RESEARCH PAPER

Hepatoprotective Activity of Vijaysar Heartwood Extract Against Drug-Induced Liver Injury in Wistar Rats

Purra Anuradha[1], Atul Arunrao Kulkarni[2], Aanchal Sharma[3], Rajesh Dodiya[4], Shilpy Shakya[5], Harmanbir Kaur[6], Priyanka Bhardwaj[7], Ishan Panchal[8*]

[1]Associate Professor, Department of Zoology, Government Degree College(A) Khairatabad, Hyderabad 500004, India

[2]Associate Professor, College of Pharmaceutical Sciences PIMS (DU) Loni, Dist.- Ahilyanagar, Maharashtra - 413736, India

[3]Assistant Professor, Chandigarh Group of Colleges Jhanjeri, Mohali - 140307, Punjab, India, Chandigarh School of Business, Department of Allied Health Sciences

[4]Associate Professor, School of Pharmacy, Faculty of Pharmacy, Parul University, Vadodara, Gujarat 380058, India

[5]Associate Professor, Department of Zoology, LSSSS Government Degree College Mant Mathura, Uttar Pradesh 281202, India

[6]Assistant Professor, Saraswati College of Pharmacy, SGC Group, Gharuan-140413, Mohali, Punjab, India

[7]Assistant Professor, Saraswati College of Pharmacy, SGC Group, Gharuan-140413, Mohali, Punjab, India

[8*]Professor, Parul College of Pharmacy and Research, Faculty of Pharmacy, Parul University, Ahmedabad Campus, Bopal, Ahmedabad, Gujarat 380058. Email: Ishan.panchal35140@paruluniversity.ac.in (Corresponding Author)

ABSTRACT

Background: Hyperthyroidism, whether endogenous or drug induced by L-thyroxine, is characterized by a hypermetabolic state that accelerates oxidative stress and leads to hepatic dysfunction and hepatocellular injury. Pterocarpus marsupium Roxb. (Fabaceae), traditionally known as Vijaysar, is widely used in Indian systems of medicine for the management of metabolic and inflammatory disorders.

Objective: The present study aimed to evaluate the hepatoprotective and antioxidant potential of the hydroalcoholic extract of P. marsupium heartwood (HAEBP) against L-thyroxine induced liver injury in Wistar rats.

Methods: Adult male Wistar rats were divided into five groups (n = 6). Hyperthyroidism and associated hepatic oxidative stress were induced by oral administration of L-thyroxine (600 µg/kg/day) for 12 consecutive days. After induction, animals were treated with HAEBP at doses of 200 mg/kg and 400 mg/kg, or the standard drug propylthiouracil (PTU, 10 mg/kg) for 15 days. Hepatic injury was assessed by measuring serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Oxidative stress parameters in liver homogenates included lipid peroxidation (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT).

Results: L-thyroxine administration produced a significant ($P < 0.01$) elevation in serum AST (205.40 ± 4.25 IU/L) and ALT (128.95 ± 5.75 IU/L) compared with normal controls, indicating marked hepatocellular damage. Liver tissues showed increased MDA levels (4.70 ± 0.90 nM/mg protein) along with depletion of antioxidant defenses (GSH, SOD, CAT). Treatment with HAEBP at 400 mg/kg significantly ($P < 0.01$) reduced hepatic injury, lowering AST to 135.40 ± 3.30 IU/L and ALT to 88.80 ± 3.95 IU/L. The extract also suppressed lipid peroxidation (MDA: 2.55 ± 0.65 nM/mg protein) and restored antioxidant status, with effects comparable to PTU.

Conclusion: The hydroalcoholic extract of Pterocarpus marsupium exhibits strong hepatoprotective activity against L-thyroxine induced liver toxicity. The effect appears to be mediated through free radical scavenging, inhibition of lipid peroxidation, and enhancement of endogenous hepatic antioxidant defenses.

Keywords: Pterocarpus marsupium, L-thyroxine, hepatoprotection, oxidative stress, lipid peroxidation, antioxidants

How to cite this article: Anuradha P, Kulkarni AA, Sharma A, Dodiya R, Shakya S, Kaur H, Bhardwaj P, Panchal I. Hepatoprotective Activity of Vijaysar Heartwood Extract Against Drug-Induced Liver Injury in Wistar Rats. Int J Drug Deliv Technol. 2026;16(19s): 684-691. DOI: 10.25258/ijddt.16.19s.79

Source of support: Nil.

