

EFFECTS OF *N*-(5-bromo-1*H*-indole-3-yl)methylene  
*nicotinohydrazide* ON THIOACETAMIDE-INDUCED  
LIVER CIRRHOSIS IN RATS

*Presented By*

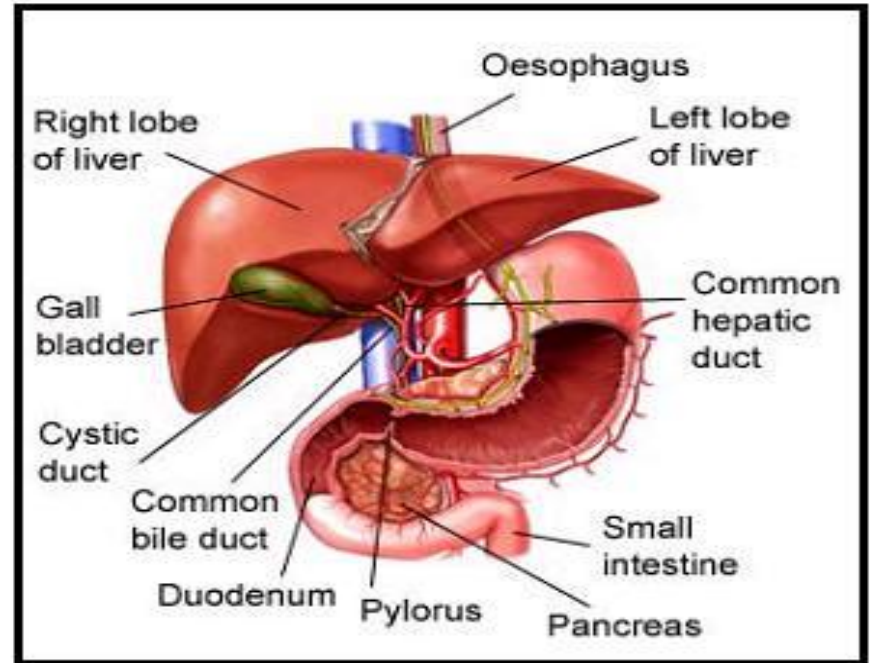
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# **INTRODUCTION**

# Liver

- Largest organ in the body
- Weights about 1.75 kg in a 70 kg adult
- Divided into 2 lobes
- Each lobe made up of thousands of lobules
- Each lobule is the functioning unit



# Functions of Liver

- Maintain metabolic homeostasis
- Synthesize, regulate, store and secrete substances that enter the liver
- Purify, detoxify and neutralized toxins, poisons and unwanted substances that enter the liver

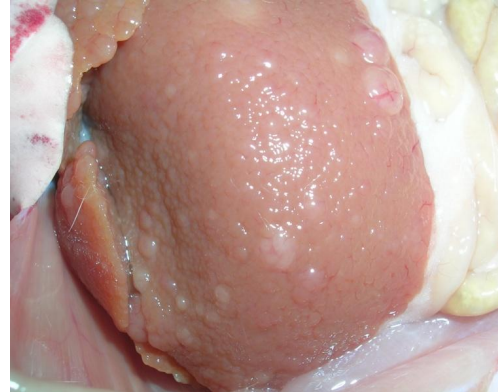
Without the **normal function** of the liver, one might not survive.

# Liver Cirrhosis

- End stages of liver disease
- Extensive build up of scar tissue in the liver caused by chronic inflammation of liver cells
- Scar tissue is tough fibrous tissue which replaced the damaged liver cells
- Blood supply is reduced
- Metabolic and detoxification processes become limited

# Causes of Liver Cirrhosis

- Chronic hepatitis B
- Chronic hepatitis C
- Tobacco smoking
- Alcohol consumption
- Biliary obstruction
- Primary or secondary biliary cirrhosis
- Non-alcoholic fatty liver disease
- Toxins and drugs



# Symptoms and Complications of Liver Cirrhosis

## Symptoms

- Asymptomatic in early stages
- Anorexia
- Weight loss
- Weakness
- Fatigue
- Osteoporosis

## Complications

- Jaundice
- Gallstones
- Edema and ascites
- Bruising and bleeding
- Itching
- Liver cancer

# Diagnosis of Liver Cirrhosis

- Analyze blood samples
- Ultrasound examination
- Computerized axial tomography (CAT) scan
- Magnetic resonance imaging (MRI)
- Radioisotope imaging
- **Liver Function Test**
- **Liver Biopsy**



