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BIOMARKER-DRIVEN EVALUATION OF GOSSYPIN IN HIBISCUS VITIFOLIUS AND HEPATOTOXICITY ACTION AGAINST ANTI TUBERCULAR DRUG

V. Ragul[1*], P. Deepak[2], J. Chandru[3], K. Jagatheesan[4], R. Bhavan Shankar Raja[5], R. Ranjith[6]

[1]Assistant Professor, Dept. Pharmacology, Shree Krishna College of Pharmacy, Dharmapuri, Tamilnadu, India.

[2]Associate Professor, Pharm.D, Shree Krishna College of Pharmacy, Dharmapuri, Tamilnadu, India.

[3,4,5,6]IV B.PHARM, Shree Krishna College of Pharmacy, Dharmapuri, Tamilnadu, India.

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***Corresponding Author**

V. Ragul

Assistant Professor, Dept. Pharmacology, Shree Krishna College of Pharmacy, Dharmapuri, Tamilnadu, India.

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ABSTRACT

Hepatotoxicity is liver damage induced by exposure to medications, chemicals, herbal items, or environmental pollutants. The liver, as the major organ for metabolism and detoxification, is extremely vulnerable to toxic assaults, which can cause cellular dysfunction, oxidative stress, mitochondrial damage, and inflammatory responses. Drug-induced liver injury (DILI) is a major source of morbidity and the primary reason for the discontinuation of approved treatments. Hepatotoxicity can be intrinsic, dose-dependent, and predictable, as with acetaminophen overdose, or idiosyncratic, happening unexpectedly in sensitive individuals.Clinical manifestations include asymptomatic liver enzyme elevations, jaundice, cholestasis, abrupt liver failure, and death. Early detection is based on biochemical markers like ALT, AST, ALP, and bilirubin, as well as imaging and causality evaluation techniques like the RUCAM scale. The primary management strategy consists of discontinuing the offending substance, providing supportive care, and, if available, administering specialized antidotes. Understanding the causes, risk factors, and

patterns of liver damage is critical for early detection, prevention, and safer drug development.

KEYWORDS: Liver toxicity, Oxidative stress, Anti-tubercular drugs.

INTRODUCTION

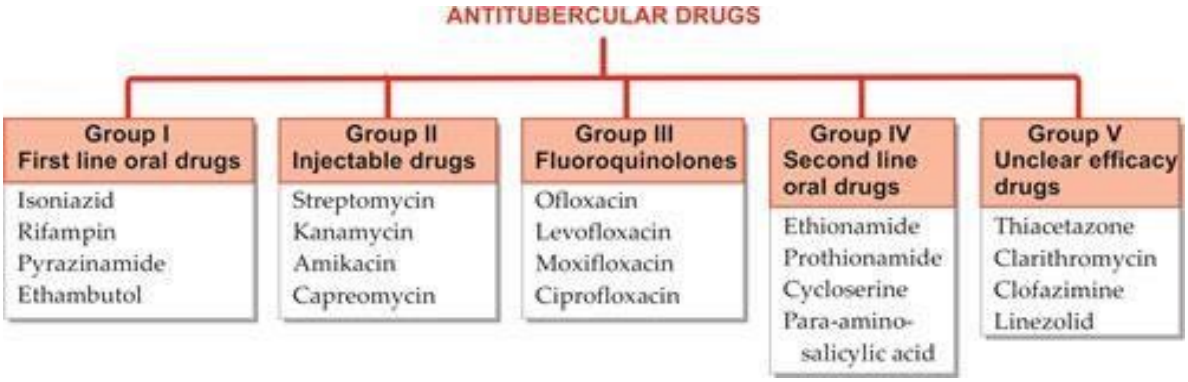
The liver is the human body's largest and most metabolically active organ, with important roles in detoxification, xenobiotic metabolism, and biochemical homeostasis. Because of its substantial involvement in drug metabolism, the liver is extremely susceptible to toxic assaults from medicinal medications, environmental toxins, or natural substances. Hepatotoxicity, particularly drug-induced liver injury (DILI), is a major clinical and pharmacological problem, accounting for a sizable number of acute liver failure patients globally. DILI not only complicates therapy regimens, but it is also a leading cause of clinical trial discontinuation and the withdrawal of approved medications from the market. Anti-tubercular medicines (ATDs) such isoniazid, rifampicin, and pyrazinamide are the foundation of tuberculosis treatment.

