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MORPHOLOGICAL HISTOLOGICAL, PHYTOCHEMICAL SCREENING AND ANTILIPIDIMIC ACTIVITY ON PSIDIUM GUAJAVA L

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ABSTRACT

Psidium guajava L. (Guava) is a widely recognized medicinal plant traditionally used for treating various ailments, including metabolic disorders. This study aimed to evaluate the pharmacognostical, phytochemical, and pharmacological properties of *P. guajava* leaves collected from two different Ethiopian regions, Babile and Gursum. Morphological and histological analyses confirmed the identity of the plant, revealing typical anatomical features such as dorsiventral leaf structure, palisade parenchyma, and collenchyma beneath the epidermis. Phytochemical screening revealed the presence of key bioactive compounds, including alkaloids, flavonoids, tannins, steroids, and saponins. Quantitative analysis showed that the Babile extract had higher total phenolic (33.71 ± 1.13 mg GAE/g) and flavonoid content (28.75 ± 1.14 mg QE/g) compared to the Gursum extract, indicating its stronger antioxidant potential. Pharmacological evaluation was conducted using Wistar albino rats divided into five groups: a control group, a high-fat diet (HFD) group, and three groups receiving HFD supplemented with *P. guajava* extract at 200 mg/kg and 400 mg/kg doses. While food consumption remained consistent, calorie intake increased significantly in extract-treated groups. Notably, the 400 mg/kg extract group demonstrated a substantial reduction in serum triglycerides (142.4 ± 6.2 mg/dL), total cholesterol (161.7 ± 5.5 mg/dL), and LDL-c (98.6 ± 4.3 mg/dL), along with an improvement in HDL-c (49.1 ± 3.7 mg/dL) levels, compared to the HFD group. In conclusion, *P. guajava* leaf extract exhibits potent lipid-lowering and antioxidant activities,

supporting its ethnomedicinal use for managing hyperlipidemia. Further studies, including clinical trials, are warranted to explore its therapeutic potential in human populations.

KEYWORDS: *Psidium guajava* L., Guava, Wistar albino rats, Phytomedicines, Hyperlipidemia.

1. INTRODUCTION

Phytomedicines, also known as plant-based medicines, derive from plants and their various parts, such as leaves, roots, bark, seeds, and flowers. These medicines are based on the principle that plants contain naturally occurring chemical compounds, many of which have therapeutic benefits. For thousands of years, humans have used these compounds to treat illnesses, injuries, and other health-related issues. In modern times, phytomedicines continue to play a vital role in healthcare, particularly in the fields of alternative and complementary medicine. The resurgence of interest in phytomedicines is attributed to their perceived safety, natural origin.[1-2]

With the advent of modern chemistry in the 19th century, scientists began isolating and identifying the active compounds within these plants.[3] This led to the development of more standardized herbal preparations and the eventual synthesis of plant-based chemicals into modern pharmaceuticals, such as aspirin, which is derived from the bark of the willow tree.

Ayurveda, the traditional medical system of India, places a strong emphasis on the use of plants and plant-derived substances for healing. The Ayurvedic pharmacopeia is vast, with thousands of plants listed as having medicinal properties.[4] Each plant is classified based on its taste, potency, and post-digestive effects, and is used to balance the doshas—Vata, Pitta, and Kapha—that govern the body's physiological functions. Common Ayurvedic herbs like ashwagandha (Withania somnifera), brahmi (Bacopa monnieri), and shatavari (Asparagus racemosus) are still widely used today for their adaptogenic, cognitive-enhancing, and reproductive health benefits, respectively.[5-6]

Despite the growing interest in phytomedicines, there are still significant challenges in their research and use. One of the major issues is the standardization of herbal medicines. The concentration of active compounds in plants can vary depending on factors such as the growing environment, harvesting methods, and storage conditions. This variability makes it difficult to ensure consistent efficacy and safety in herbal products. Furthermore, there is a

need for more clinical trials to scientifically validate the claims made about many traditional plant-based treatments.[7-8]

1.1. Uses of phytomedicines

The uses of phytomedicines vary widely, covering a broad spectrum of health conditions. They are commonly employed to treat chronic conditions such as inflammation, cardiovascular diseases, digestive disorders, and respiratory issues. For example, turmeric, known for its anti-inflammatory properties, is widely used to manage arthritis and other inflammatory conditions.[9]

- **Chronic conditions:** *Turmeric*: Anti-inflammatory; used for arthritis. *Ginger*: Aids digestion, relieves nausea and indigestion.
- **Mental health:** *St. John's Wort & Valerian Root*: Used for depression, anxiety, and sleep disorders.[10]
- **Immune support:** *Echinacea*: Boosts immunity; helps with colds and respiratory infections. *Garlic*: Offers antimicrobial and heart health benefits.
- **Antioxidant protection:** *Green Tea & Berries*: Help prevent cancer and heart disease via antioxidant effects.[11]
- **Women's health:** *Evening Primrose Oil*: Used for PMS and breast pain as a natural alternative to HRT.
- **Skin & Dermatology:** *Aloe Vera*: Soothes burns, wounds, and skin irritations. *Tea Tree Oil*: Treats acne, fungal infections, and skin conditions.[12]
- **Infectious diseases:** *Neem*: Antibacterial/antiviral; used for skin infections and malaria.
- **Cardiovascular health:** *Hawthorn*: Improves heart function and circulation. *Flaxseed*: Lowers cholesterol and cardiovascular risk.[13]
- **Preventative & Holistic health:** *Turmeric*, *Green Tea*, *Ginseng*: Adaptogens that reduce stress and support longevity.[14]

1.2. Advantages and Disadvantages of phytomedicines

Advantages of phytomedicines

1. **Fewer side effects:** Being natural, they are often gentler on the body compared to synthetic drugs.[15]
2. **Holistic benefits:** Work on multiple body systems simultaneously; e.g., turmeric is anti-inflammatory, antioxidant, and antimicrobial.

3. **Affordable & Accessible:** Easier to grow, prepare, and use in low-resource settings, especially in rural or low-income areas.[16]
4. **Sustainability & Biodiversity:** Support organic farming and eco-friendly healthcare; promote environmental conservation.
5. **Cultural acceptance:** Align with traditional healing systems like Ayurveda and TCM, fostering patient trust and cultural continuity.[17]

Disadvantages of phytomedicines

1. **Inconsistent potency:** Active ingredient levels vary by plant part, harvest method, or preparation, leading to unpredictable effects.
2. **Drug interactions:** Can interfere with prescription medications, causing enhanced or reduced effects if not guided properly.[18]
3. **Lack of scientific validation:** Many lack rigorous clinical trials, limiting their integration into mainstream healthcare.
4. **Overharvesting issues:** Popular medicinal plants like ginseng are at risk due to unsustainable harvesting, harming biodiversity.[19]
5. **Limited insurance coverage:** Often not covered by health insurance, making high-quality herbal products costly for some.

