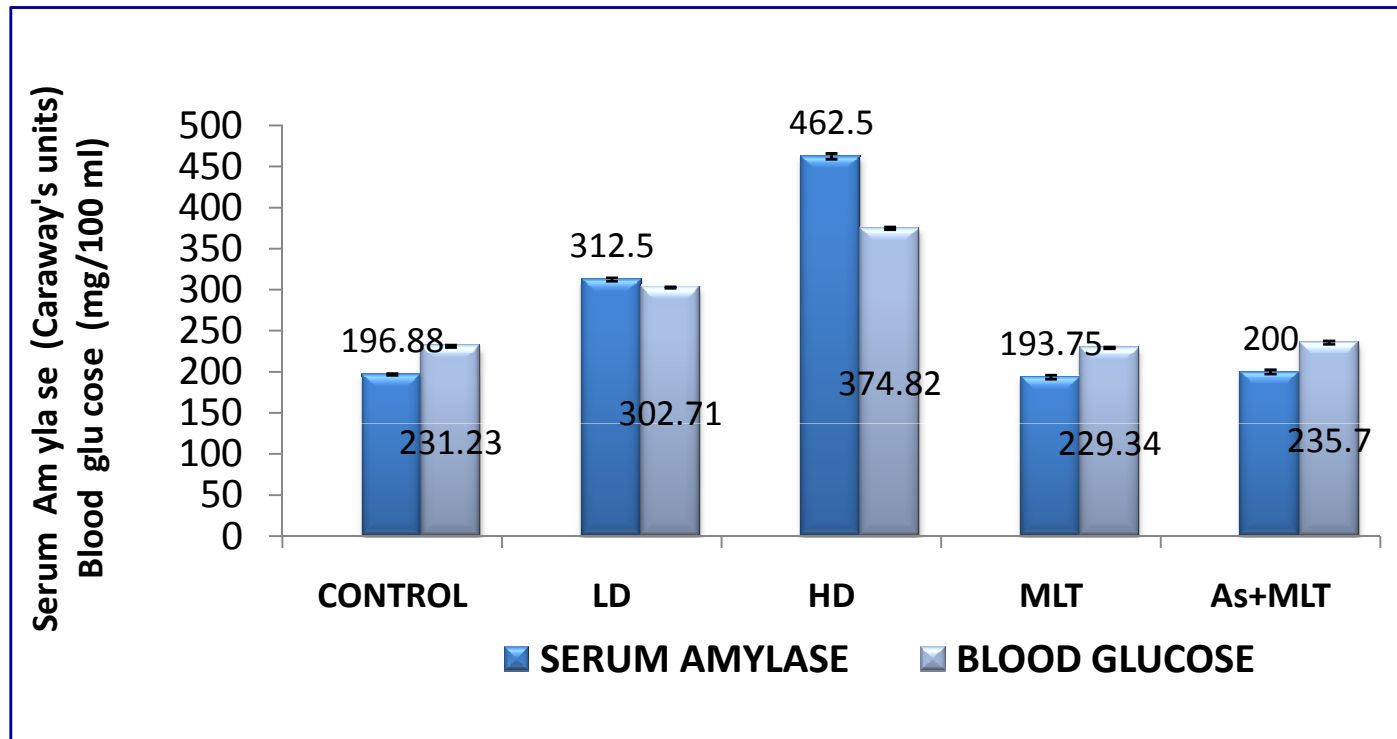


PROTEIN & TOTAL -SH

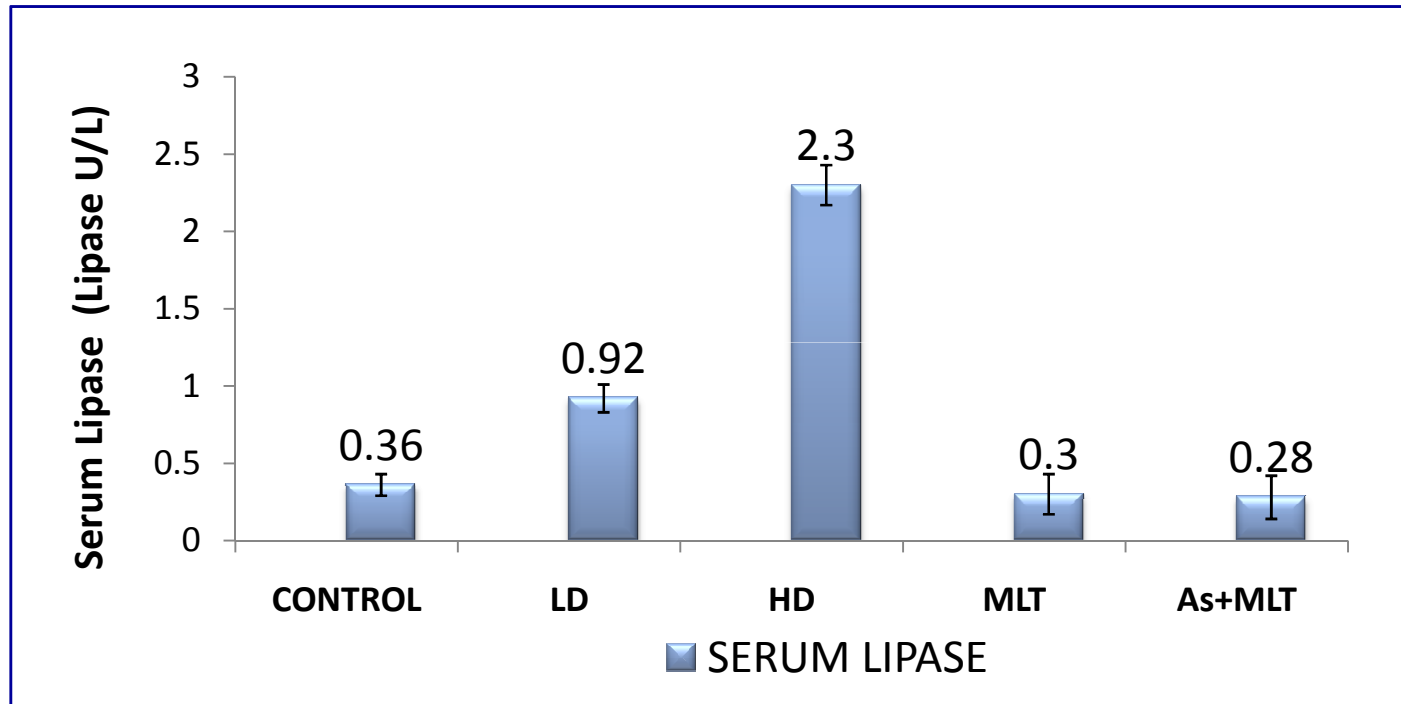


SERUM AMYLASE

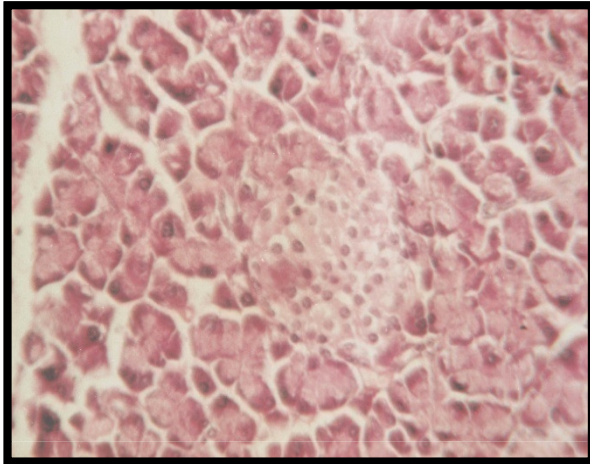
BLOOD GLUCOSE



SERUM LIPASE

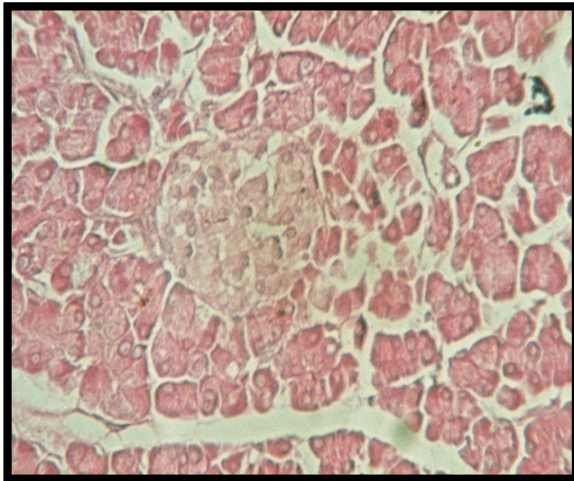


HISTOPATHOLOGICAL ANALYSIS



CONTROL

- Normal architecture of Pancreas