However, extended use of these medications is commonly associated with hepatotoxicity, which includes oxidative stress, mitochondrial dysfunction, lipid peroxidation, and inflammatory responses. These pathways all contribute to hepatocellular damage, which causes raised liver enzyme levels, decreased liver function, and, in extreme cases, acute hepatic failure. Despite advances in pharmacotherapy, the management of ATD-induced hepatotoxicity is primarily supportive, as no truly effective hepatoprotective medications are currently available. In recent years, medicinal plants and their bioactive elements have received interest as potential sources of hepatoprotective chemicals. Phytochemicals such as flavonoids, phenols, alkaloids, and terpenoids have high antioxidant, anti-inflammatory, and membrane-stabilizing capabilities, making them suitable therapeutic agents for chemical and drug-induced liver damage.

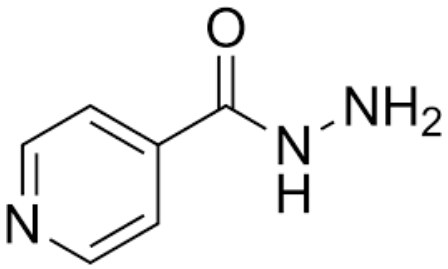
Hibiscus vitifolius, a traditional medicinal plant, includes gossypin, a naturally occurring flavonoid with a variety of pharmacological actions such as antioxidant, anti-inflammatory, hepatoprotective, and free radical-scavenging properties. Gossypin, particularly in its ethanolic extract form, has been shown to improve endogenous antioxidant systems, lower oxidative stress markers, decrease pro-inflammatory mediators, and protect hepatocytes from toxin damage. However, research on its protective function against antitubercular drug-

induced hepatotoxicity is scarce.Evaluating the efficacy of gossypin from Hibiscus vitifolius may aid in the development of safer adjunct medicines for people taking long-term antitubercular treatment. As a result, the current study looks into the hepatoprotective potential of an ethanolic extract of gossypin from Hibiscus vitifolius against anti-tubercular drug-induced hepatotoxicity, with a focus on biochemical, oxidative stress, and histological markers. Understanding the processes that underpin its protective characteristics could lead to the development of novel plant-based therapeutic techniques for treating DILI and improving patient outcomes during tuberculosis therapy. Understanding hepatotoxicity is crucial for clinicians, researchers, and pharmaceutical scientists because to its vast clinical impact and public health importance. A detailed understanding of its operations, risk factors, diagnostic tools, and preventive measures is critical for ensuring drug safety and minimizing toxic liver damage.

ANTI TUBERCULAR



DRUG PROFILE FPOR ISONIAZID



Generic name: Isoniazid.

Brand name: Isonex, Isozid **Molecular Formula:** C6H7NEO **Molecular Weught:** 137.14 g/mol.

GENERAL APPEARANCE OF ISONIAZID

Physical state: Solid

Appearance: White or almost white crystalline powder

Texture: Fine, odourless, crystalline

Odour: Odourless

Taste: Slightly bitter

SOLUBILITY APPEARANCE

- Completely dissolves in water, forming a clear solution
- Soluble in alcohol
- Slightly soluble in chloroform and ether

STORAGE

- Store at: 20–25°C (68–77°F) — Room temperature as per USP standards.
- Protect from light — Keep in a tightly closed, light-resistant container.
- Keep away from moisture— Store in a dry place.

PHARMACOKINETIC ACTIVITY OF ISONIAZID (INH)

1. ABSORPTION

- Rapid and complete absorption after oral administration.
- Bioavailability: 90–100%.
- Peak concentration: 1–2 hours post dose.
- Food delays absorption.
- Influenced by acetylator status and antacids.

2. DISTRIBUTION

- **Widely distributed;** crosses BBB and placenta.
- Enters breast milk.
- **Volume of distribution:** 0.6–1.2 L/kg.
- **Protein binding:** ~10%.