Fig. 1: Advantages and Disadvantages of Phytomedicines.[20]

1.3. *Psidium guajava* L.

Psidium guajava, commonly known as guava, is a small evergreen tree or shrub native to tropical and subtropical regions of the Americas, particularly Central America and northern South America. Belonging to the Myrtaceae family, *Psidium guajava* has been cultivated for thousands of years for its nutritious fruit and medicinal properties. The plant is highly valued not only for its delicious fruit but also for the extensive range of traditional remedies derived from various parts of the plant, including the leaves, bark, and roots.[21]

The guava fruit is rich in vitamins, particularly vitamin C, with one guava providing more than four times the daily recommended intake of the vitamin. It also contains essential minerals like potassium, calcium, and magnesium, along with dietary fiber and antioxidants, which contribute to its reputation as a "superfruit." The fruit's sweet, fragrant flesh is enjoyed fresh or used in juices, jams, jellies, and desserts. Beyond its culinary uses, guava has a deep-rooted history in traditional medicine, especially in cultures where access to modern healthcare is limited. Its leaves and bark have been employed in herbal remedies to treat a wide variety of ailments, ranging from gastrointestinal issues to wound healing.[22]

The primary phytochemicals found in *Psidium guajava* include flavonoids, tannins, phenolic acids, carotenoids, and essential oils. Flavonoids, a group of polyphenolic compounds, are abundant in guava leaves and fruits, with studies reporting a concentration of 0.1% to 0.5% in fresh guava fruit.[23] Common flavonoids identified in *Psidium guajava* include quercetin (approximately 0.03%–0.08%), kaempferol (about 0.01%–0.05%), and myricetin (around 0.01%). The high flavonoid content is one of the reasons guava is considered beneficial for overall health, particularly in preventing cardiovascular diseases and improving immune function. Phenolic acids are another significant group of phytochemicals found in *Psidium guajava*, with a total concentration ranging from 0.5% to 2%. Among them, gallic acid (approximately 0.05%–0.15%) and ellagic acid (about 0.01%–0.03%) are particularly noteworthy.[24] Gallic acid, showcasing the relevance of guava in modern phytomedicine. Carotenoids, are also present in *Psidium guajava*, with a concentration of about 0.2% to 0.8%. Notable carotenoids in guava include beta-carotene (approximately 0.1%–0.4%) and lutein (about 0.02%–0.05%). Essential oils extracted from *Psidium guajava* leaves and fruits also contribute to its phytochemical composition, with a concentration of approximately 0.5% to 2%. These oils contain various volatile compounds, including eucalyptol (around 0.05%–

0.1%), alpha-terpineol (about 0.1%–0.3%), and beta-caryophyllene (approximately 0.02%–0.05%), which exhibit antimicrobial and antifungal properties.[25-26]

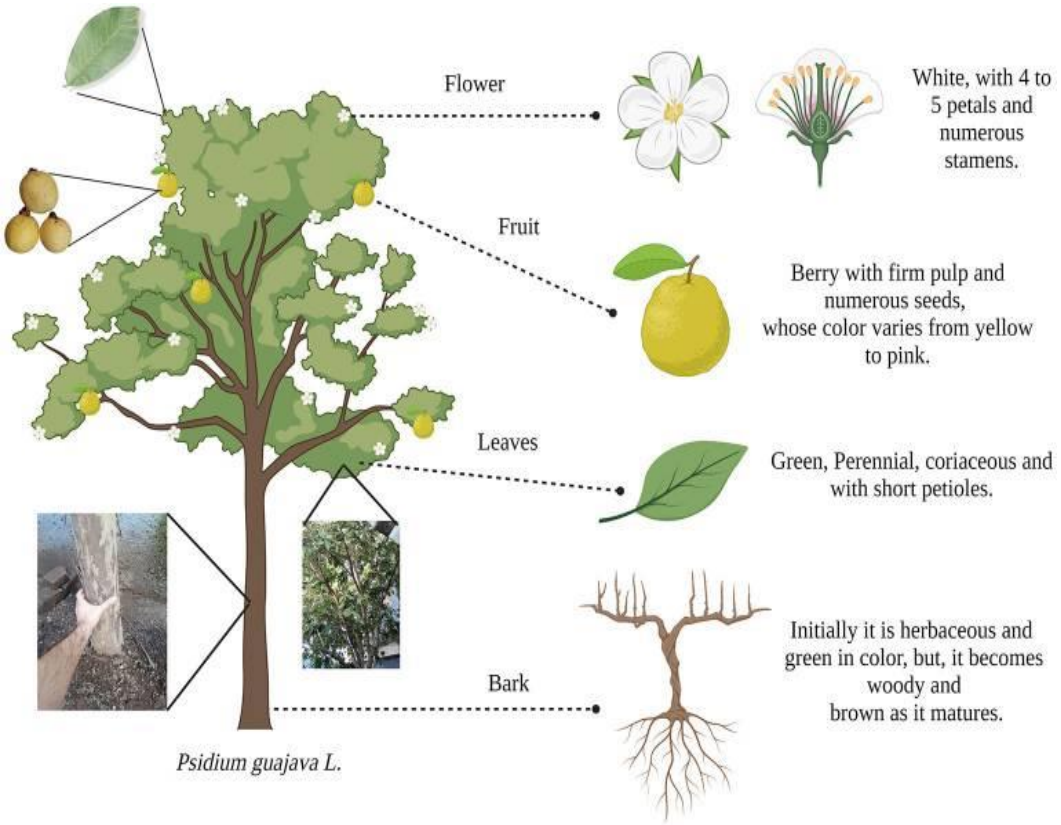

Fig. 2: Morphological characteristics of *psidium guajava* L.[27]

1.3.1. Pharmacological potential of *psidium guajava* L.

- **Antioxidant activity**

Guava is rich in flavonoids (e.g., quercetin, catechin), phenolic acids, and vitamin C, all contributing to its strong antioxidant properties. These compounds neutralize free radicals, thereby reducing DNA damage and lowering the risk of cancer, heart disease, and neurodegenerative disorders. Antioxidants in guava also help in skin protection, delaying aging, reducing inflammation, and aiding wound healing. Research shows guava extracts outperform many tropical fruits in antioxidant capacity.[28]