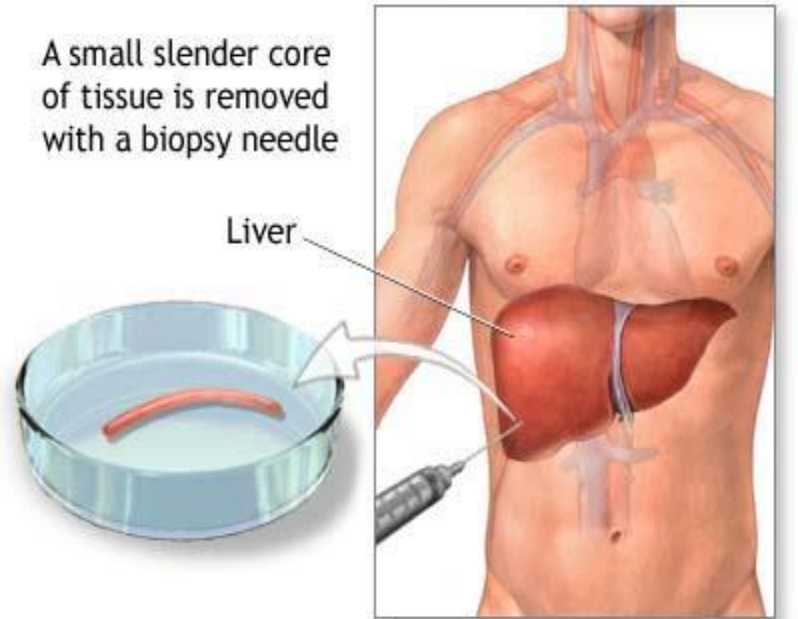
# Liver Function Test

Common blood test to evaluate liver function

- Albumin
- Alpha 1-antitrypsin (A1AT)
- Alkaline phosphatase (ALP)
- **Alanine aminotransferase (ALT)**
- **Aspartate aminotransferase (AST)**
- Gamma glutamyl transferase (GGT)
- Prothrombin time (PT)
- Serum bilirubin
- Urine bilirubin

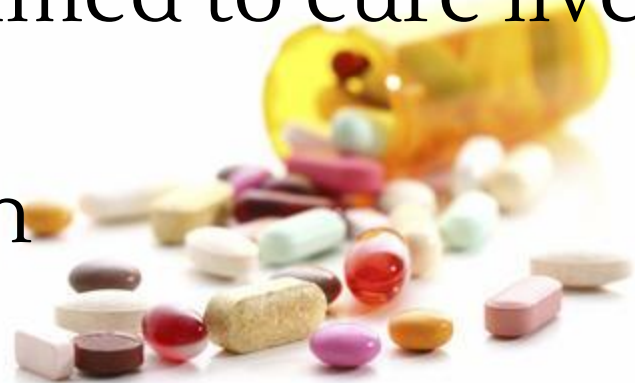
# Liver Biopsy

- A procedure whereby tiny pieces of liver tissue are removed and sent to a laboratory for examination
- The tissue is then prepared and stained and views under the microscope
- Histology of the tissue helps the physician make a specific diagnosis



# Current Therapeutic Approaches for Liver Cirrhosis

- Stop or delay further progression
- Reduce the possible complications
- No drug in the modern system of medicine can be claimed to cure liver cirrhosis
- Liver transplantation



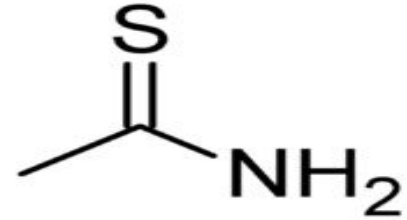
# Objectives

- To synthesized N-(5-bromo-1H-indol-3-yl)methylene) nicotinohydrazide.
- To investigate the 5-bromo-1H-indol-3-yl) methylene) nicotinohydrazide therapeutic effect in preventing thioacetamide-induced liver cirrhosis in rats.