- Normal Islet size & cell population
- Normal acinar tissue
- Normal capillary number in Islet

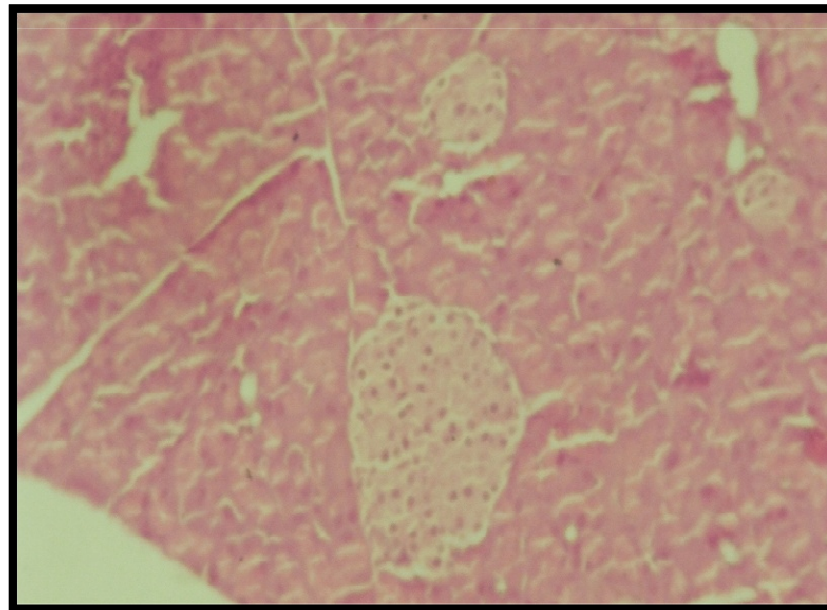


ARSENIC TREATED

(Pathological changes)

- Shrunken islets with vacuolization
- Reduction in Islet cell number
- Damaged acinar tissue
- Increased capillary number & diameter

**T.S of pancreas of MLT+
As₂O₃ treated mouse
showing revival in the
morphology and population
of cells**



CONCLUSION

➤ **Arsenic trioxide treatment**

- Reduction in body and organ weights
- Declined levels of protein and total sulfhydryl groups
- Elevated levels of serum amylase, serum lipase & blood glucose
- Arsenic retention