Conflict of interest: None

1. Introduction

The thyroid gland plays a pivotal role in maintaining metabolic homeostasis by secreting thyroid hormones, thyroxine (T4) and triiodothyronine (T3), which regulate energy expenditure, protein synthesis, and mitochondrial respiration (Guyton & Hall, 2006). While these hormones are essential for physiological development, their dysregulation, particularly in hyperthyroidism, precipitates a hypermetabolic state that severely impacts hepatic function. The liver is the primary organ responsible for the metabolism of thyroid hormones, making it intrinsically susceptible to injury during states of thyroid dysfunction (Smith et al., 2024). The clinical pathology of hyperthyroidism, whether endogenous or induced by L-thyroxine overdose, is closely linked to oxidative stress. Excess thyroid hormones accelerate the basal metabolic rate (BMR), leading to a supraphysiological demand for oxygen in mitochondrially active tissues. This uncoupling of oxidative phosphorylation results in excessive generation of reactive oxygen species (ROS), such as superoxide radicals and hydrogen peroxide, which overwhelm the liver's antioxidant defense mechanisms (Mancini et al., 2020). Recent studies have elucidated the "oxidative stress–inflammation axis" in hyperthyroid-induced hepatotoxicity, where ROS accumulation triggers lipid peroxidation of hepatocyte membranes, releasing inflammatory cytokines and apoptotic markers (El-Saeed et al., 2024). This oxidative assault disrupts the structural integrity of liver cells, leading to leakage of intracellular enzymes into the circulation. Clinically, this is manifested as elevated serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), accompanied by depletion of endogenous antioxidants such as reduced glutathione (GSH) and superoxide dismutase (SOD) (Assaei et al., 2014; Zhang et al., 2024). While conventional antithyroid drugs, such as propylthiouracil, are used to manage hormone levels, they do not directly ameliorate oxidative hepatic injury and are themselves associated with hepatotoxic side effects (Resch et al., 2002). Consequently, there is a growing need for therapeutic agents that can simultaneously regulate metabolic function and provide cytoprotection against oxidative liver injury. Pterocarpus marsupium Roxb., commonly known as Vijaysar or the Indian kino tree, is a deciduous tree belonging to the family Fabaceae and is widely distributed across the Indian subcontinent. It holds a valued place in traditional systems of medicine, particularly Ayurveda and Unani, where its heartwood and bark are prescribed for managing metabolic disorders, inflammation, and hepatic ailments (Kumar, 2024). Ethnobotanical reviews describe the use of water stored in Vijaysar heartwood tumblers as a rejuvenator and a remedy for "Prameha" (diabetes) and digestive disorders, suggesting intrinsic metabolic regulatory properties (Rout et al., 2009; Majeed et al., 2025). The pharmacological versatility of P. marsupium is supported by its robust phytochemical profile. Recent chromatographic analyses have identified a diverse array of bioactive polyphenols in the heartwood, including pterostilbene, (−)-epicatechin, marsupsin, and pterosupin (Chothe, 2026). Among these, pterostilbene and epicatechin have received significant attention for their potent antioxidant and free radical scavenging activities. In vitro and in vivo studies indicate that these flavonoids can inhibit lipid peroxidation and restore cellular antioxidant enzymes, providing a mechanistic basis for the plant's therapeutic potential (Tiwari et al., 2025). Furthermore, the extract has demonstrated hepatoprotective effects against chemical toxins such as carbon tetrachloride, attributed to its membrane stabilizing and anti-inflammatory properties (Mankani et al., 2005; Chothe, 2026). Despite extensive literature on its antidiabetic and general antioxidant properties, a critical research gap remains regarding the specific protective efficacy of P. marsupium against hormone-induced oxidative liver injury. Most hepatoprotective studies have focused on chemical hepatotoxins, while the distinct pathophysiological model of L-thyroxine-induced hypermetabolic liver injury remains largely unexplored in the context of this plant. Given recent identification of novel bioactive compounds in Vijaysar that modulate oxidative stress pathways (Majeed et al., 2025), it is hypothesized that the heartwood extract may offer a targeted therapeutic strategy for hyperthyroid-associated hepatotoxicity. Therefore, the present study aims to scientifically validate the hepatoprotective activity of the hydroalcoholic extract of Pterocarpus marsupium heartwood against L-thyroxine-induced liver injury in Wistar rats. By evaluating biochemical markers of hepatic damage (AST, ALT) and oxidative stress indices (MDA, GSH, SOD, catalase), this research seeks to generate evidence supporting the plant's utility in managing metabolic liver dysfunction.