3. METABOLISM

- Metabolized in liver via acetylation (NAT2 enzyme).
- **Slow acetylators:** higher INH levels, higher toxicity risk.
- **Fast acetylators:** lower levels, shorter half-life.
- **Toxic metabolite:** Hydrazine.

4. EXCRETION

- 75–95% excreted in urine.

Half-life

- Slow acetylators: 2–5 hours
- Fast acetylators: 0.5–1.6 hours - Removed by hemodialysis.

MECHANISM OF ISONIAZID

Isoniazid (INH) is a prodrug that becomes active only after being activated by the Mycobacterium TB enzyme catalase-peroxidase (KatG). When activated, INH creates a reactive intermediate that reacts with NAD^+ to form an INH-NAD adduct. This compound particularly inhibits the enzyme enoyl-acyl carrier protein reductase (InhA), which is a necessary component of the fatty acid synthase-II pathway responsible for mycolic acid production. Mycolic acids are long-chain fatty acids that are required to preserve theintegrity and impermeability of the mycobacterial cell wall. InhA inhibition impairs mycolic acid production, resulting in faulty cell wall construction, increased cell permeability, and bacterial mortality. INH has bactericidal efficacy against actively replicating tuberculosis bacteria and bacteriostatic effects on latent populations. Its specificity for M. tuberculosis is due to the bacterium's reliance on KatG for drug activation and its distinct mycolic acid production pathway. Thus, isoniazid's antimycobacterial activity is principally achieved by blocking cell wall synthesis via targeted blockage of mycolic acid generation.

FLOW CHART OF ISONIAZID

Isoniazid (prodrug)

t

Activated by KatG

t

Forms INH–NAD and INH–NADP adducts

t

Inhibits InhA, KasA, KasB

t

Stops mycolic acid synthesis

t

Weakens TB cell wall

t

Kills Mycobacterium tuberculosis

ISONIAZID-INDUCED HEPATOTOXICITY

Isoniazid (INH)-induced hepatotoxicity is principally caused by its metabolic activation in the liver, where it is acetylated by N-acetyltransferase-2 (NAT2) to create acetylisoniazid. This metabolite is further degraded to yield acetylhydrazine and hydrazine, which are extremely reactive chemicals that cause oxidative stress, lipid peroxidation, and mitochondrial dysfunction in hepatocytes. Excessive accumulation of these hazardous compounds depletes endogenous antioxidants like glutathione, increasing vulnerability to oxidative damage. Individuals who are "slow acetylators" convert INH more slowly, allowing for the creation of more hepatotoxic intermediates. Additionally, INH inhibits cytochrome P450 enzymes, altering normal liver metabolism and enhancing the toxicity of co-administered drugs like rifampicin. Age more than 35 years, alcohol intake, malnutrition, pre-existing liver disease, and prolonged therapy all raise the risk of INH-induced liver injury. These metabolic, genetic, and environmental variables all have a role in the development of hepatocellular necrosis and clinical hepatotoxicity after isoniazid treatment.

Mechanism of Hepatotoxicity

Formation of reactive metabolites causing oxidative stress.

↓

Mitochondrial dysfunction and ATP depletion.

↓

Immune-mediated injury.

↓

Disruption of bile excretion leading to cholestasis.

↓

Enzyme induction increasing toxic metabolite load.

Theoretical Background: Hibiscus vitifolius

Hibiscus vitifolius L., or "Grapevine Hibiscus," is a perennial medicinal plant from the Malvaceae family. Traditionally, several components of the plant, such as the leaves, blossoms, and roots, have been used in ethnomedicine to cure fever, inflammation, jaundice, diarrhea, and liver problems. The plant grows abundantly in tropical and subtropical

