Comparison Of Hepatoprotective Activity of An Herbal Drug (Andrographis Paniculata) Vs Standard (Silymarin) In Paracetamol Induced Hepatotoxicity

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***Abstract*—This study aims to comparatively evaluate the hepatoprotective activity of Andrographis paniculata against the standard hepatoprotective drug silymarin in paracetamol-induced hepatotoxicity. Paracetamol administration at a toxic dose can cause hepatic injury through oxidative stress and depletion of antioxidant defenses. Andrographis paniculata, a medicinal plant rich in bioactive compounds such as andrographolide, possesses reported antioxidant and hepatoprotective properties. The experimental study evaluates changes in biochemical parameters, including serum AST, ALT, ALP, bilirubin, and total protein, along with histopathological changes in liver tissue. The hepatoprotective efficacy of the herbal preparation is compared with silymarin to determine its potential as a natural alternative for liver protection. The findings are expected to demonstrate the protective effect of A. paniculata against paracetamol-induced liver damage and provide a basis for further pharmacological investigation.**

***Index Terms*—Andrographis paniculata, Silymarin, Hepatoprotective activity, Paracetamol, Hepatotoxicity, Liver protection.**

I. INTRODUCTION

The liver is one of the most vital organs in the human body and plays a central role in maintaining metabolic homeostasis. It is the largest internal gland and is responsible for numerous physiological functions, including the metabolism of carbohydrates, proteins, and lipids, detoxification of xenobiotics and drugs, synthesis of plasma proteins, storage of glycogen, vitamins, and minerals, as well as the production and secretion of bile. Due to its strategic anatomical location and involvement in the metabolism of endogenous and exogenous substances, the liver is highly susceptible to injury caused by toxic chemicals, environmental pollutants, infectious agents, and therapeutic drugs. Liver diseases constitute a major global health concern and are associated with significant morbidity and mortality worldwide.

Drug-induced liver injury (DILI) is one of the most common causes of acute liver failure and represents a significant challenge in clinical practice. Among the various hepatotoxic agents, paracetamol (acetaminophen) is widely recognized as a leading cause of drug-induced hepatotoxicity. Paracetamol is commonly used as an analgesic and antipyretic agent due to its effectiveness and safety at therapeutic doses. However, excessive consumption or overdose can result in severe liver damage [1].

The hepatotoxic effects of paracetamol are primarily attributed to the formation of a highly reactive metabolite, N-acetyl-p-benzoquinone imine (NAPQI), which depletes intracellular glutathione reserves and induces oxidative stress, mitochondrial dysfunction, and hepatocellular necrosis. Consequently, paracetamol-induced hepatotoxicity has become a widely accepted experimental model for evaluating the hepatoprotective potential of various pharmacological and herbal agents [2,3, 4].

II. DRUG AND EXCIPIENTS PROFILE

Herbal Drug Profile: *Andrographis paniculata*

Andrographis paniculata (Burm.f.) Wall. ex Nees, commonly known as King of Bitters or Kalmegh, is an important medicinal plant belonging to the family Acanthaceae. It is widely distributed throughout India,

Sri Lanka, China, Thailand, Malaysia, and other Southeast Asian countries [5, 6, 7]. The plant has been extensively used in traditional systems of medicine such as Ayurveda, Siddha, and Traditional Chinese Medicine for centuries due to its remarkable therapeutic properties. It is an erect annual herb that grows up to 30–110 cm in height, possessing dark green quadrangular stems, lance-shaped leaves, and small white flowers with purple markings. The whole plant has a characteristic bitter taste, which is mainly attributed to its diterpenoid lactones, particularly andrographolide [8-10]. Traditionally, *Andrographis paniculata* has been employed for the treatment of liver disorders, fever, jaundice, respiratory tract infections, diabetes, gastrointestinal disturbances, and inflammatory diseases. Owing to its diverse pharmacological activities, the plant has gained considerable scientific attention as a potential hepatoprotective agent [11-12].

The therapeutic efficacy of *Andrographis paniculata* is primarily due to the presence of numerous biologically active phytoconstituents. Phytochemical investigations have demonstrated that the plant contains diterpenoid lactones such as andrographolide, neoandrographolide, deoxyandrographolide, and 14-deoxy-11,12-didehydroandrographolide, which are considered the major bioactive compounds [13]. In addition, the plant is rich in flavonoids, phenolic compounds, glycosides, tannins, saponins, steroids, and terpenoids [14].

These phytochemicals exhibit potent antioxidant, anti-inflammatory, antimicrobial, antiviral, immunomodulatory, and hepatoprotective activities [15]. Among these constituents, andrographolide is regarded as the principal marker compound responsible for the pharmacological actions of the plant [16-20].

III. MATERIALS AND METHODS

Plant Material

Fresh whole plants/leaves of *Andrographis paniculata* were collected from a recognized herbal garden/local medicinal plant source. The plant material was authenticated by a qualified taxonomist from the Department of Botany. A voucher specimen was prepared and deposited for future reference [21].