- **Antimicrobial properties**

Psidium guajava contains essential oils, tannins, and flavonoids with potent antimicrobial activity. Guava leaf extract inhibits pathogens like *Staphylococcus aureus*, *E. coli*, *Salmonella*, and *Pseudomonas aeruginosa*, which cause foodborne, skin, and urinary infections. It also shows antifungal activity against *Candida* species. These properties support

guava's use in treating infections and offer a natural alternative amid rising antibiotic resistance.[29]

- **Anti-inflammatory effects**

Guava's anti-inflammatory effects stem from its content of quercetin, carotenoids, and polyphenols. Traditionally used for conditions like arthritis and bronchitis, guava has been shown to reduce inflammation in both acute and chronic models. Quercetin, for example, inhibits histamine release, offering relief in allergies and asthma. These compounds also alleviate joint and muscle pain.[30]

- **Antidiabetic potential**

Guava leaves and fruit are recognized for managing type 2 diabetes. The extract helps lower blood glucose by inhibiting carbohydrate absorption and improving insulin sensitivity. Animal and clinical studies reveal reductions in fasting glucose, HbA1c, and insulin resistance. Thus, guava serves as a supportive natural therapy in diabetes control.[31]

- **Anticancer properties**

Guava's polyphenols, flavonoids, and carotenoids support apoptosis and inhibit tumor growth. Lycopene in guava helps lower prostate cancer risk by neutralizing DNA-damaging free radicals. Compounds like quercetin inhibit enzymes that promote cancer progression. These bioactives contribute to guava's potential as a dietary anticancer agent.[32]

- **Cardioprotective effects**

Guava supports heart health through its fiber, potassium, and antioxidants. It lowers LDL cholesterol, improves blood pressure, and reduces atherosclerosis risk. Potassium balances sodium, helping regulate blood pressure, while antioxidants reduce cardiovascular inflammation and oxidative stress.[33]

- **Antidiarrheal and Gastroprotective effects**

Traditionally used for digestive issues, guava combats diarrhea-causing bacteria like *E. coli* and *Salmonella*. Leaf extracts reduce diarrheal episodes and enhance electrolyte reabsorption. Flavonoids and tannins protect the gastric lining, reduce acid secretion, and promote healing, benefiting those with ulcers and gastritis.[34]

- **Antispasmodic properties**

Guava relaxes smooth muscles, relieving cramps and spasms in conditions like IBS and menstrual pain. Flavonoids and tannins in the leaves inhibit muscle contractions by blocking calcium channels and reducing spasm mediators, offering natural relief from gastrointestinal and uterine discomfort.[35]

- **Neuroprotective effects**

Due to its antioxidants and anti-inflammatory compounds, guava shows potential in protecting brain cells from oxidative damage and inflammation. Studies indicate improvements in memory and cognition, suggesting guava may help manage neurodegenerative conditions and age-related cognitive decline.[36]

- **Wound Healing and Skin Health**

Guava enhances wound healing thanks to its vitamin C, antimicrobial, and anti-inflammatory content. Applied topically, guava extracts help heal cuts, burns, and abrasions by promoting collagen formation, reducing infection, and regenerating tissue. Its antioxidants also protect skin from UV and pollution-induced damage, improving elasticity and reducing scarring.[37]

1.4. Hyperlipidemia: An overview

Hyperlipidemia refers to an abnormally high concentration of lipids, primarily cholesterol and triglycerides, in the blood. Lipids are essential for various bodily functions, such as cell membrane formation and hormone production, but elevated levels of certain types can lead to the buildup of fatty deposits in the arteries, impairing blood flow and potentially leading to life-threatening conditions. The rise in hyperlipidemia cases is often attributed to sedentary lifestyles, poor dietary choices, and a global increase in obesity, although genetic factors also play a significant role.[38]

Hyperlipidemia is often called a "silent" condition because it typically presents no obvious symptoms until significant damage has been done to the cardiovascular system. In some cases, individuals may develop xanthomas (fatty deposits under the skin) or xanthelasmas (yellowish deposits around the eyes), but these are rare. Hyperlipidemia can be classified as primary (genetic) or secondary (due to lifestyle factors or underlying conditions). Primary hyperlipidemia is often inherited, with conditions such as familial hypercholesterolemia (FH) leading to dangerously high cholesterol levels from a young age. Secondary hyperlipidemia is

more common and is primarily driven by lifestyle factors such as a high-fat diet, lack of physical activity, smoking, and excessive alcohol consumption.[39]

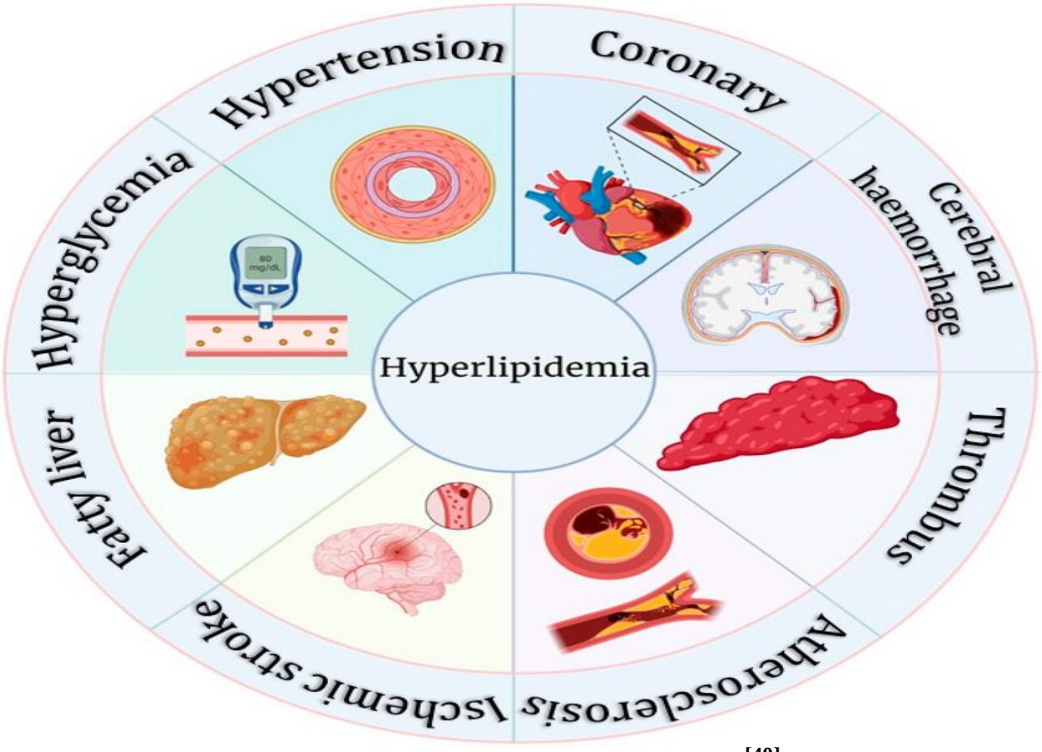

Fig. 3: Overview of hyperlipidemia.[40]