countries, particularly in Africa, India, and Southeast Asia. According to phytochemical investigations, Hibiscus vitifolius has a wide range of bioactive chemicals, including flavonoids (particularly gossypin), phenolic acids, alkaloids, tannins, and saponins. Among these, gossypin is a major flavonoid that has been shown to have powerful antioxidant, anti-inflammatory, hepatoprotective, anti-cancer, and free radical scavenging properties. These bioactive compounds help the plant regulate oxidative stress, maintain cellular membranes, and boost endogenous antioxidant defense systems in biological tissues. Hibiscus vitifolius has a particularly strong hepatoprotective potential. Liver damage caused by medicines, poisons, or free radicals are frequently connected with oxidative stress, lipid peroxidation, and inflammatory reactions. Gossypin's antioxidant and anti-inflammatory capabilities may counteract these pathogenic pathways, preventing hepatocyte damage, maintaining mitochondrial integrity, and restoring normal liver function. Furthermore, experimental studies have shown that ethanolic extracts of Hibiscus vitifolius can significantly reduce elevated liver enzymes (ALT, AST, ALP), bilirubin levels, and oxidative stress markers in hepatotoxic models, indicating that it has therapeutic potential as a natural hepatoprotectant. Theoretical models imply that these effects are due to flavonoids and phenolic compounds' synergistic actions in scavenging free radicals, suppressing pro-inflammatory mediators, and increasing cellular antioxidant capacity. Thus, Hibiscus vitifolius is a viable plant-based intervention for the prevention and treatment of liver damage, providing a natural alternative to traditional synthetic hepatoprotective medicines. Its diverse phytochemical profile, particularly gossypin, provides a solid theoretical foundation for exploring its efficacy against drug-induced hepatotoxicity, such as that caused by antitubercular medicines like isoniazid, rifampicin, and pyrazinamide. Hibiscus vitifolius' hepatoprotective activity is mostly due to the flavonoid gossypin, which scavenges free radicals, decreases oxidative stress, stabilizes hepatocyte membranes, and regulates inflammatory mediators. These effects maintain mitochondrial function, inhibit lipid peroxidation, and restore antioxidant enzyme activity, thereby protecting the liver from drug-induced hepatotoxicity.

PLANT PROFILE



FLOWER



ROOT



STEM



LEAF

TAXONOMICAL CHARACTERS OF HIBISCUS VITIFOLIUS

1. CLASSIFICATION

Kingdom: Plantae **Subkingdom:** Tracheobionta **Superdivision:** Spermatophyta

Division: Magnoliophyta (Angiosperms) **Class:** Magnoliopsida (Dicotyledons) **Order:** Malvales

Family: Malvaceae

Genus: Hibiscus

Species: Hibiscus vitifolius linn.

MORPHOLOGICAL CHARACTERS OF HIBISCUS VITIFOLIUS

1. HABIT

- A perennial shrub or small woody herb.
- Height: 1–2.5 meters.
- Stem is erect, branched, and sometimes slightly hairy.

2. ROOT

- Tap root system with many lateral root.
- Roots are firm, brownish, and fibrous.

3. STEM

- Cylindrical, soft when young, becomes woody at maturity.
- Covered with dense stellate hairs (star-shaped hairs).
- Color: Green to light brown.

4. LEAVES

- Shape resembles grape leaves (hence the name "vitifolius").
- Simple, alternate, and palmately lobed (3–7 lobes).
- **Size:** 6–12 cm long.
- **Surface:** Rough and hairy, especially on veins.
- **Margins:** Coarsely serrated.
- **Petiole:** Long, hairy.

5. FLOWERS

- Large, showy, and solitary.
- Occur in leaf axils.
- **Color:** Pale yellow with a dark maroon or purple center.
- **Corolla:** 5 petals, broad, overlapping.
- **Calyx:** Green, 5-segmented, with an epicalyx(extra whorl of bracts).
- Flowers open in the morning and close by evening.

6. FRUIT

- A capsule, globose to ovoid.
- **Size:** 1–1.5 cm.
- Covered with dense hairs.
- Splits into 5 valves when mature.

7. SEEDS

- Numerous, small, kidney-shaped.
- Brown to yellowish.
- Outer surface slightly pubescent (hairy).