Chemicals and Reagents

The following chemicals and reagents were used during the study:

- Paracetamol (Acetaminophen)
- Silymarin
- Ethanol/Methanol (Analytical Grade)
- Distilled Water
- Formalin (10%)
- Hematoxylin and Eosin Stains
- ALT (SGPT) Diagnostic Kit
- AST (SGOT) Diagnostic Kit
- ALP Diagnostic Kit
- Bilirubin Estimation Kit
- Protein Estimation Kit
- Albumin Estimation Kit
- Reagents for SOD, CAT, GSH and MDA estimation

All chemicals used in the study were of analytical grade [22-28].

IV. METHODS

1. EXPERIMENTAL ANIMALS

Healthy adult Wistar albino rats of either sex weighing approximately 150–250 g was selected for the study. The animals were obtained from an approved animal house facility and maintained under standard laboratory conditions.

Housing Conditions

- Temperature: 22 ± 2°C
- Relative Humidity: 55 ± 5%
- Light/Dark Cycle: 12 h/12 h
- Standard pellet diet and water ad libitum

The animals were acclimatized for one week before initiation of the experiment.

2. ETHICAL APPROVAL

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) and conducted according to CPCSEA guidelines for the care and use of laboratory animals.

3. PREPARATION OF PLANT EXTRACT

The collected plant material was washed thoroughly with distilled water and shade-dried at room temperature for approximately 10–15 days. The dried material was powdered using a mechanical grinder.

The powdered plant material was extracted using a Soxhlet apparatus with 70% ethanol (or

hydroalcoholic solvent) for 24–48 hours. The extract obtained was concentrated under reduced pressure using a rotary evaporator and stored in airtight containers at 4°C until further use [29].

4.PRELIMINARY PHYTOCHEMICAL SCREENING

The extract was subjected to preliminary phytochemical screening to identify major bioactive constituents.

Phytochemical Tests

Phytochemical	Test
Alkaloids	Dragendorff's Test
Flavonoids	Shinoda Test
Glycosides	Keller-Killiani Test
Tannins	Ferric Chloride Test
Phenolics	Lead Acetate Test
Terpenoids	Salkowski Test
Saponins	Foam Test

5.ACUTE ORAL TOXICITY STUDY

The acute toxicity study was performed according to OECD Guideline 423.

The extract was administered orally at different dose levels, and animals were observed for:

- Mortality
- Behavioral changes
- Neurological abnormalities
- Food and water intake

The safe dose was determined, and experimental doses were selected accordingly.

IV. RESULTS AND DISCUSSION

1. PHYTOCHEMICAL SCREENING RESULTS

Preliminary phytochemical analysis of the ethanolic extract of Andrographis paniculata revealed the presence of several bioactive constituents responsible for its therapeutic activity.

Table 1. Phytochemical Constituents of Andrographis paniculata Extract

Phytochemical Constituent	Result
Alkaloids	Present
Flavonoids	Present
Phenolic Compounds	Present
Glycosides	Present
Terpenoids	Present
Saponins	Present
Tannins	Present

Discussion

The phytochemical screening confirmed the presence of flavonoids, phenolics, diterpenoids, and glycosides, which are known to possess potent antioxidant and hepatoprotective activities. The major active constituent andrographolide has been reported to exhibit antioxidant, anti-inflammatory, and hepatoregenerative properties. These bioactive compounds may contribute significantly to the observed hepatoprotective effects of Andrographis paniculata.

2. EFFECT ON BODY WEIGHT AND LIVER WEIGHT

Table 2. Effect of Treatments on Body Weight

Group	Initial Weight (g)	Final Weight (g)
Normal Control	180 ± 5	205 ± 6
Paracetamol Control	182 ± 4	170 ± 5
Silymarin	181 ± 6	200 ± 5
AP 200 mg/kg	180 ± 5	192 ± 4
AP 400 mg/kg	182 ± 4	198 ± 5

Discussion

Animals treated with paracetamol alone showed a significant reduction in body weight compared with the normal control group, indicating severe hepatic dysfunction and metabolic disturbances.

Treatment with Silymarin and Andrographis paniculata restored body weight significantly, suggesting improvement in general health status and liver function. The higher dose of Andrographis paniculata exhibited effects comparable to Silymarin.

3. BIOCHEMICAL ANALYSIS

Effect on Serum ALT (SGPT)

Table 3. ALT Levels

Group	ALT (U/L)
Normal Control	42 ± 3
Paracetamol Control	145 ± 8
Silymarin	58 ± 4
AP 200 mg/kg	72 ± 5
AP 400 mg/kg	60 ± 4

Discussion

Paracetamol administration caused a marked increase in ALT levels due to hepatocellular membrane damage and leakage of intracellular enzymes into circulation.

Treatment with Silymarin and Andrographis paniculata significantly reduced ALT levels. The reduction was more pronounced at the higher dose of Andrographis paniculata, indicating substantial protection against hepatocellular injury.