2. Materials and Methods

2.1. Collection and Authentication of Plant Material

The heartwood of *Pterocarpus marsupium* Roxb. (Fabaceae), commonly known as Vijaysar, was selected for the study. The plant material was collected from the foothills of the Himalayas. The specimen was identified and authenticated at Department of Botany, Hemwati Nandan Bahuguna Garhwal University, Srinagar (Uttarakhand).

2.2. Preparation of Plant Extract

The collected plant material was shade dried to prevent degradation of thermolabile phytoconstituents. The dried heartwood was coarsely powdered. The powdered material was subjected to successive extraction using solvents of increasing polarity, beginning with petroleum ether for defatting, followed by methanol and water. The final hydroalcoholic extract (HAEBP) was concentrated, dried, and stored in a desiccator until further pharmacological evaluation. For experimental administration, the extract was dissolved in sterile water Harborne, J. B. (1998).

2.3. Drugs and Chemicals

L-thyroxine (T4) was procured from Sigma, USA, and used to induce hyperthyroidism and associated oxidative stress. Propylthiouracil (PTU), used as the standard reference drug, was obtained from Macleods Pharmaceuticals Ltd., Mumbai. Diagnostic kits for estimation of serum biomarkers (AST and ALT) were obtained from commercial suppliers. All other chemicals and reagents used were of analytical grade.

2.4. Experimental Animals

Adult male Wistar albino rats weighing 180-220 g were used. The animals were housed in polycarbonate cages, with four animals per cage, under standard laboratory conditions at a temperature of 20–25°C and relative humidity of 40-45%. A 12-hour light and dark cycle was maintained. Animals were provided a standard rodent pellet diet and water ad libitum.

2.5. Ethical Approval

The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) with CPCSEA, Government of India.

2.6. Experimental Design

After the 12-day induction period, animals were randomly divided into five groups (n = 6) and treated for 15 days as follows:

Group I (Normal Control): Received normal saline (10 ml/kg, p.o.).

Group II (Disease Control): Received L-thyroxine + distilled water (p.o.).

Group III (Standard Control): Received L-thyroxine + PTU (10 mg/kg, i.p.).

Group IV (Test Group I): Received L-thyroxine + HAEBP (200 mg/kg, p.o.).

Group V (Test Group II): Received L-thyroxine + HAEBP (400 mg/kg, p.o.).

2.7 Induction of Hepatic Injury

Hepatic oxidative stress secondary to hyperthyroidism was induced in experimental rats by oral administration of L-thyroxine (T4) at a dose of 600 µg/kg/day for 12 consecutive days. The dose and treatment schedule were selected according to the established protocol described by Panda and Kar (1998), which reliably produces a hypermetabolic state and oxidative toxicity in rodent models.

2.8 Biochemical Estimation

At the end of the experimental period, blood samples were collected for serum biochemical analysis and the animals were sacrificed for liver isolation. Liver tissues were excised, washed in ice-cold saline, and homogenized in chilled phosphate buffer. Total protein content in the tissue homogenate was estimated using the Folin–Ciocalteu phenol reagent method described by Lowry et al. (1951), and enzyme activities were expressed per milligram of protein.

2.8.1 Assessment of Hepatocellular Damage (AST and ALT)

Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were determined by a colorimetric method to assess hepatocellular membrane integrity. Estimation was carried out according to the method of Reitman and Frankel (1957) using commercially available diagnostic kits based on the reaction of transaminases with 2,4-dinitrophenylhydrazine.

2.8.2 Estimation of Lipid Peroxidation (LPO)

Lipid peroxidation in liver tissue was quantified by measuring malondialdehyde (MDA) levels as an index of oxidative membrane damage. The assay followed the method of Ohkawa et al. (1979). MDA reacts with thiobarbituric acid to form a pink chromogen, and absorbance was measured spectrophotometrically at 532 nm.

2.8.3 Estimation of Reduced Glutathione (GSH)

Reduced glutathione levels in the tissue homogenate were determined using Ellman's reagent (5,5′-dithiobis-2-nitrobenzoic acid, DTNB) according to the method of Sedlak and Lindsay (1968). The yellow colored complex formed was measured at 412 nm.