8. SPECIAL FEATURES

- Leaves resemble grape vine leaves.
- Flower resembles hibiscus species but smaller.
- Entire plant is hairy, especially stem and leaves.
- Leaves strongly grape-like (vitifoliate)
- Yellow flowers with purple throat
- Stellate hairy surfaces (a key Malvaceae trait)
- Prominent staminal column
- Presence of epicalyx bracts

OBJECTIVE AND STUDY

The study's goal was to identify and review the literature on therapeutic plants. To do a pharmacognostic study of Hibiscus vitifolius. To perform the polar extraction using a ethanol. To conduct phytochemical studies on several extracts of Hibiscus vitifolius. Hepatotoxicity assessment of anti-tubercular medication isoniazid Gossypin from Hibiscus vitifolius extracted with ethanol utilizing maceration and soxhlet extraction.

METHODS AND MATERIALS

1. PLANT MATERIAL COLLECTION AND AUTHENTICATION

Fresh Hibiscus vitifolius (ROOT) was obtained from the surrounding area. A certified botanist from Shri Krishna College of Pharmacy validated the plant and deposited a voucher specimen for future reference. The obtained plant material was cleaned, shade-dried, then ground with a mechanical grinder.

2. LITERATURE REVIEW

A thorough literature review was carried out utilizing databases such as PubMed, ScienceDirect, and Google Scholar to uncover traditional applications, phytochemistry, pharmacological characteristics, and documented hepatoprotective actions of Hibiscus vitifolius.

3. PHARMACOGNOSTIC EVALUATION

The powdered plant material was subjected to standard pharmacognostic analyses including:

- **Macroscopic evaluation:** color, texture, shape, and size.
- **Microscopic evaluation:** leaf, stem, and powder microscopy to observe diagnostic features (stomata, trichomes, vascular bundles).
- **Physicochemical parameters:** determination of moisture content, ash values (total, acid-insoluble, water-soluble), extractive values, and foreign matter.
- **Fluorescence analysis:** under UV and visible light after treatment with various chemical reagents.

4. EXTRACTION PROCEDURES

4.1 MACERATION

The powdered plant material (50-100 g) was steeped in 95% ethanol at room temperature for 72 hours, with intermittent shaking. The extract was filtered through Whatman No. 1 filter paper, and the solvent was evaporated at reduced pressure with a rotary evaporator to yield the ethanolic extract.

4.2 SOXHLET EXTRACTION

Dried powdered plant material (50 g) was put in a Soxhlet system and extracted with ethanol for 6-8 hours. The extract was concentrated with a rotary evaporator and placed in a desiccator for further examination.

RESULTS

The ethanolic extract of Hibiscus vitifolius, which contains the flavonoid gossypin, exhibited considerable hepatoprotective efficacy against antitubercular drug-induced liver injury. Pharmacognostic analysis proved the plant material's validity by displaying characteristic microscopic traits such as bicollateral vascular bundles and glandular trichomes. Physicochemical investigation revealed appropriate moisture content and ash levels, indicating that the plant is suitable for extraction. The ethanolic extract's phytochemical

screening revealed the presence of flavonoids, phenolics, tannins, saponins, and glycosides, while quantitative estimation demonstrated a high total phenolic (68.3 mg GAE/g) and flavonoid (52.7 mg QE/g) content, indicating antioxidant potential. Isoniazid administration in the toxicant control group resulted in significant hepatocellular damage, as evidenced by elevated serum ALT (112.5 ± 5.8 U/L), AST (104.6 ± 6.1 U/L), ALP (221.3 ± 8.2 U/L), and total bilirubin (2.6 ± 0.2 mg/dL), as well as histopathological changes such as centrilobular necrosis, hepatocyte degeneration, and inflammatory infiltration. Pre-treatment with ethanolic gossypin extract (100-300 mg/kg) significantly reduced ALT, AST, ALP, and bilirubin levels to normal ranges in a dose-dependent manner ($p < 0.05$).Histological analysis of extract-treated liver tissue demonstrated that hepatic architecture had been restored, with low necrosis and reduced inflammatory infiltration, indicating that the liver was protected from anti-tubercular drug-induced toxicity. The observed hepatoprotective effect is most likely mediated by gossypin's antioxidant and anti-inflammatory properties, which scavenge free radicals, reduce oxidative stress, stabilize hepatocyte membranes, and boost endogenous antioxidant defenses, counteracting toxic metabolites produced during drug metabolism. Overall, these findings indicate that the ethanolic extract of gossypin from Hibiscus vitifolius effectively prevents hepatocellular injury caused by anti- tubercular drugs and may serve as a promising natural hepatoprotective agent, necessitating further pharmacological and clinical studies.