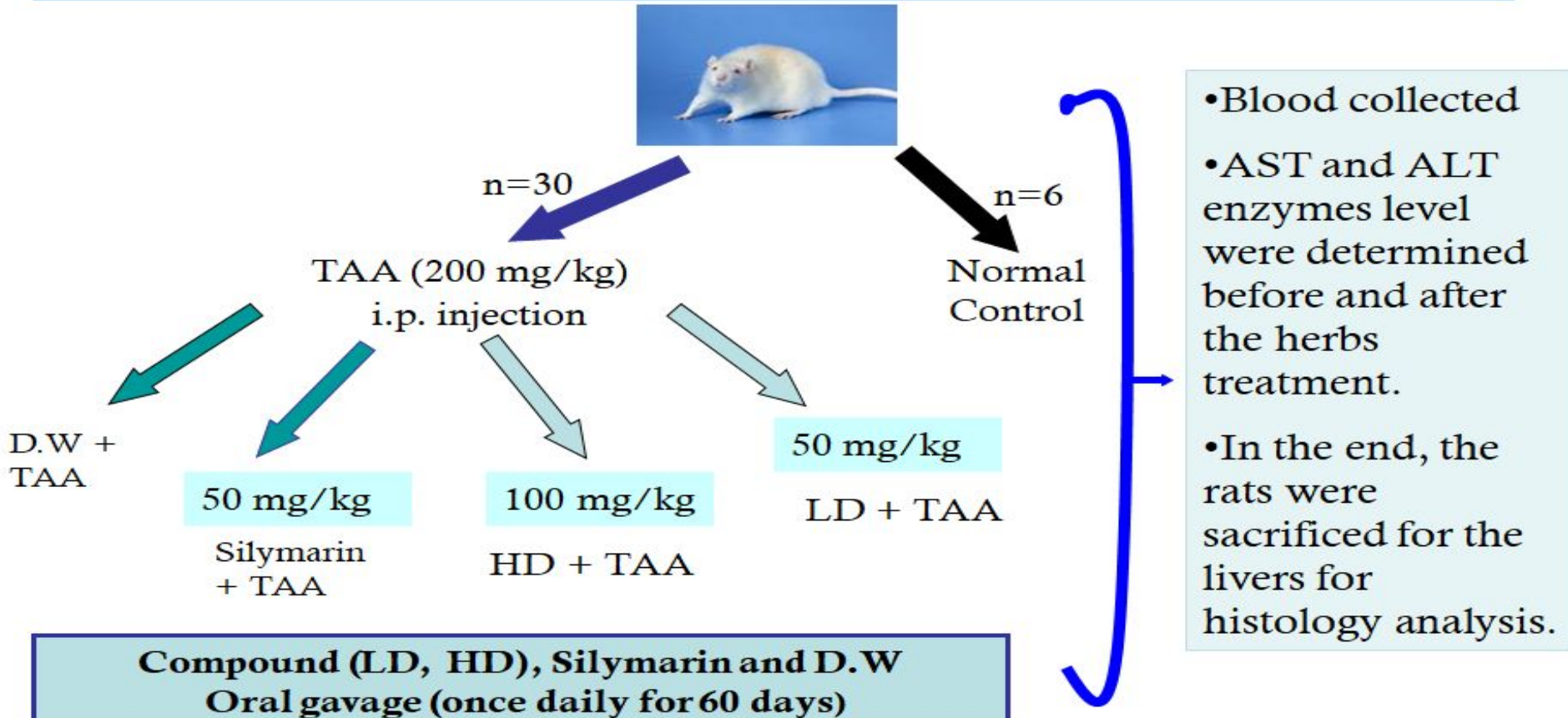
**MATERIALS  
AND  
METHODS**

# Thioacetamide (TAA)

- $\text{CH}_3\text{CSNH}_2$
- An organic compound
- White crystal under standard conditions
- Soluble in water and ethanol
- **Hepatotoxic** and **hepatocarcinogenic** agent
- Induced rat liver cirrhosis which is to resemble the human liver cirrhosis



# Experimental Design



# ALT and AST Level

## ALT

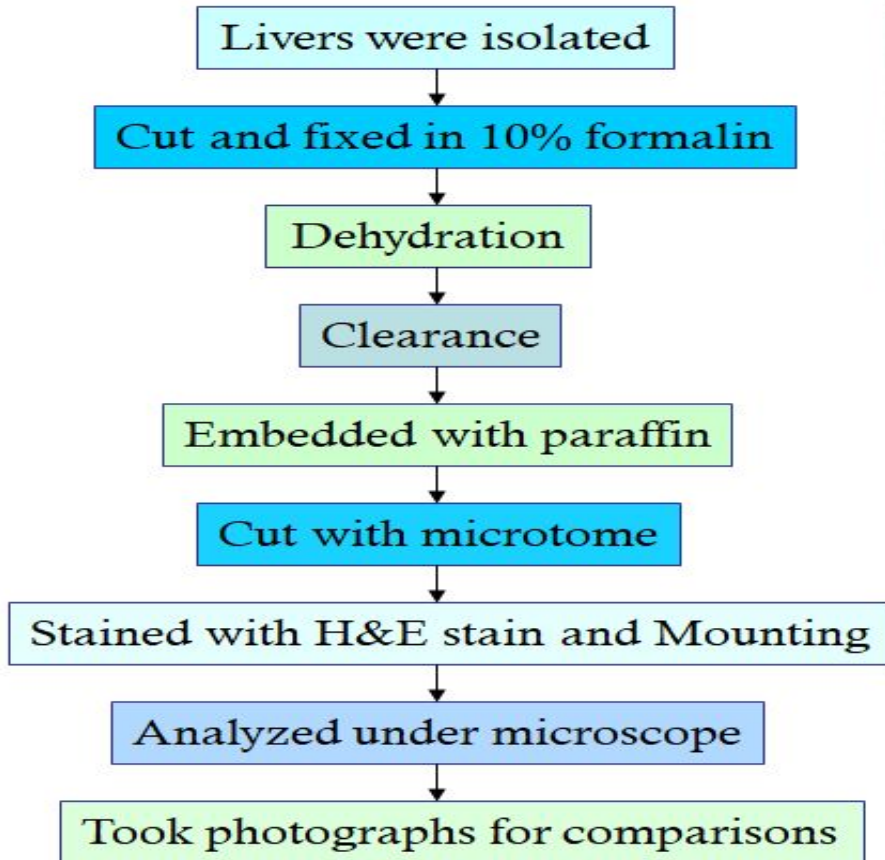
- Alanine aminotransferase
- enzyme produced within the hepatocytes
- leaks into the bloodstream
  - caused the level in the blood increased when the cells are damaged
- the most sensitive marker for liver cell damage.
- may or may not correlate with the degree of cell death or inflammation

## AST

- Aspartate aminotransferase
- enzyme that reflects hepatocytes injury
- less specific for liver disease
  - might also rise in other situation such as during heart attack

# ratio between AST to ALT is highly specific but not diagnostic for the presence of cirrhosis

# Preparation of Histology Slides



# **RESULTS AND DISCUSSION**

# AST and ALT Enzyme Level

Group	Type of Treatment (oral + i.p. injection)	Enzyme Level (IU/L)	
		AST	ALT
Normal Control	DW + DW	157.00 ± 6.08	60.33 ± 7.22
LD, 50 mg/kg compound	Compound + TAA	*185.17 ± 8.78	86.83 ± 7.19
HD, 50 mg/kg compound	Compound + TAA	*170.00 ± 7.00	78.00 ± 7.11
Silymarin 50mg/kg Positive control	Silymarin + TAA	165.33 ± 6.29	73.17 ± 2.28
Cirrhosis Control	DW + TAA	*369.60 ± 24.27	*124.10 ± 12.42

Table 1: Enzymes level for different groups.