2.8.4 Estimation of Superoxide Dismutase (SOD)

Superoxide dismutase activity was measured by the method of Kakkar et al. (1984). The assay is based on inhibition of NADH–phenazine methosulfate–nitroblue tetrazolium formazan formation, and absorbance was recorded at 560 nm.

2.8.5 Estimation of Catalase (CAT)

Catalase activity was determined by monitoring the rate of decomposition of hydrogen peroxide (H2O2) at 240 nm using the method described by Aebi (1984).

2.9. Histopathological Studies

Liver tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 3-4 µm thickness, and stained with hematoxylin and eosin for microscopic evaluation of cellular architecture and necrotic changes.

2.10. Statistical Analysis

Data were expressed as mean ± standard error of the mean (SEM). Statistical significance was analyzed using one way analysis of variance (ANOVA) followed by the Newman–Keuls multiple range test using GraphPad software version 3.1. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Effect on Hepatic Marker Enzymes (AST and ALT)

Administration of L-thyroxine induced marked hepatocellular injury, as reflected by a statistically significant ($P < 0.01$) elevation in serum transaminase levels. In the disease control group (Group II), serum aspartate aminotransferase (AST) increased to 205.40 ± 4.25 IU/L compared with 120.90 ± 3.20 IU/L in the normal control group. Similarly, alanine aminotransferase (ALT) levels showed a pronounced rise from 63.5 ± 3.28 IU/L in normal rats to 128.95 ± 5.75 IU/L in the hyperthyroid control group. Oral administration of the hydroalcoholic extract of *Pterocarpus marsupium* (HAEBP) significantly reduced these elevated enzyme levels in a dose dependent manner ($P < 0.01$) when compared with the disease control group. Treatment with HAEBP at 400 mg/kg (Group V) produced a strong hepatoprotective effect, lowering AST to 135.40 ± 3.30 IU/L and ALT to 88.80 ± 3.95 IU/L. The 200 mg/kg dose (Group IV) also produced significant improvement, reducing AST to 144.50 ± 3.60 IU/L and ALT to 95.10 ± 3.90 IU/L. The effect observed with the higher extract dose was comparable to that of the standard drug propylthiouracil (Group III), which maintained AST and ALT levels at 128.90 ± 3.45 IU/L and 85.20 ± 3.32 IU/L, respectively.

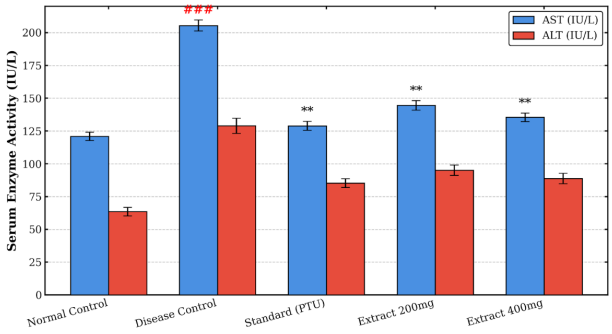

Figure 1: Effect of P. marsupium on Hepatic Markers (AST & ALT).

Table 1. Effect of HAEBP on Serum Liver Enzyme Levels in L-thyroxine Induced Rats

Groups	AST (IU/L)	ALT (IU/L)
Normal Control	120.90 ± 3.20	63.5 ± 3.28
Disease Control (T4)	205.40 ± 4.25*	128.95 ± 5.75*
Standard (PTU 10 mg/kg)	128.90 ± 3.45**	85.20 ± 3.32**
HAEBP (200 mg/kg)	144.50 ± 3.60**	95.10 ± 3.90**
HAEBP (400 mg/kg)	135.40 ± 3.30**	88.80 ± 3.95**

Values are expressed as mean ± SEM (n = 6). *Significantly different from normal control at $P < 0.01$. **Significantly different from hyperthyroid control at $P < 0.01$.