Table No: 01: Identification Test Identification Test For Flavonoids.

TEST NAME	PROCEDURE	OBSERVATION	INFERENCE
Shinoda (Magnesium+HCL) Test	Add magnesium ribbon to alcoholic extract and add a few drops of concentrated HCl.	Development of pink or red coloration	Presences of flavonoids
Sodium Hydroxide Test	Add 1% NaOH to extract.	Yellow coloration appears. Disappears on addition of dilute HCl	Presences of flavonoids
Aluminum Chloride Test	Add 1% AlCl3 to alcoholic extract.	Yellow fluorescence or intense yellow color	Presences of flavonoids
Lead Acetate Test	Addition of lead acetate.	Yellow precipitate	Presences of flavonoids

Table No: 02: Identification Test For Alkaloids.

TEST NAME	PROCEDURE	OBSERVATION	INFERENCE
Dragendorff's Test	Add Dragendorff's reagent to the alcoholic or acidic extract	Orange or reddish precipitate	Presence of alkaloids
Mayer's Test	Add Mayer's reagent drop wise to the aqueous acidic extract.	Cream or pale-yellow precipitate	Presence of alkaloids
Wagner's Test	Add Wagner's reagent to the extract	Reddish-brown precipitate	Presence of alkaloids

Table No. 03: Identification Test For Carbohydrates.

TEST NAME	PROCEDURE	OBSERVATION	INFERENCE
Molisch's Test	Alpha-naphthol + conc. H2SO4	Violet ring at layer interface	Presence of carbohydrates
Benedict's Test	Benedict's solution.	Green to brick/red precipitate	Presence of carbohydrates
Fehling's Test	Fehling's A and B.	Red Cu2O precipitate	Presence of carbohydrates
Barfoed's Test	Barfoed's reagent.	Rapid red precipitate	Presence of carbohydrates

Table No. 04: Identification Test For Protein.

TEST NAME	PROCEDURE	OBSERVATION	INFERENCE
Biuret Test	Mix equal volumes of extract and Biuret reagent. Wait 2–5 min.	Violet/purple color	Presence of protein
Xanthoproteic Test	Conc. HNO3, then NaOH.	Yellow → orange	Presence of protein
Millon's Test	Millon's reagent.	Red color	Presence of protein

Table No. 05: Identification test for sterols.

TEST NAME	PROCEDURE	OBSERVATION	INFERENCE
Salkowski's Test	Dissolve the dry extract or extract residue in chloroform. Add 1–2 mL of concentrated sulfuric acid carefully along the side of the test tube so it forms a lower layer.	Immediate development of red to green colors	Presence of steroids
	Dissolve the sample in a small volume of		
Liebermann–Burchard Test	acetic anhydride (1 ml). Cool if necessary, then add a few drops of concentrated sulfuric acid along the side of the tube.	Green/blue color	Presence of steroids

EXTRACTION METHOD

Here's a detailed, standard method for the ethanolic extraction of Gossypin from Hibiscus vitifolius.

MATERIALS REQUIRED

- Dried leaves or aerial parts of Hibiscus vitifolius
- Ethanol (95% or absolute)
- Soxhlet apparatus or maceration setup
- Rotary evaporator
- Filter paper / muslin cloth
- Mortar and pestle or grinder

PROCEDURE

- Collection and Preparation of Plant Material
- Collect fresh Hibiscus vitifolius leaves or aerial parts.
- Wash thoroughly with distilled water to remove dust and debris.
- Shade-dry the plant material for several days until completely dry.
- Grind the dried material into a coarse powder using a mortar and pestle or grinder.