\* Indicates  $p < 0.05$  when compared to value from cirrhosis control group

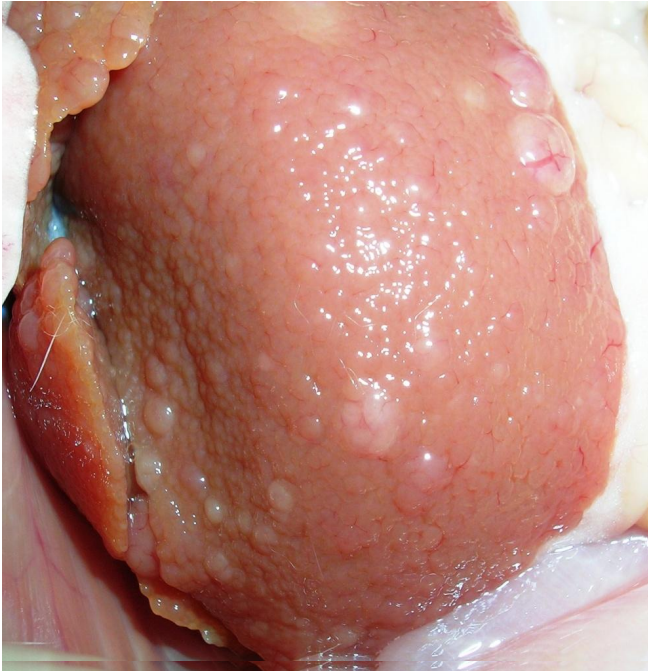
# Gross Images

Normal rat liver



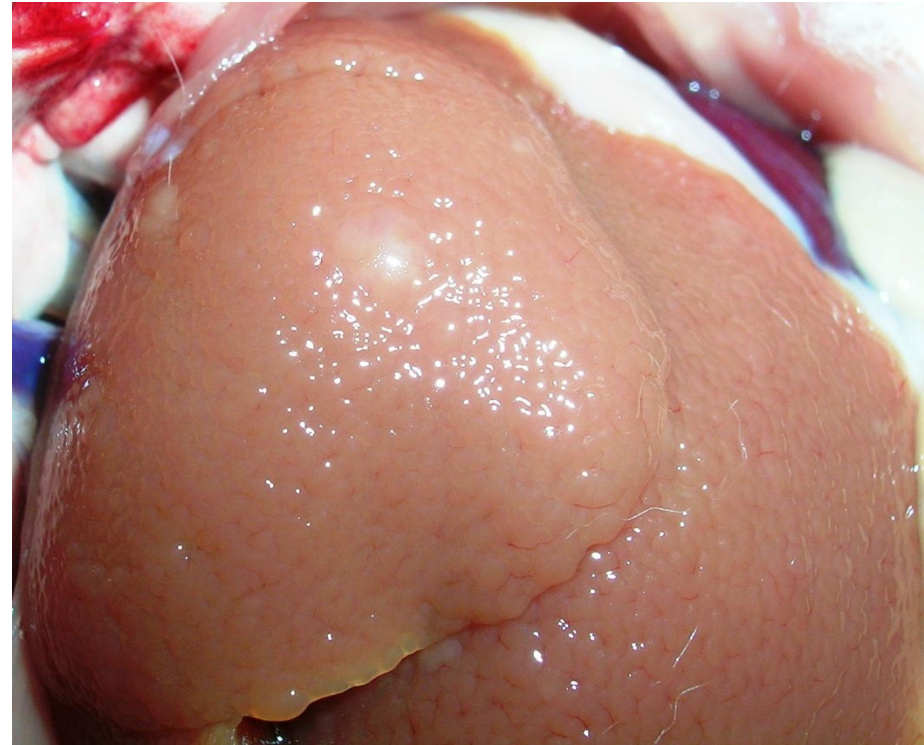
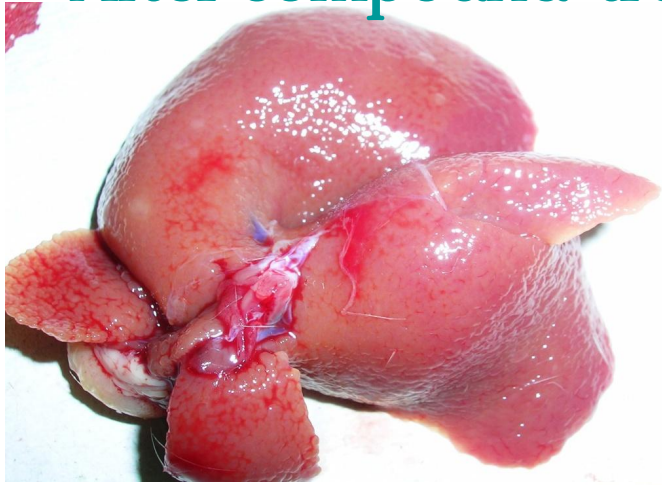
# Gross Images