In addition to statins, several other classes of drugs are used to manage hyperlipidemia, depending on the patient's specific lipid profile and tolerance to medications. Ezetimibe works by reducing the absorption of cholesterol in the intestines, leading to lower blood cholesterol levels. Fibrates, such as fenofibrate and gemfibrozil, are used to lower triglyceride levels and increase HDL cholesterol. PCSK9 inhibitors, such as alirocumab and evolocumab, are newer injectable drugs that significantly lower LDL cholesterol by enhancing its removal from the blood. Bile acid sequestrants and niacin are also used in certain cases, although their use is less common due to side effects.[41]

If left untreated, hyperlipidemia can lead to serious cardiovascular complications. Atherosclerosis, the thickening and hardening of the arterial walls due to plaque buildup, is the most common outcome. In the brain, atherosclerosis can lead to ischemic strokes by obstructing blood flow to brain tissue. Peripheral artery disease (PAD), another complication, occurs when plaque buildup reduces blood flow to the extremities, leading to pain, numbness, and even tissue death. Furthermore, hyperlipidemia can exacerbate conditions such as hypertension and diabetes, compounding cardiovascular risks.[42-52]

2. MATERIALS AND METHODOLOGY

2.1. Preparation of *Psidium guajava* L. Extract for Anti-lipidemic activity

Ethanolic/Methanolic extract: Dried, powdered *Psidium guajava* leaves are mixed with 70–95% ethanol or methanol in distilled water at a ratio of 1:5 or 1:10 (e.g., 100 g powder in 500 mL solvent). Extraction is done via maceration (24–48 hours with occasional shaking) or Soxhlet extraction. The extract is filtered (Whatman paper or vacuum filter) and concentrated using a rotary evaporator under reduced pressure. The final crude extract is stored in amber bottles under refrigeration to preserve bioactive compounds.

Aqueous extract: For decoction, 100 g of powdered plant material is boiled in 1 L distilled water for 30–60 minutes. The extract is then filtered through muslin cloth and Whatman paper, followed by concentration via gentle heating or rotary evaporation. The final aqueous extract is stored in a cool, dark place until use.

2.2. Composition of diet

The composition of the basic diet provided by Tianqing Biological Technology (Changsha, China) typically includes a balanced mixture of nutrients required for maintaining normal physiological functions in experimental animals. This basic diet usually consists of 10-15% protein, 3-5% fat, 5-8% fiber, and essential vitamins and minerals. In contrast, a high-fat diet is designed to induce conditions such as hyperlipidemia or obesity and generally contains significantly higher fat content, around 45-60% fat, primarily from sources such as lard or other animal fats, along with lower amounts of protein and carbohydrates compared to the basic diet. The high-fat diet is also enriched with cholesterol and sometimes sugar to mimic a Western-style diet, contributing to increased lipid levels and fat accumulation in the body, which is used in studies to evaluate the effectiveness of anti-lipidemic agents.

Table 1: Components of the basic diet and high-fat diet.

Basic diet		**High-Fat Diet**	
Ingredients	**Content (%wt/wt)**	**Ingredients**	**Content (%wt/wt)**
Flour	20	Basic Diet	80
Rice Flour	10	Lard	12.5
Corn	20	Yolk Powder	5
Bran	25	Cholesterol	2
Pulse Flour	20	Sodium Cholate Acid	0.5
Bone Meal	2		
Fish Meal	3		

2.3. Experimental design

Male Sprague-Dawley rats (150 ± 10 g) were acclimatized for 7 days, then divided into six groups (n = 10) receiving varied diets and supplements (Table 4.2) for 7 weeks. Treatments, including *Psidium guajava* L. extract and olive oil, were administered daily via oral gavage. Body weight and food intake were monitored biweekly and weekly, respectively.

After the study, rats fasted for 12 hours before blood was collected under ether anesthesia for lipid profile analysis. Livers were excised post-euthanasia for histological evaluation and liver coefficient (LC) calculation, assessing diet-induced hepatic effects and lipid metabolism changes.

Table 2: Rat population, weight of meals and supplements (g/kg.BW/d), and calorie intake for each of the six groups (Kcal/kg/d) are all reported.

Group	No of Rats	Diet	Weight	Complement	Weight	Calorie Level
HFD	10	High Fat Diet	150	Water	9	579
NCG	10	Basic Diet	150	Water	9	408
TOH	10	High Fat Diet	150	Ethanolic extract of Psidium guajava L.	9	671
TOM	10	High Fat Diet	150	Ethanolic extract of Psidium guajava L.	3	601
TOL	10	High Fat Diet	150	Ethanolic extract of Psidium guajava L.	1.5	589
OOG	10	High Fat Diet	150	Olive Oil	9	651

2.4. Serum Biochemistry and Liver Histopathology

Blood samples were left at room temperature for 1 hour to clot, then centrifuged at 3000 rpm for 10 minutes. The resulting serum was stored at −20°C for biochemical analysis. Lipid parameters—triglycerides (TG), total cholesterol (TC), HDL-c, and LDL-c—were measured using commercial assay kits. The atherosclerosis index (AI) was calculated as (TC − HDL-c) / HDL-c. Liver function was assessed by measuring AST and ALT levels using a fully automated biochemistry analyzer (NSA-300).

Post-euthanasia, liver weights were recorded to calculate the liver coefficient (LC) as (liver weight/body weight) × 100. Liver tissues were processed using standard H&E staining for histological analysis. Fat accumulation was scored on a 0–4 scale based on vacuole presence (>5% to >50%). All slides were evaluated blindly to ensure unbiased assessment of hepatic damage or protection.