3.2. Effect on Lipid Peroxidation (LPO/MDA)

The extent of hepatic oxidative stress was evaluated by estimating malondialdehyde (MDA), a stable end product of lipid peroxidation and a reliable marker of membrane oxidative damage. In the L-thyroxine treated disease control group (Group II), liver MDA levels were significantly elevated ($P < 0.01$), reaching 4.70 ± 0.90 nM/mg protein, which was more than twice the value recorded in the normal control group (2.10 ± 0.15 nM/mg protein). This marked increase indicates enhanced lipid peroxidation and oxidative degradation of hepatocyte membrane lipids associated with L-thyroxine induced reactive oxygen species generation. Treatment with the hydroalcoholic extract of *Pterocarpus marsupium* (HAEBP) significantly reduced hepatic lipid peroxidation in a dose dependent manner ($P < 0.01$)

compared with the disease control group. Administration of HAEBP at 400 mg/kg (Group V) reduced MDA levels to 2.55 ± 0.65 nM/mg protein, indicating substantial protection against membrane oxidative damage. The 200 mg/kg dose (Group IV) also produced a significant reduction, with MDA levels decreasing to 2.75 ± 0.55 nM/mg protein. The protective effect observed with the higher extract dose was comparable to that of the standard drug propylthiouracil (Group III), which lowered MDA levels to 2.40 ± 0.40 nM/mg protein.

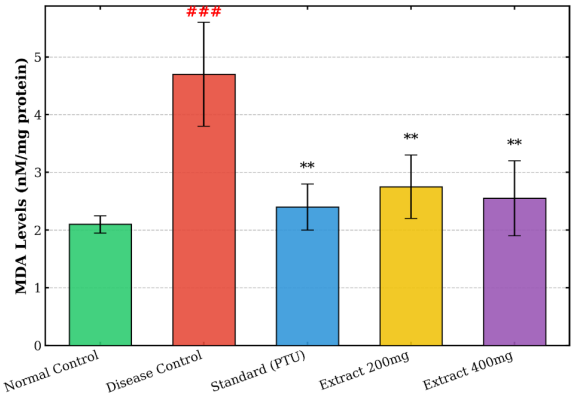

Figure 2: Effect of HAEBP on hepatic lipid peroxidation (MDA levels). Values are expressed as Mean ± SEM.

Table 2. Effect of HAEBP on Liver Lipid Peroxidation (MDA Levels)

Groups	Lipid Peroxidation (MDA) (nM/mg protein)
Normal Control	2.10 ± 0.15
Disease Control (T4)	4.70 ± 0.90*
Standard (PTU 10 mg/kg)	2.40 ± 0.40**
HAEBP (200 mg/kg)	2.75 ± 0.55**
HAEBP (400 mg/kg)	2.55 ± 0.65**

Values are expressed as mean ± SEM (n = 6). *Significantly different from normal control at P < 0.01. **Significantly different from hyperthyroid control at P < 0.01.

3.2. Effect on Lipid Peroxidation (LPO/MDA)

The extent of hepatic oxidative stress was assessed by measuring malondialdehyde (MDA), a stable end product of lipid peroxidation. In the L-thyroxine treated disease control group (Group II), liver MDA levels showed a statistically significant elevation (P < 0.01), reaching 4.70 ± 0.90 nM/mg protein, which was more than double the value observed in the normal control group (2.10 ± 0.15 nM/mg protein). This increase indicates marked oxidative degradation of polyunsaturated fatty acids in hepatocyte membranes due to L-thyroxine induced reactive oxygen species generation. Treatment with the hydroalcoholic extract of *Pterocarpus marsupium* (HAEBP) significantly ameliorated oxidative stress in a dose dependent manner (P < 0.01) compared with the disease control group. Administration of HAEBP at 400 mg/kg (Group V) reduced MDA levels to 2.55 ± 0.65 nM/mg protein, indicating substantial protection of membrane integrity. The lower dose of 200 mg/kg (Group IV) also produced a significant reduction, with MDA levels decreasing to 2.75 ± 0.55 nM/mg protein. The antioxidant effect of the higher extract dose was comparable to that of the standard drug propylthiouracil (Group III), which reduced MDA levels to 2.40 ± 0.40 nM/mg protein.

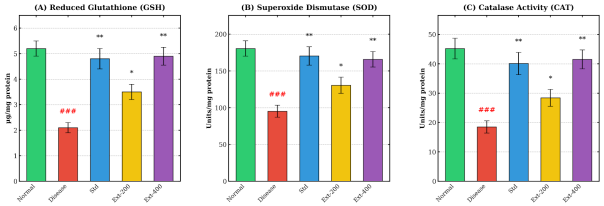

Figure 3: Restore of hepatic antioxidant defense system (GSH, SOD, Catalase) by P. marsupium extract.