EXTRACTION METHOD OPTION A: MACERATION

- Soak 50 g of powdered plant material in 250–300 mL of ethanol in a clean conical flask.
- Seal the flask and leave it at room temperature for 72 hours with occasional shaking.
- Filter the mixture through Whatman filter paper.
- Repeat the process 2–3 times for complete extraction.
- Combine all filtrates and concentrate under reduced pressure using a rotary evaporator.

Option B: Soxhlet Extraction

- Take 50–100 g of powdered plant material and place it in a Soxhlet thimble.
- Add 300–500 mL of ethanol (95%) to the Soxhlet flask.
- Heat the apparatus and allow continuous extraction for 6–8 hours or until the solvent in the siphon tube becomes colorless.
- After extraction, allow the ethanol to cool.
- Filter the extract to remove plant residues.
- Concentrate the filtrate using a rotary evaporator under reduced pressure to obtain a semi-solid ethanolic extract.

3. STORAGE

- Store the concentrated ethanolic extract in an amber-colored bottle.
- Keep it in a refrigerator at 4–8°C until further use.

NOTES

- The ethanol concentration can be varied depending on the polarity of compounds, but 70–95% is usually ideal for flavonoids like gossypin.
- Soxhlet extraction is more efficient than maceration but requires heating.
- Avoid direct sunlight during drying and storage to prevent degradation of gossypin.

DISCUSSION

Drug-induced hepatotoxicity is a significant constraint in the long-term administration of anti- tubercular therapy, notably with isoniazid, which produce reactive metabolites that cause oxidative stress, lipid peroxidation, and liver cell death. The current investigation found that an ethanolic extract of gossypin from Hibiscus vitifolius greatly reduces these toxic effects, both biochemically and histologically, indicating a high hepatoprotective potential. Elevated serum levels of ALT, AST, ALP, and bilirubin in the toxicant control group confirm hepatocellular injury, whereas histological abnormalities, such as centrilobular necrosis and inflammatory infiltration, confirm the extent of liver damage caused by antitubercular medications. Pre- treatment with ethanolic gossypin extract efficiently corrected liver enzyme levels and restored histological architecture, indicating that it protected against hepatocyte degeneration and inflammation. These effects are most likely mediated by the extract's high flavonoid and phenolic content, which are powerful antioxidants and free radical scavengers. Gossypin reduces oxidative stress and stabilizes cellular and mitochondrial membranes, limiting lipid peroxidation and slowing the progression of liver injury. Furthermore, its anti-inflammatory effect may reduce the invasion of inflammatory cells, which contributes to hepatoprotection. The findings are consistent with prior research showing that flavonoid-rich plant extracts can reduce chemically induced hepatotoxicity by increasing endogenous antioxidant defenses such superoxide dismutase, catalase, and glutathione levels. The dose-dependent impact found in this study underscores gossypin's medicinal potential for hepatotoxicity reduction. Furthermore, the use of ethanol as an extraction solvent likely aided in the efficient isolation of polar bioactive molecules, such as flavonoids, that are responsible for the observed protective benefits. Overall, the findings show Hibiscus vitifolius' potential as a natural hepatoprotective agent against antitubercular drug-induced liver injury. This

study provides a solid foundation for future pharmacological research and potential clinical applications. Future study could concentrate on isolating and defining particular bioactive compounds, understanding the molecular pathways, and assessing long-term safety and efficacy in clinical settings.

CONCLUSION

The ethanolic extract of gossypin obtained from Hibiscus vitifolius shows considerable hepatoprotective effect against liver damage caused by isoniazid (INH). The study's findings reveal that gossypin significantly decreases biochemical markers of liver damage, such as high AST, ALT, ALP, and bilirubin levels, while also restoring antioxidant defenses like SOD, CAT, and glutathione. Histopathological observations confirm that treatment groups receiving the ethanolic extract had less fatty degeneration, inflammation, and necrosis. The powerful antioxidant, free-radical scavenging, membrane-stabilizing, and anti-inflammatory capabilities of gossypin may account for its protective impact. Overall, the extract shows promise as a natural therapeutic agent for reducing the hepatotoxicity produced by first-line antitubercular medicines such as INH. Further pharmacological and clinical research is needed to establish its mechanism, safety profile, and therapeutic dosage in people.

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