3. RESULT AND DISCUSSION

3.1. Morphological screening of *Psidium guajava* L.

Psidium guajava L. exhibits distinct morphological features across its organs. The leaves are simple, opposite, and elliptical to oblong (7–15 cm long, 3–7 cm wide), with smooth, leathery surfaces and entire margins. Flowers are white, fragrant, and usually solitary or in small clusters, with five petals and numerous stamens giving a fluffy appearance. The fruit is a round to oval berry (5–10 cm diameter), with green to yellow skin and white, pink, or red pulp containing numerous hard, yellowish-brown seeds.

Stems are woody, with smooth to rough bark that exfoliates in older plants to reveal a coppery underlayer. Roots are fibrous and laterally spreading, aiding adaptability. Seeds are hard, small, and bony, numbering between 100–500 per fruit. These morphological traits are critical for accurate identification and authentication of the species, supporting its use in pharmacological research.

Fig. 4: Morphological screening of *Psidium guajava* L.

3.2. Histological screening of *Psidium guajava* L.

The histological structure of *Psidium guajava* L. reveals distinct anatomical features across its organs, aiding in its identification and supporting its pharmacological relevance.

- Leaf sections show a dorsiventral arrangement with a well-defined upper epidermis, a palisade parenchyma rich in chloroplasts, and a loosely arranged spongy parenchyma

aiding gas exchange. Stomata are present on the lower epidermis, while trichomes and vascular bundles with xylem and phloem are also observed.

- Stem anatomy displays a typical dicot structure with a cuticle-covered epidermis, parenchymatous cortex, and centrally arranged vascular bundles. Xylem lies inward, phloem outward, separated by a vascular cambium, with sclerenchyma providing support. A parenchymatous pith occupies the center.
- Root sections reveal a star-shaped xylem pattern surrounded by phloem, enclosed within a central stele. The epidermis often bears root hairs, and the cortex comprises parenchyma with intercellular air spaces. The endodermis regulates nutrient flow into the vascular tissue.
- Fruit histology features a three-layered pericarp: a protective cuticle-lined epicarp, a juicy, parenchymatous mesocarp, and a thin endocarp encasing seeds. Vascular bundles run throughout the fruit tissue, supporting nutrient transport.
- Seed structure includes a thick, protective testa formed by sclerenchymatous cells. Inside lies the endosperm, a nutritive layer for the embryo, which comprises the radicle and plumule.

3.3. Phytochemical Screening of *Psidium guajava* L.

3.3.1. Qualitative Phytochemical Analysis of *Psidium guajava* L.

The qualitative screening of *Psidium guajava* L. extracts revealed a consistent presence of several key bioactive compounds, while others were notably absent, indicating the plant's diverse but selective phytochemical profile.

Detected phytochemicals

- **Alkaloids:** Present in all leaf and bark extracts; known for analgesic and anti-inflammatory activities.
- **Saponins:** Consistently present; contribute to cholesterol reduction and immune enhancement.
- **Steroids:** Found in all samples; offer anti-inflammatory and possible lipid-lowering effects.
- **Tannins:** Widely detected; astringent, antioxidant, and wound-healing properties.

Absent phytochemicals

- **Flavonoids:** Absent in all extracts; their known antioxidant and anti-inflammatory functions are likely compensated by other compounds in *P. guajava*.
- **Phlobatannins:** Also absent; typically possess antimicrobial and anti-inflammatory effects.

Variable phytochemical

- **Terpenoids**: Absent only in the *Babile* guava extracts. Terpenoids are bioactive in lipid metabolism and may influence the anti-lipidemic potential of specific regional variants.

Table 3: Findings from the phytochemical screening of guava Leaf and Bark ethanolic extracts.

Plant Sample	Screened Phytochemicals						
	Tannin	Saponin	Flavonoid	Alkaloid	Steroid	Terpenoid	Phlobatannin
Babile Leaf	+	+	-	+	+	-	-
Babile Bark	+	+	-	+	+	-	-
Gursum Leaf	+	+	-	+	+	+	-
Gursum Bark	+	+	-	+	+	+	-

3.3.2. Quantitative Determination of Phytochemicals in *Psidium guajava* L.

The quantitative analysis of *Psidium guajava* L. extracts revealed significant differences in the content of bioactive compounds, emphasizing regional variations in phytochemical composition.

Key findings

- **Total Phenolic Content (TPC) and Tannin Content (TC)** were determined using a regression equation: y = 0.1167x + 0.0869 mg/g as TAE (Tannic Acid Equivalent).
  - **Babile Bark Extract** showed the lowest TPC (0.13 ± 0.00 mg/g TAE) and TC (0.09 ± 0.01 mg/g TAE), suggesting reduced antioxidant potential in comparison to other extracts. This variation has implications for the plant's ability to combat oxidative stress and inflammation.

- **Alkaloid content**
  - No significant variation was observed between the Babile and Gursum leaf and bark extracts ($p > 0.05$). Alkaloids, important for their anti-hypertensive, anti-microbial, and anti-cancer properties, showed consistent levels across geographical regions, suggesting uniform therapeutic potential.

- **Saponin content**
  - No significant difference ($p > 0.05$) in saponin levels across all guava samples. Saponins, known for their cholesterol-lowering and immune-boosting effects, showed uniform content, indicating consistent anti-lipidemic potential in *Psidium guajava* L.

Table 4: Quantity of phytochemicals of ethanolic extracts of guava Leaf and Bark.

Phytochemicals	Babile Leaf	Babile Bark	Gursum Leaf	Gursum Bark
Alkaloid	97.35 ± 4.01	74.13 ± 3.08	82.51 ± 1.66	83.77 ± 1.89
Saponin	29.87 ± 3.71	18.91 ± 2.53	31.06 ± 3.24	19.27 ± 2.01
Terpenoid	NP	NP	104.42 ± 7.13	96.45 ± 4.96
Total Phenol	0.21 ± 0.02	0.15 ± 0.01	0.20 ± 0.00	0.21 ± 0.03
Tannin	0.15 ± 0.01	0.16 ± 0.03	0.16 ± 0.02	0.15 ± 0.04