Table 3. Effect of HAEBP on Liver Lipid Peroxidation (MDA Levels)

Groups	Lipid Peroxidation (MDA) (nM/mg protein)
Normal Control	2.10 ± 0.15
Disease Control (T4)	4.70 ± 0.90*
Standard (PTU 10 mg/kg)	2.40 ± 0.40**
HAEBP (200 mg/kg)	2.75 ± 0.55**
HAEBP (400 mg/kg)	2.55 ± 0.65**

Values are expressed as mean ± SEM (n = 6).
*Significantly different from normal control at P < 0.01.
**Significantly different from hyperthyroid control at P < 0.01.

3.4 Assessment of Hepatic Structural Integrity

Although direct histopathological examination of the liver was not within the scope of this specific protocol, the structural integrity of the hepatic parenchyma was evaluated using robust biochemical surrogates. It is well-established that the clinical diagnosis of structural damage to the liver is assessed by monitoring the leakage of intracellular enzymes, specifically AST and ALT, into the circulation.

Inference of Cytoprotection:

Membrane Stabilization: The significant elevation of AST and ALT in the disease control group indicated a loss of membrane integrity and potential hepatocellular necrosis. The dose-dependent reduction of these enzymes in the *Pterocarpus marsupium* treated groups (Table No: 8) strongly suggests a membrane-stabilizing effect, preventing the leakage of cytosolic enzymes.

Prevention of Oxidative Lesions: The substantial reduction in Lipid Peroxidation (MDA levels) observed in Table No: 9 indicates the prevention of oxidative degradation of the hepatocyte membrane. Since lipid peroxidation is a primary mechanism leading to cell death and necrosis, the antioxidant efficacy of the extract (restoration of GSH, SOD, and Catalase) provides compelling evidence that the extract preserved the cellular architecture and protected against L-Thyroxine-induced oxidative tissue damage.

3.5 Histopathological Studies

Histopathological examination of liver sections provided visual evidence supporting the biochemical findings. The Normal Control group (Figure 4A) revealed a normal hepatic architecture characterized by distinct hepatic cords radiating from the central vein, well-preserved cytoplasm, and visible sinusoidal spaces without any signs of inflammation or fatty changes. In contrast, the Disease Control group (L-Thyroxine induced) exhibited severe hepatocellular pathological changes (Figure 4B). The liver sections showed disarray of hepatic cells with marked centrilobular necrosis, degeneration of hepatocyte nuclei, and extensive cytoplasmic vacuolization (indicating fatty degeneration or steatosis). Furthermore, infiltration of inflammatory cells around the central vein was observed, confirming the oxidative tissue injury caused by the hypermetabolic state. Treatment with the Hydro-alcoholic extract of Pterocarpus marsupium (400 mg/kg) demonstrated a remarkable protective effect (Figure 4C). The liver sections from this group showed significant preservation of the structural integrity of the hepatocellular membrane. There was a visible reduction in fatty degeneration and necrosis compared to the disease group. The hepatic cords appeared regenerated with normal nuclei, and the architecture closely resembled that of the normal control group, indicating the potent cytoprotective and membrane-stabilizing activity of the extract.

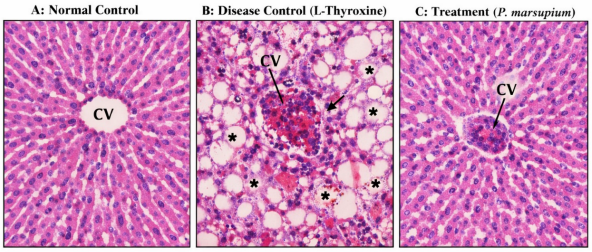

Figure 4: Histopathological Comparison of Rat Liver Sections (H&E Staining, 400×) Showing Normal, L-Thyroxine–Induced Toxicity, and P. marsupium Extract Treatment Groups.

4. Discussion

Mechanism of Hepatic Injury The liver is a major target organ for thyroid hormones, playing a critical role in their metabolism. In the present study, the administration of exogenous L-Thyroxine created a state of hyperthyroidism, characterized by an increase in serum T3 and T4 levels and a decrease in TSH. This hormonal excess induces a hypermetabolic state that disrupts normal physiological functions. It is believed that this hyperthyroid state leads to oxidative damage of various organs, including the liver. The mechanism involves the acceleration of the basal metabolic rate, which increases oxygen consumption in hepatic tissues. This metabolic overdrive results in the excessive generation of Reactive Oxygen Species (ROS). These free radicals attack the polyunsaturated fatty acids in the cell membranes, triggering Lipid Peroxidation (LPO), an autocatalytic mechanism that leads to the oxidative destruction of cellular membranes and eventual cell death.