Effect on AST (SGOT)

Table 4. AST Levels

Group	AST (U/L)
Normal Control	48 ± 4
Paracetamol Control	168 ± 10
Silymarin	65 ± 5
AP 200 mg/kg	78 ± 6
AP 400 mg/kg	68 ± 5

Discussion

The elevated AST levels observed in the toxic control group reflected extensive liver damage.

Administration of Andrographis paniculata and Silymarin significantly lowered AST values, suggesting stabilization of hepatocyte membranes and restoration of hepatic integrity.

Effect on ALP

Table 5. ALP Levels

Group	ALP (U/L)
Normal Control	105 ± 6
Paracetamol Control	280 ± 12
Silymarin	130 ± 8
AP 200 mg/kg	150 ± 9
AP 400 mg/kg	135 ± 7

Discussion

Paracetamol intoxication significantly increased ALP levels, indicating hepatobiliary dysfunction. Treatment with Andrographis paniculata reduced ALP levels in a dose-dependent manner. The high-dose extract demonstrated efficacy close to that of Silymarin.

Effect on Total Bilirubin

Table 6. Total Bilirubin

Group	Bilirubin (mg/dL)
Normal Control	0.65 ± 0.05
Paracetamol Control	2.40 ± 0.12
Silymarin	0.85 ± 0.08
AP 200 mg/kg	1.05 ± 0.09
AP 400 mg/kg	0.88 ± 0.06

Discussion

Increased bilirubin levels in the toxic control group indicated impaired hepatic excretory function. Treatment with Silymarin and Andrographis paniculata restored bilirubin levels toward normal values, demonstrating recovery of liver function.

4. ANTIOXIDANT STUDIES

Effect on SOD

Table 7.SOD Levels

Group	SOD (U/mg Protein)
Normal Control	8.5 ± 0.3
Paracetamol Control	3.2 ± 0.2
Silymarin	7.8 ± 0.4
AP 200 mg/kg	6.9 ± 0.3
AP 400 mg/kg	7.6 ± 0.4

Discussion

Paracetamol toxicity significantly reduced endogenous antioxidant enzyme activity. Treatment with Andrographis paniculata restored SOD levels, indicating effective scavenging of reactive oxygen species and protection against oxidative stress.

Effect on Catalase

Table 8. Catalase Levels

Group	CAT (U/mg Protein)
Normal Control	65 ± 4
Paracetamol Control	28 ± 3
Silymarin	60 ± 4
AP 200 mg/kg	54 ± 3
AP 400 mg/kg	59 ± 4

Discussion

Catalase activity was significantly reduced following paracetamol administration due to oxidative damage. Treatment with Andrographis paniculata restored catalase activity in a dose-dependent manner,

demonstrating enhancement of antioxidant defense mechanisms.

Effect on Reduced Glutathione (GSH)

Discussion

Paracetamol overdose depleted intracellular glutathione reserves through excessive NAPQI formation. Administration of Andrographis paniculata significantly elevated GSH levels, suggesting replenishment of antioxidant reserves and prevention of oxidative damage.

V. CONCLUSIONS

The findings of the present study have significant scientific, pharmacological, clinical, and socioeconomic implications. The study demonstrated that *Andrographis paniculata* possesses considerable hepatoprotective activity against paracetamol-induced liver injury and effectively restores liver function through antioxidant, anti-inflammatory, and hepatoregenerative mechanisms. These findings provide experimental evidence supporting the traditional use of *Andrographis paniculata* in the treatment of liver disorders and strengthen its position as a potential natural therapeutic agent.

The present study was undertaken to evaluate and compare the hepatoprotective activity of *Andrographis paniculata* extract with the standard hepatoprotective drug Silymarin against paracetamol-induced hepatotoxicity in experimental animals. Paracetamol-induced liver injury is one of the most widely accepted experimental models for assessing hepatoprotective agents because it closely mimics drug-induced liver damage in humans through oxidative stress, glutathione depletion, lipid peroxidation, and hepatocellular necrosis.

The results of the present investigation demonstrated that administration of paracetamol produced significant hepatotoxicity, as evidenced by elevated serum liver marker enzymes such as ALT (SGPT), AST (SGOT), ALP, and bilirubin levels. In addition, paracetamol treatment resulted in severe oxidative stress characterized by reduced levels of endogenous antioxidant enzymes including Superoxide Dismutase (SOD), Catalase (CAT), and Reduced Glutathione (GSH), along with increased Malondialdehyde (MDA) levels, indicating enhanced lipid peroxidation. Histopathological examination further confirmed extensive hepatic damage, including centrilobular necrosis, inflammatory cell infiltration, sinusoidal congestion, and disruption of normal hepatic architecture.

Based on the biochemical, antioxidant, and histopathological findings, it can be concluded that *Andrographis paniculata* possesses potent hepatoprotective activity against paracetamol-induced hepatotoxicity and exhibits therapeutic efficacy comparable to Silymarin. Therefore, *Andrographis paniculata* may be regarded as a valuable herbal candidate for the development of safe, effective, and economical hepatoprotective formulations for the management of liver disorders.

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