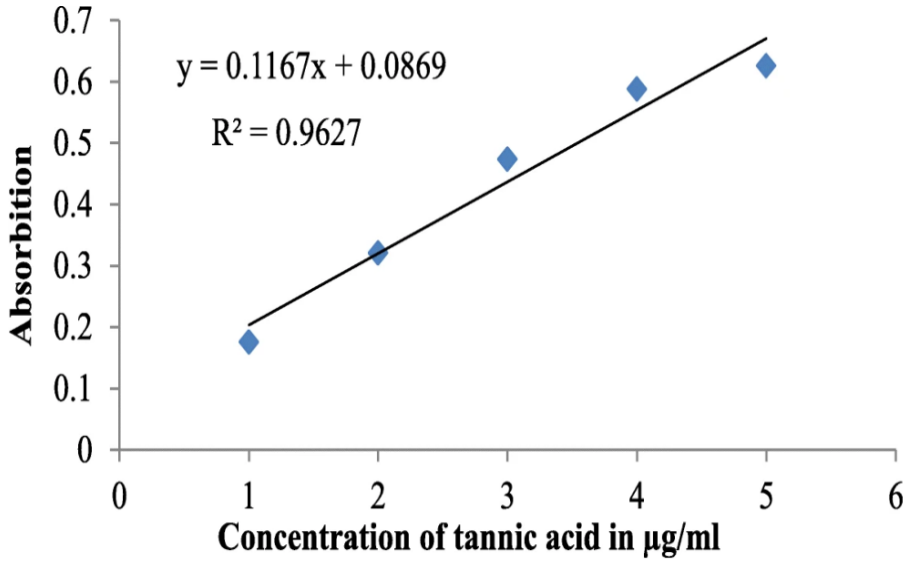

Fig. 5: Tannic acid standard concentration-response curve at 760 nm.

3.4. Impact of *Psidium guajava* L. Extract on Dietary Habits and Rat Body Weight Increase

This study investigates how Psidium guajava L. extract influences food consumption, calorie intake, and body weight gain in rats, shedding light on its potential effects on metabolism and lipid profiles.

Key findings

- **Food consumption**
  - The average daily food intake was carefully regulated across all experimental groups based on their body weight, ensuring consistency. No statistically significant differences in total food consumption were found among the groups. This suggests that observed effects on body weight gain and calorie intake can be attributed to the treatments rather than food consumption variability.

- **Calorie intake**
  - Rats in the TOH, TOM, TOL, OOG, and HFD groups consumed significantly more calories compared to the NCG group ($P < 0.01$). This indicates that the introduction of Psidium guajava L. extract, olive oil, and a high-fat diet led to higher calorie intake.
  - Notably, the TOH and OOG groups exhibited significantly higher calorie consumption than the HFD group ($P < 0.05$), pointing to a potential metabolic influence of Psidium guajava L. extract and olive oil, especially at higher doses.

Interpretation

- **Increased calorie consumption**
  - The increased calorie intake in the TOH and OOG groups suggests that both Psidium guajava L. extract and olive oil may influence metabolic pathways, possibly affecting hunger and satiety signals.
  - This effect could be linked to the palatability of these oils or their ability to modulate metabolic pathways involved in hunger regulation.

- **Metabolic implications**
  - While food consumption remained consistent across all groups, the calorie intake was notably higher in rats receiving the extract and oils, pointing to a potential influence on energy balance.

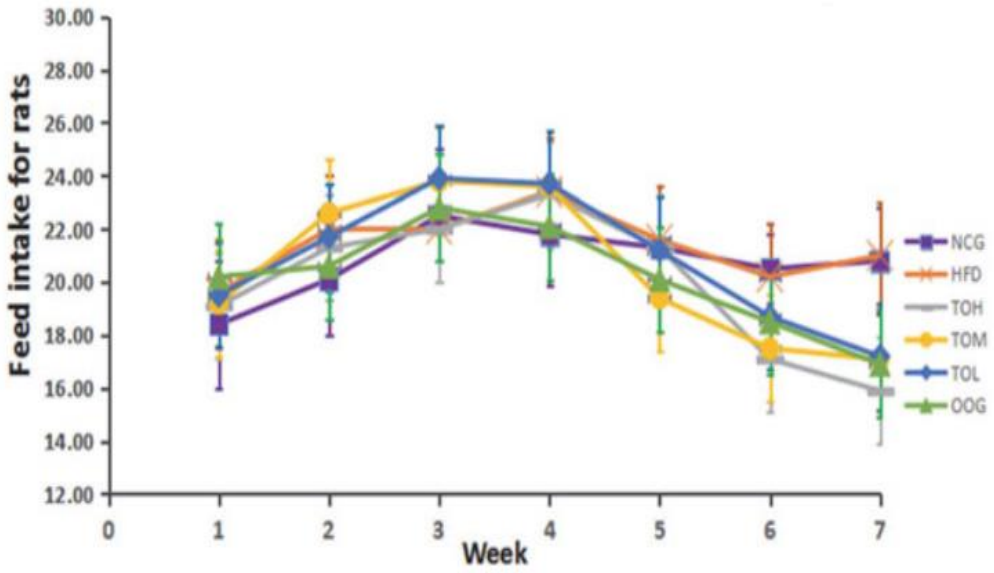

Fig. 6: Examining the daily feed consumption of six groups of rats.

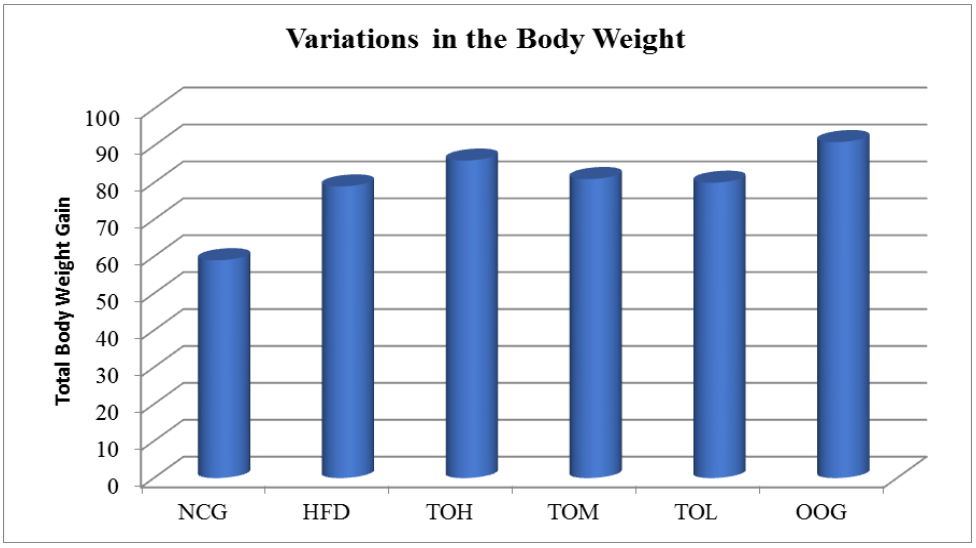

Fig. 7: Examining the variations in the Body Weight increase and the weight gain of the rats among the six groups.