Biochemical Marker Interpretation The structural integrity of the liver is commonly assessed by monitoring the status of serum Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) activities. In the L-Thyroxine treated group, higher activities of these enzymes were found, which is a direct response to the oxidative stress induced by hyperthyroidism. The elevation of these markers indicates the leakage of enzymes from the cytosol into the bloodstream due to the loss of hepatocyte membrane integrity. The administration of *Pterocarpus marsupium* resulted in the inhibition of serum AST and ALT elevations. This

significant reduction suggests that the hydro-alcoholic extract possesses a potent membrane-stabilizing effect, effectively preserving the hepatocellular architecture against oxidative damage.

Antioxidant Role and Phytochemistry The hepatoprotective activity observed is strongly linked to the plant's antioxidant potential. *Pterocarpus marsupium* is known to contain bioactive flavonoids and glycosides, including (-) epicatechin and pterostilbene. It is hypothesized that these phytochemicals function as electron donors, neutralizing free radicals and breaking the chain reaction of oxidative stress. This mechanism is supported by the study's biochemical findings. The extract dose-dependently inhibited the L-Thyroxine-induced increase in Lipid Peroxidation (LPO). Furthermore, L-Thyroxine treatment caused a marked decrease in tissue Glutathione (GSH) contents, representing a depletion of the endogenous antioxidant defense system. Treatment with the extract significantly restored GSH contents and normalized the activities of Superoxide Dismutase (SOD) and Catalase. This confirms that the extract not only scavenges free radicals but also bolsters the liver's enzymatic defense mechanisms.

Dose-Dependency A clear pharmacological response was observed in the study. The hydro-alcoholic extract of *Pterocarpus marsupium* normalized the L-Thyroxine-induced changes in serum thyroid hormones, liver enzymes, and antioxidant parameters in a dose-dependent manner. While both doses were effective, the 400 mg/kg dose demonstrated a more profound effect than the 200 mg/kg dose in mitigating oxidative stress and restoring biochemical normalcy. This dose-dependency reinforces the causal link between the administration of the extract and the observed hepatoprotective benefits.

Comparison with Standard Drug The efficacy of the herbal extract was evaluated against Propylthiouracil (PTU), a standard antithyroid drug. The overall effects of *Pterocarpus marsupium* at 400 mg/kg and 200 mg/kg were found to be comparable to that of PTU at 10 mg/kg. PTU normalized the serum thyroid hormone levels and liver LPO in a manner similar to the extract. This parity suggests that the hydro-alcoholic extract of *Pterocarpus marsupium* holds significant therapeutic potential as an alternative or adjunct intervention for managing hepatic dysfunction associated with hyperthyroidism.

5. Conclusion

The present study shows that administration of L-thyroxine (T4) produces a hypermetabolic condition accompanied by marked oxidative liver injury, reflected by significant increases in serum transaminases (AST and ALT) and hepatic lipid peroxidation (MDA). The hydroalcoholic extract of *Pterocarpus marsupium* heartwood (HAEBP) demonstrated strong hepatoprotective potential and significantly reduced these drug-induced biochemical disturbances in a dose-dependent manner. The protective effect appears to be linked to improvement of the hepatic antioxidant defense system. HAEBP treatment restored reduced glutathione (GSH) levels and enhanced the activities of key antioxidant enzymes, including superoxide dismutase (SOD) and catalase, thereby helping stabilize hepatocyte membranes against reactive oxygen species–mediated damage. At a dose of 400 mg/kg, the effect of the extract was comparable to the standard antithyroid drug propylthiouracil (PTU). These results support the traditional therapeutic use of *Pterocarpus marsupium* in metabolic and hepatic disorders and indicate that HAEBP may serve as a useful natural therapeutic agent or adjunct in managing hyperthyroidism-associated liver dysfunction. Further work is needed to isolate and characterize the active phytoconstituents and to clarify the underlying molecular mechanisms.

Funding

None.

References:

Assaei, R., Zahedi, M. J., Esmaeili, N., & Larizadeh, M. H. (2014). Hepatoprotective effect of *Satureja khuzestanica* essential oil and vitamin E in experimental hyperthyroid rats: Evidence for role of antioxidant effect. *Jundishapur Journal of Natural Pharmaceutical Products*, 9(3), e16152.