After Induced with TAA



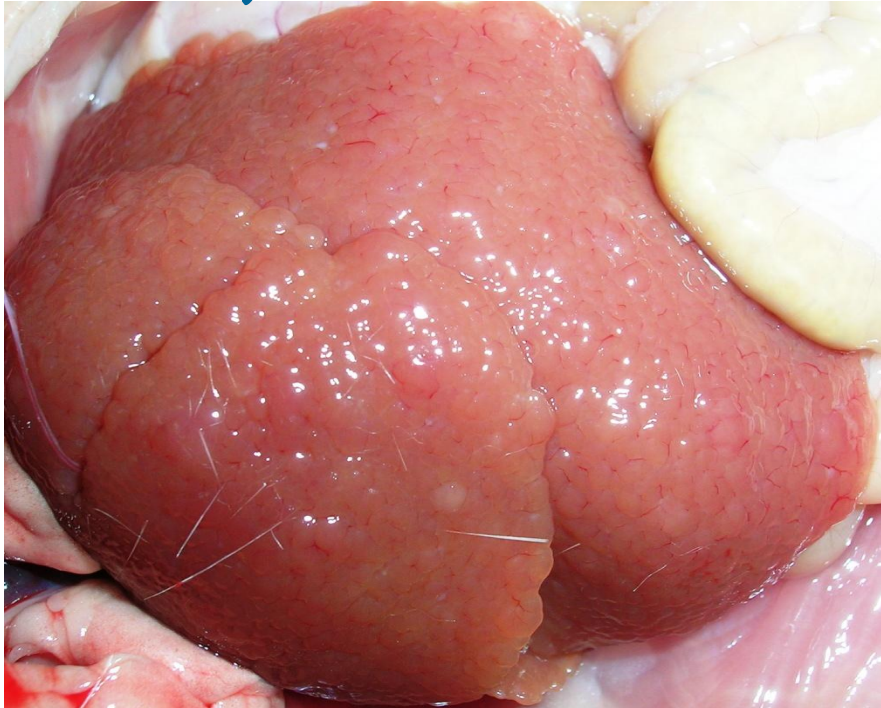
# Gross Images

After compound treatment



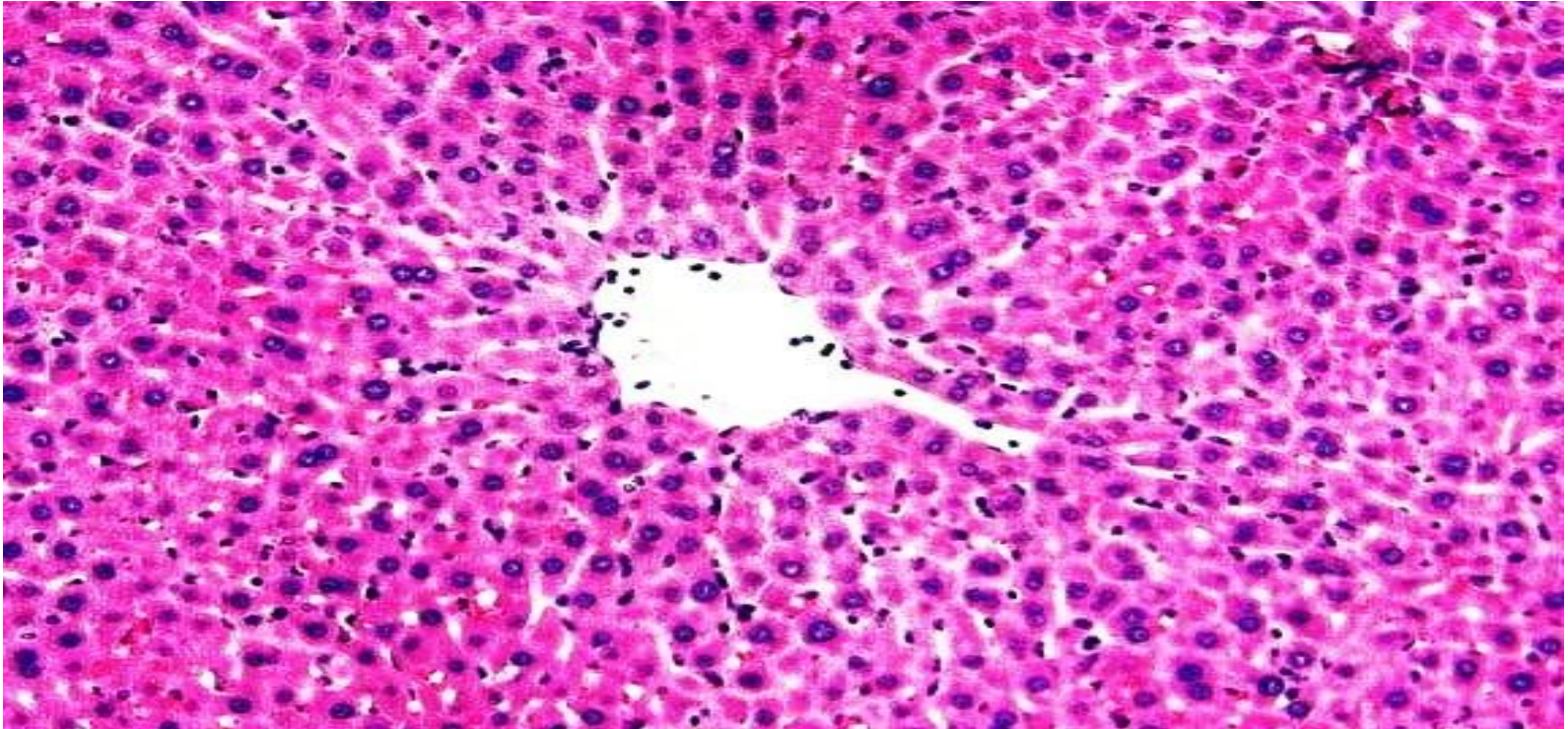