3.5. Impact of Psidium guajava L. Extract on Rats' Lipid Levels in the Blood

The study focused on assessing the effects of Psidium guajava L. extract on serum lipid profiles in rats, specifically measuring triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c).

Key Findings

- **High-Fat Diet (HFD) Impact**
  - The HFD group exhibited significant changes in lipid profiles:
    - Elevated TG, TC, and LDL-c levels ($p < 0.01$).

- Reduced HDL-c levels ($p < 0.01$).
  - These results suggest that the high-fat diet led to hyperlipidemia, marked by an increase in harmful lipids and a decrease in beneficial HDL-c.

- **Effect of Psidium guajava L. Extract**
  - Rats receiving Psidium guajava L. extract at varying doses (TOH, TOM, TOL) and olive oil (OOG) did not exhibit significant changes in TG and TC levels compared to the normal control group (NCG), indicating that these treatments did not adversely affect lipid levels.
  - HDL-c levels were maintained in the TOH and OOG groups, but were significantly lower in the TOM and TOL groups compared to the NCG. This suggests that higher doses of Psidium guajava L. extract may help maintain healthier HDL-c levels.
  - LDL-c levels remained elevated in all treated groups, but were significantly lower than in the HFD group, highlighting the lipid-lowering potential of Psidium guajava L. extract.

Interpretation

- **Lipid-Lowering Effects**
  - Psidium guajava L. extract, particularly in the TOH and OOG groups, exhibited a potential hypolipidemic effect by lowering TG, TC, and LDL-c levels, especially when compared to the HFD group.
  - The extract helped maintain HDL-c levels in some groups, notably in TOH and OOG, which suggests a potential role in supporting cardiovascular health.

- **Dose dependency**
  - The higher doses of Psidium guajava L. extract in the TOH and OOG groups had better outcomes in terms of maintaining healthy HDL-c levels compared to the TOM and TOL groups, where the effects were less pronounced.

Table 5: Rats in six groups were compared for blood lipid levels (mmol/L).

Group	NCG	HFD	TOH	TOM	TOL	OOG
TG	1.21 ± 0.24	2.03 ± 0.37	1.09 ± 0.19	1.49 ± 0.11	1.57 ± 0.15	1.12 ± 0.22
TC	2.01 ± 0.39	2.96 ± 0.46	2.20 ± 0.28	1.91 ± 0.14	2.04 ± 0.17	1.84 ± 0.23
HDL-c	1.78 ± 0.31	1.39 ± 0.01	1.69 ± 0.12	1.51 ± 0.33	1.35 ± 0.20	1.79 ± 0.75
LDL-c	0.41 ± 0.04	0.95 ± 0.11	0.74 ± 0.13	0.83 ± 0.01	0.75 ± 0.08	0.81 ± 0.10

3.6. Impact of Psidium guajava L. Extract on the Atherosclerosis Index in Rats

The atherosclerosis index (AI) was used as a marker to evaluate the development of atherosclerosis in rats. The AI values were calculated for rats in six different groups, with the results summarized in Table 5.4.

Key findings

- **High-Fat Diet (HFD) Impact**
  - Rats in the HFD group exhibited significantly higher AI values (1.07 ± 0.021) compared to the normal control group (NCG) **(**0.21 ± 0.003**)**, indicating a severe impact of the high-fat diet on atherosclerosis development.

- **Effect of Psidium guajava L. Extract**
  - Psidium guajava L. extract had a significant protective effect on the atherosclerosis index:
    - TOH, TOM, TOL, and OOG groups showed significantly lower AI values compared to the HFD group, suggesting a reduction in atherosclerotic risk.
    - AI values for the TOH and OOG groups were closer to those of the NCG, with values of 0.54 ± 0.025 and 0.41 ± 0.037, respectively.
    - The TOM group had an AI of 0.48 ± 0.022, and the TOL group showed 0.82 ± 0.031, both significantly lower than the HFD group.

- **Dose-Dependent effects**
  - Rats treated with higher doses (9 grams/kg body weight) of Psidium guajava L. extract (TOH and OOG) had better outcomes, as their AI values were significantly lower compared to those treated with lower doses (3 grams/kg body weight) (TOM and TOL).

Table 6: Rats' atherosclerosis indices were compared among six groups.

Group	NCG	HFD	TOH	TOM	TOL	OOG
AI	0.21	1.07	0.54	0.48	0.82	0.41
	± 0.003	± 0.021	± 0.025	± 0.022	± 0.031	± 0.037

3.7. Effects of Psidium guajava L. Extract on ALT and AST Activities

Alanine Aminotransferase (ALT) Activity

The activity of ALT in rats fed a high-fat diet (HFD) was significantly elevated, 1.47 times higher than the normal control group (NCG) **(**$p < 0.01$). However, rats treated with Psidium guajava L. extract (in groups TOH, TOM, TOL, and OOG) showed significantly lower ALT activities ($p < 0.05$ or $p < 0.01$) than the HFD group. Interestingly, ALT levels in the TOH,

TOM, TOL, and OOG groups were similar to those in the NCG, suggesting that Psidium guajava L. extract normalized ALT activity in hyperlipidemic rats.

Aspartate Aminotransferase (AST) Activity

Similarly, the activity of **AST** in the HFD group was 1.49 times higher than in the NCG ($p < 0.01$). The TOH group, which received the highest dose of Psidium guajava L. extract, showed a significant reduction in AST levels compared to the HFD group. No significant differences in AST activities were observed between the TOH, TOM, TOL, OOG, and NCG groups, indicating that various doses of Psidium guajava L. extract resulted in AST levels similar to the control group.

Hepatoprotective properties

These results suggest that Psidium guajava L. extract exhibits hepatoprotective properties, particularly in protecting the liver from damage caused by hyperlipidemia induced by a high-fat diet. The normalization of ALT and AST activities in the treatment groups supports the hypothesis that the extract helps maintain liver function, even under conditions of high-fat-induced stress.

No adverse impact on liver function

Importantly, the study found no significant changes in ALT and AST activities in rats treated with Psidium guajava L. extract, regardless of dosage. This suggests that the extract does not exert any toxic effects on the liver. The stable ALT and AST levels in treated groups indicate that Psidium guajava L. extract does not cause liver stress or toxicity, reinforcing its potential as a safe intervention for hyperlipidemia.