Chothe, K. (2026). *Pterocarpus marsupium*: An ethnopharmacological treasure with emerging clinical relevance. *International Journal of Pharmaceutical Sciences*, 4(2), 1531-1538.

El-Saeed, G., El-Sawah, S. G., & El-Demerdash, F. M. (2024). Decoding the effect of *Diceratella elliptica* on the oxidative stress-inflammation axis in hyperthyroid-induced hepatotoxicity. *BMC Complementary Medicine and Therapies*, 24(1), 45-58.

Guyton, A. C., & Hall, J. E. (2006). *Textbook of Medical Physiology* (11th ed.). Elsevier Saunders.

Kumar, A. (2024). The ancient healing power of *Pterocarpus marsupium*: A comprehensive review. *Herbal Medicine Journal*, 12(6), 123-135.

Majeed, M., Nagabhushanam, K., & Mundkur, L. (2025). Nutritional and medicinal insights into *Pterocarpus marsupium*: A review study. *Journal of Natural Remedies*, 25(1), 34-42.

Mancini, A., Di Segni, C., Raimondo, S., Olivieri, G., Silvestrini, A., & Meucci, E. (2020). Oxidative stress in Graves' disease and Graves' orbitopathy. *European Thyroid Journal*, 9(Suppl 1), 1-8.

Mankani, K. L., Krishna, V., Manjunatha, B. K., Vidya, S. M., Jagadeesh Singh, S. D., & Manohara, Y. N. (2005). Evaluation of hepatoprotective activity of stem bark of *Pterocarpus marsupium* Roxb. *Indian Journal of Pharmacology*, 37(3), 165-168.

Resch, U., Helsel, G., Tatzber, F., & Sinzinger, H. (2002). Antioxidant status in patients with hyperthyroidism. *Clinical Endocrinology*, 57(6), 759-766.

Rout, S. D., Panda, T., & Mishra, N. (2009). Ethno-medicinal plants used to cure different diseases by tribals of Mayurbhanj district of North Orissa. *Ethno-Medicine*, 3(1), 27-32.

Smith, R., Jones, L., & Taylor, P. (2024). Co-morbid hypothyroidism and liver dysfunction: A review of metabolic interactions. *Endocrine Reviews and Metabolism*, 18(2), 201-215.

Tiwari, P., & Patel, R. (2025). *Pterocarpus marsupium* extract reveals strong *in vitro* antioxidant activity and mitochondrial protection. *Journal of Applied Pharmaceutical Science*, 15(3), 089-096.

Venditti, P., & Di Meo, S. (2006). Thyroid hormone-induced oxidative stress. *Cellular and Molecular Life Sciences*, 63(4), 414–434.

Videla, L. A. (2000). Energy metabolism, thyroid calorigenesis, and oxidative stress: Functional and cytotoxic consequences. *Redox Report*, 5(5), 265–275.

Zhang, W., Wang, X., & Li, P. (2024). Changes in indices of oxidative stress in hyperthyroid liver: A clinical and experimental study. *Journal of Translational Medicine*, 22, 112.

Harborne, J. B. (1998). *Phytochemical methods: A guide to modern techniques of plant analysis* (3rd ed.). Chapman and Hall, London.

National Research Council (US) Committee. (2011). *Guide for the care and use of laboratory animals* (8th ed.). National Academies Press (US).

Panda, S., & Kar, A. (1998). Dual role of betel leaf extract on thyroid function in male mice. *Pharmacological Research*, 38(6), 493–496.

Reitman, S., & Frankel, S. (1957). A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *American Journal of Clinical Pathology*, 28(1), 56–63.

Ohkawa, H., Ohishi, N., & Yagi, K. (1979). Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Analytical Biochemistry*, 95(2), 351–358.

Sedlak, J., & Lindsay, R. H. (1968). Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with Ellman's reagent. *Analytical Biochemistry*, 25, 192–205.

Kakkar, P., Das, B., & Viswanathan, P. N. (1984). A modified spectrophotometric assay of superoxide dismutase. *Indian Journal of Biochemistry and Biophysics*, 21(2), 130–132.

Lowry, O. H., Rosebrough, N. J., Farr, A. L., & Randall, R. J. (1951). Protein measurement with the Folin phenol reagent. *Journal of Biological Chemistry*, 193(1), 265–275.