# Gross Images

After Sylmarin Treatment



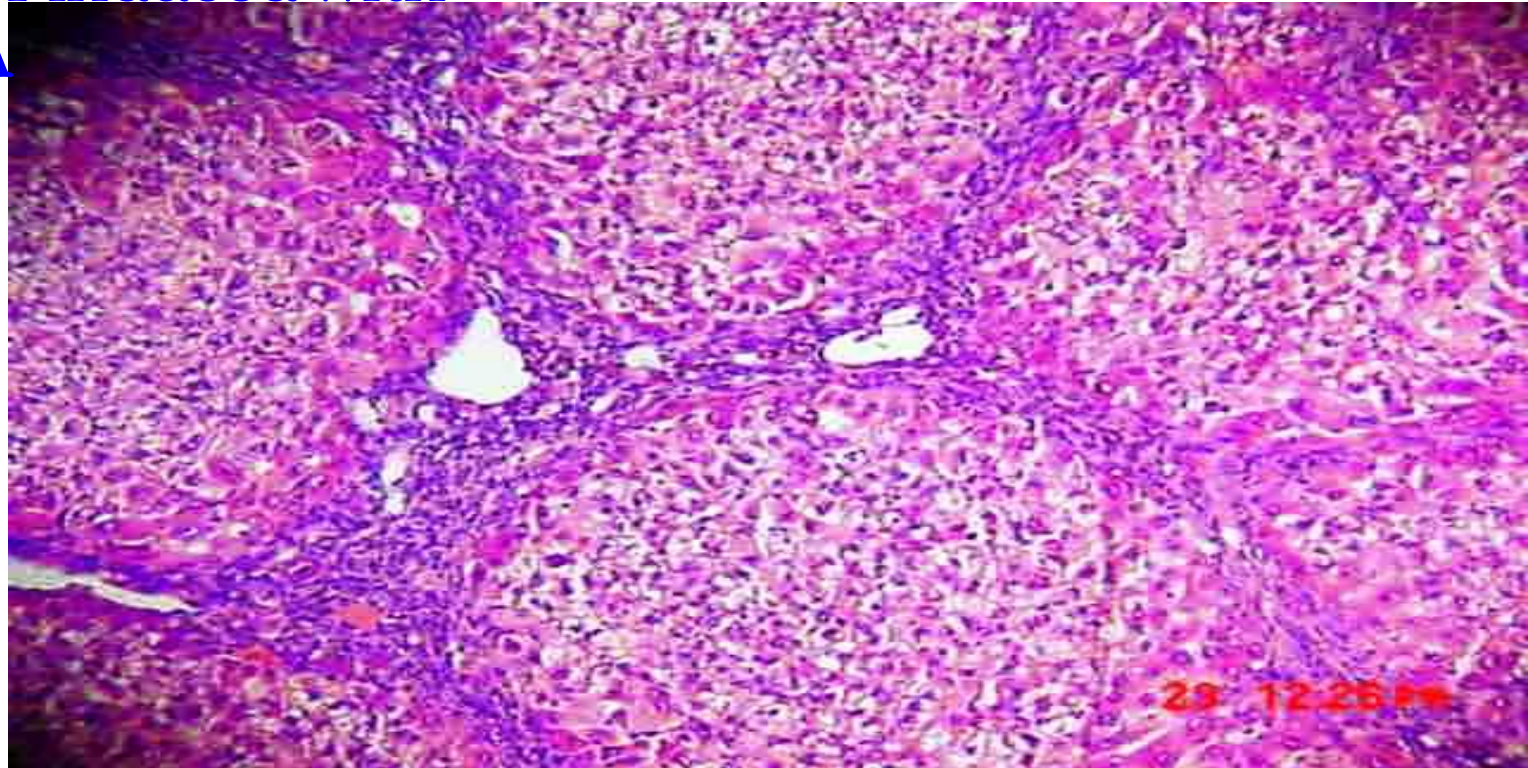
# Histology

## Normal liver



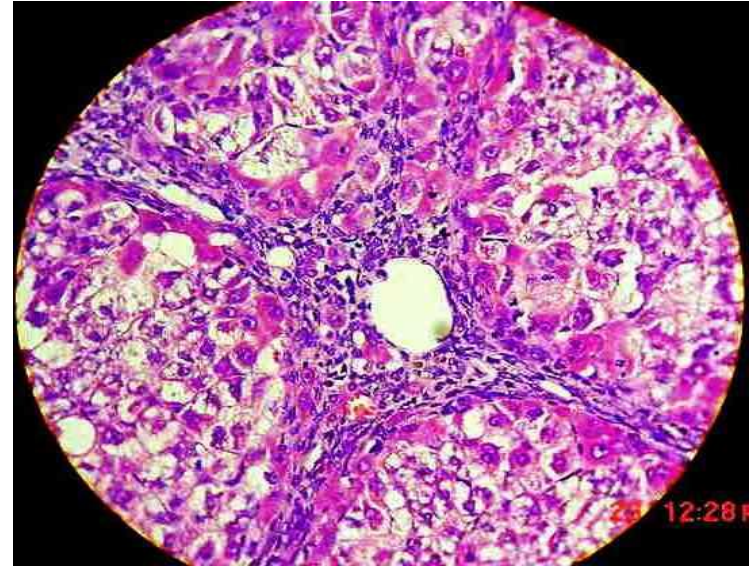