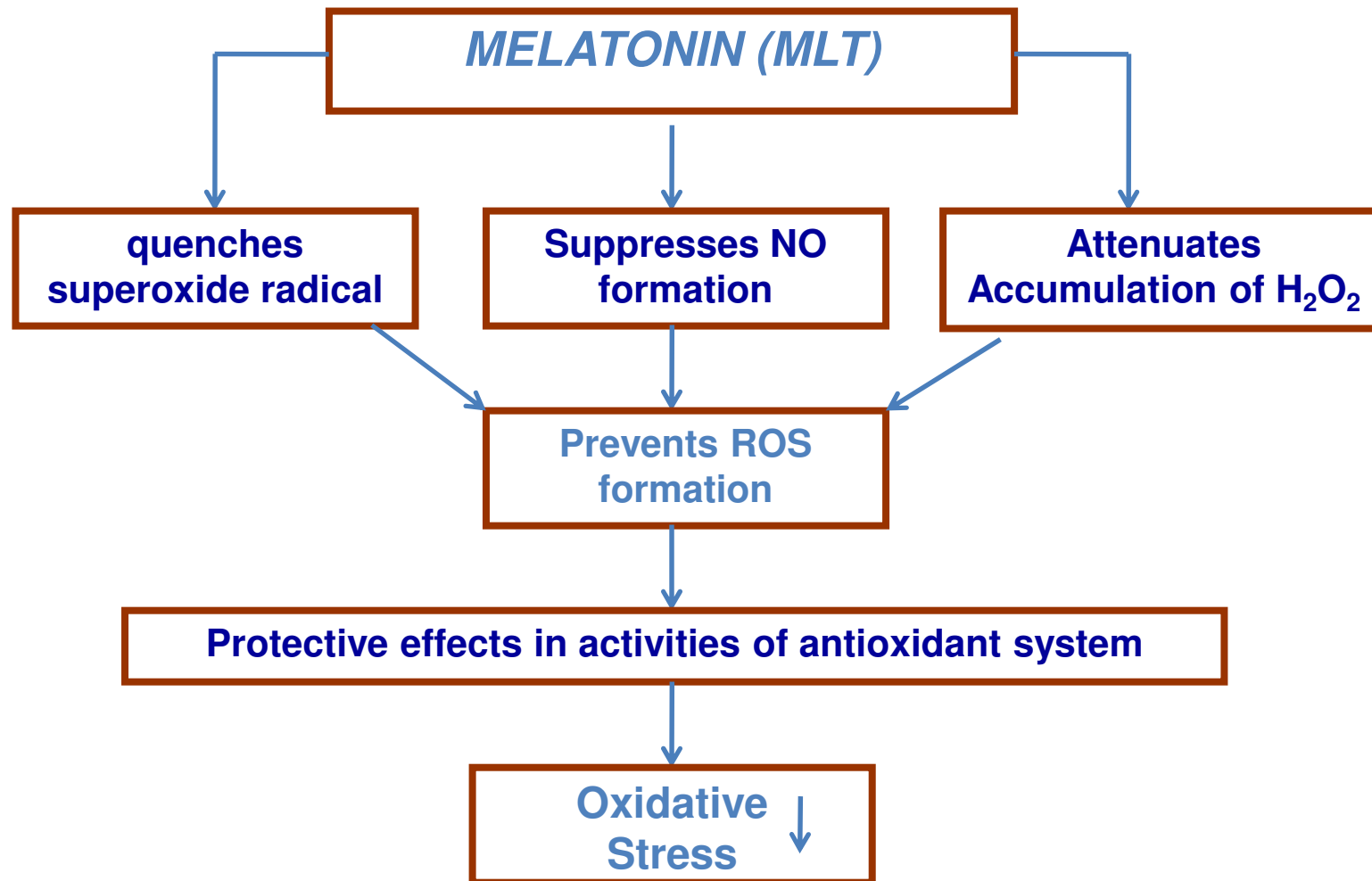
➤ **Histological analysis**

- Destruction of the exocrine and endocrine tissue

➤ **Administration of melatonin (MLT)**

Reversed the above toxic effects and improved the arsenic induced altered function in pancreas

PROBABLE MECHANISM BY WHICH MELATONIN PROTECTS AGAINST ARSENIC TOXICITY



Thank you