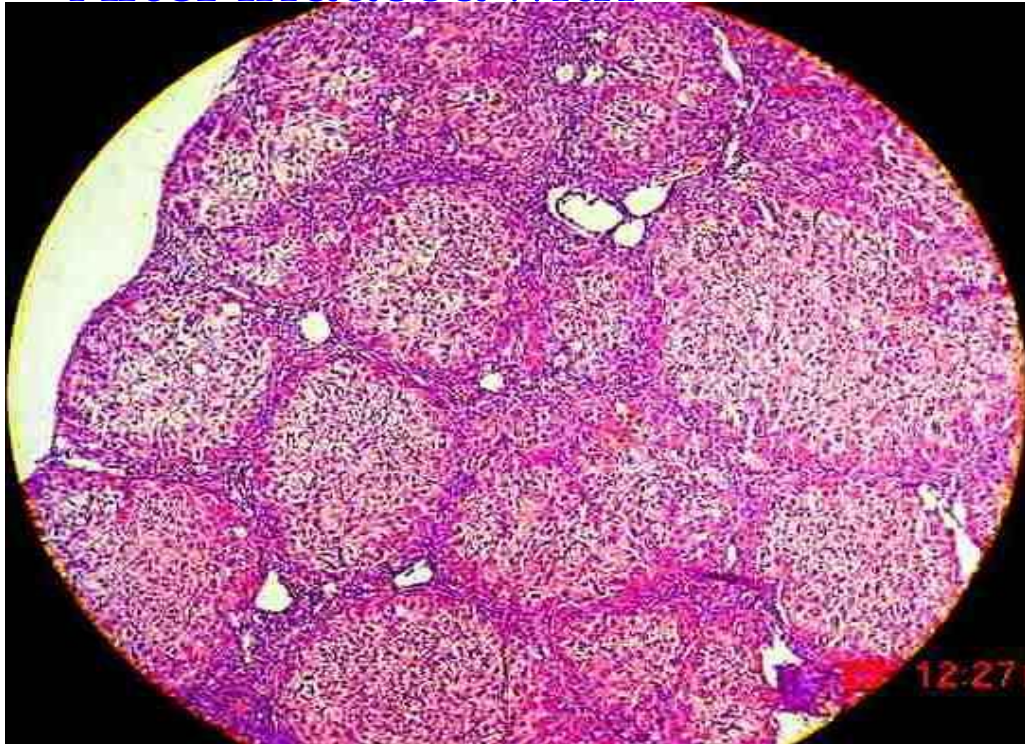
# Histology

After induced with  
TAA



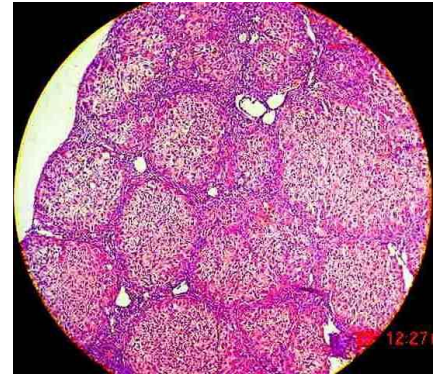
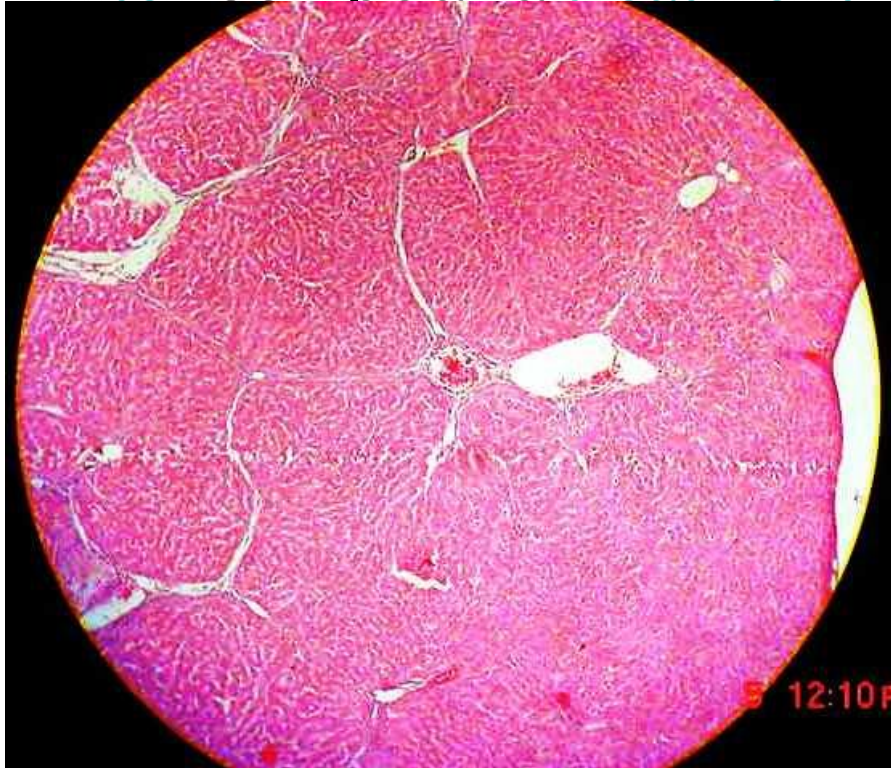
# Histology

After induced with



# Histology

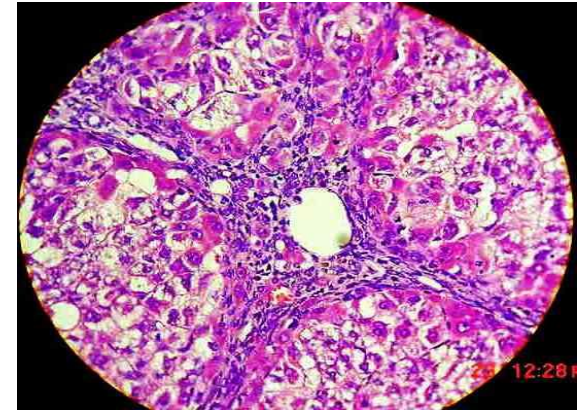
After Compound treatment



Cirrhosis control (TAA)

# Histology

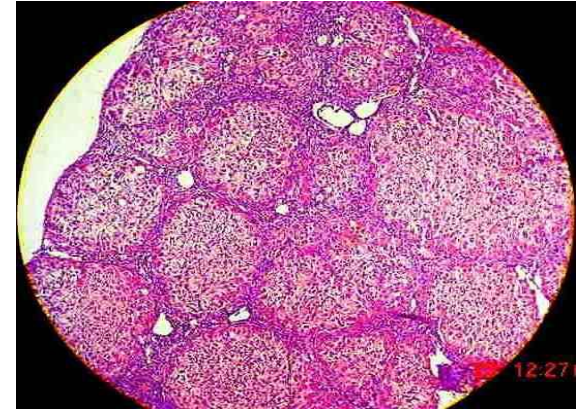
After silymarin treatment



Cirrhosis control (TAA)

# Histology

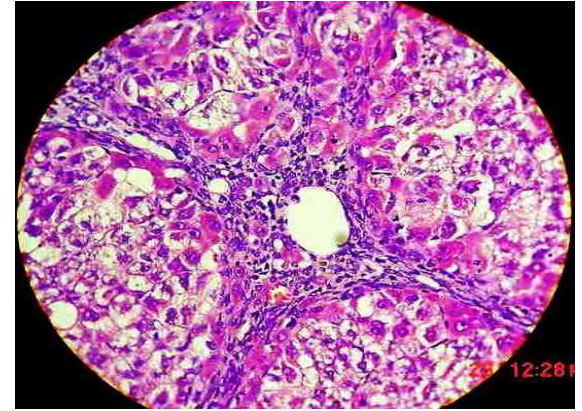
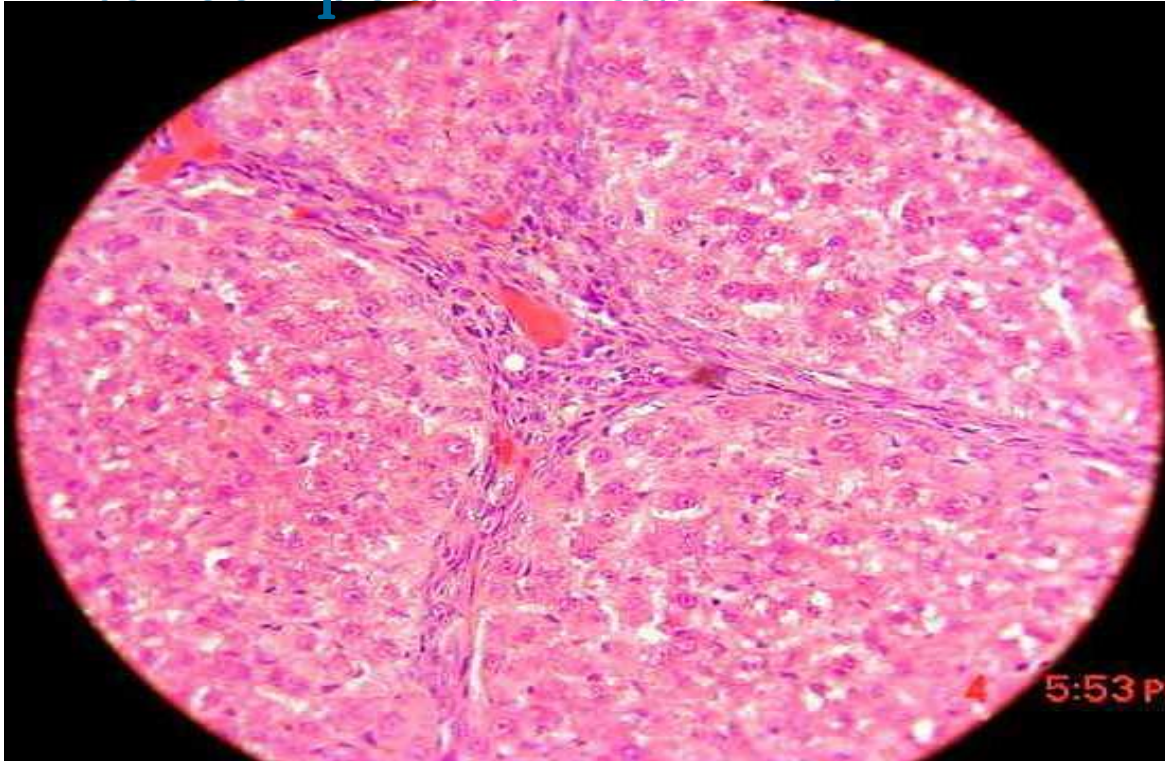
After Compound Treatment



Positive control (TAA)

# Histology

After compound Treatment



Positive control (TAA)

# CONCLUSION

- Compound has significant effective to relieve liver cirrhosis in TAA-induced liver cirrhosis.

THANK YOU

# References

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