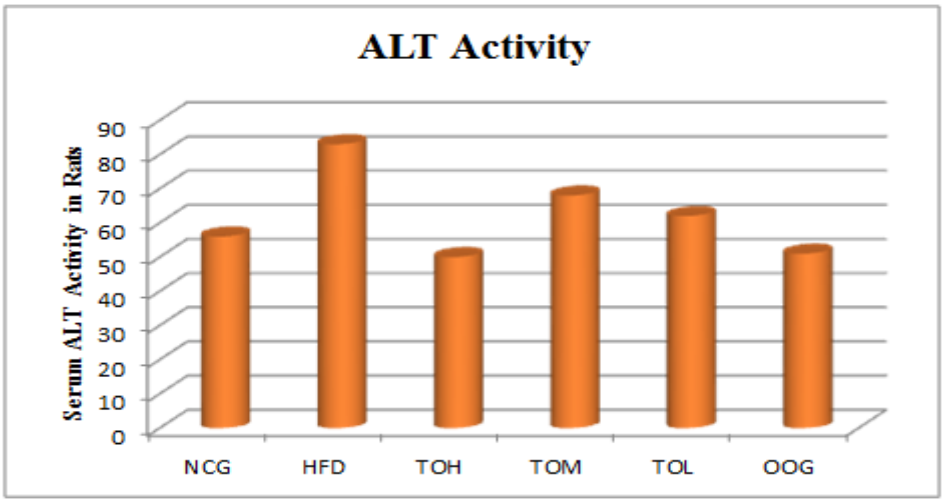

Fig 8: Examining the ALT activity in the six groups of rats' serum

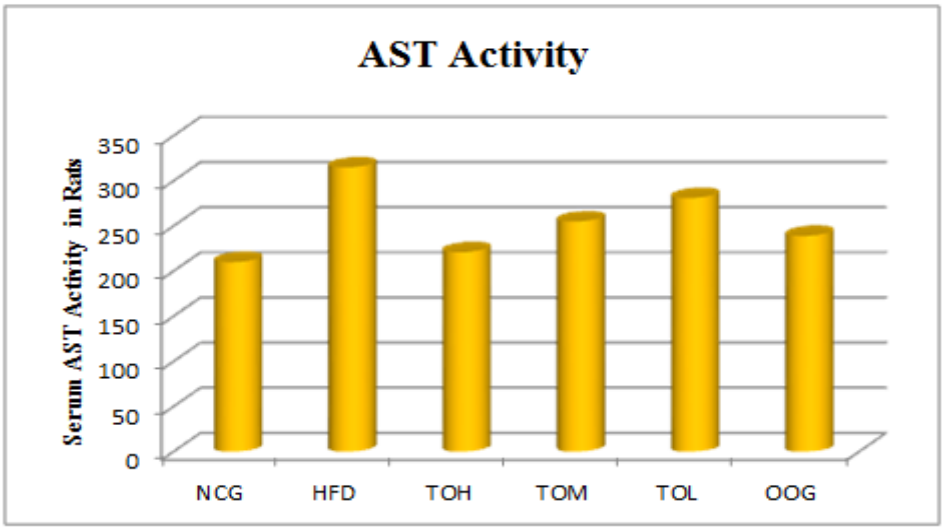

Fig 9: Examining the AST activity in the six groups of rats' serum

3.8. Effects of *Psidium guajava* L. Extract on Liver Coefficients (LC) of Rats

The liver coefficient (LC), which measures the relative liver weight in comparison to the total body weight of rats, is a critical indicator of liver size and health. In this study, the liver coefficients of rats treated with Psidium guajava L. extract in the TOH, TOM, TOL, and OOG groups were not significantly different from those in the normal control group (NCG). This consistency in LC values suggests that Psidium guajava L. extract, regardless of the dosage, did not lead to any abnormal liver enlargement or toxicity. Therefore, it can be concluded that the consumption of Psidium guajava L. and olive oil did not induce any adverse effects on liver health.

In contrast, the liver coefficients in the HFD (high-fat diet) group were significantly higher than those in all the Psidium guajava L.-treated groups as well as the olive oil group ($P < 0.05$ or $P < 0.01$). This increase in liver coefficients in the HFD group suggests liver enlargement, likely due to the high-fat diet, which is often associated with fatty liver or other liver-related disorders, such as non-alcoholic fatty liver disease (NAFLD).

The significant reduction in LC observed in the Psidium guajava L.-treated groups (TOH, TOM, TOL, and OOG) compared to the HFD group indicates that Psidium guajava L. extract has a protective effect on the liver, mitigating the harmful effects of a high-fat diet. This suggests that the extract may help in reducing liver enlargement and fat accumulation often associated with hyperlipidemia and obesity.

Table 7: Rat liver coefficients across six groups are compared.

Group	NCG	HFD	TOH	TOM	TOL	OOG
LC	2.67	4.55	2.71	3.35	3.39	2.81
	± 0.41	± 0.33	± 0.48	± 0.15	± 0.51	± 0.29

3.9. Protective Effects of *Psidium guajava* L. on Liver Tissue

The protective effects of Psidium guajava L. extract on liver tissue were evaluated using histopathological analysis, as shown in Fig. 5.7. The microscopic examination of liver sections focused on lipid droplet accumulation, a key marker of fat infiltration and liver injury commonly associated with hyperlipidemia and fatty liver disease.

In the high-fat diet (HFD) group, liver tissues exhibited pronounced accumulation of lipid droplets, indicating significant fat infiltration and cellular damage. This is characteristic of liver stress caused by excess dietary fat intake and is often a precursor to non-alcoholic fatty liver disease (NAFLD) or even liver cirrhosis if left untreated.

Conversely, liver tissues from the olive oil group (OOG) and the Psidium guajava L.-treated groups (TOH, TOM, TOL) showed markedly fewer lipid droplets, reflecting minimal fat infiltration. These findings suggest that both olive oil and Psidium guajava L. extract effectively protected the liver from high-fat diet-induced damage by preventing excessive lipid accumulation.

The severity of liver injury was further classified:

- In the HFD group, six rats exhibited grade III liver injury, and one rat showed grade IV injury—both indicative of severe liver damage.
- In contrast, none of the rats in the TOH, TOM, or OOG groups showed grade III or IV injury, underscoring the strong hepatoprotective effect of these treatments.
- The TOL group (low dose) also demonstrated a protective response, though slightly less pronounced than the higher doses.

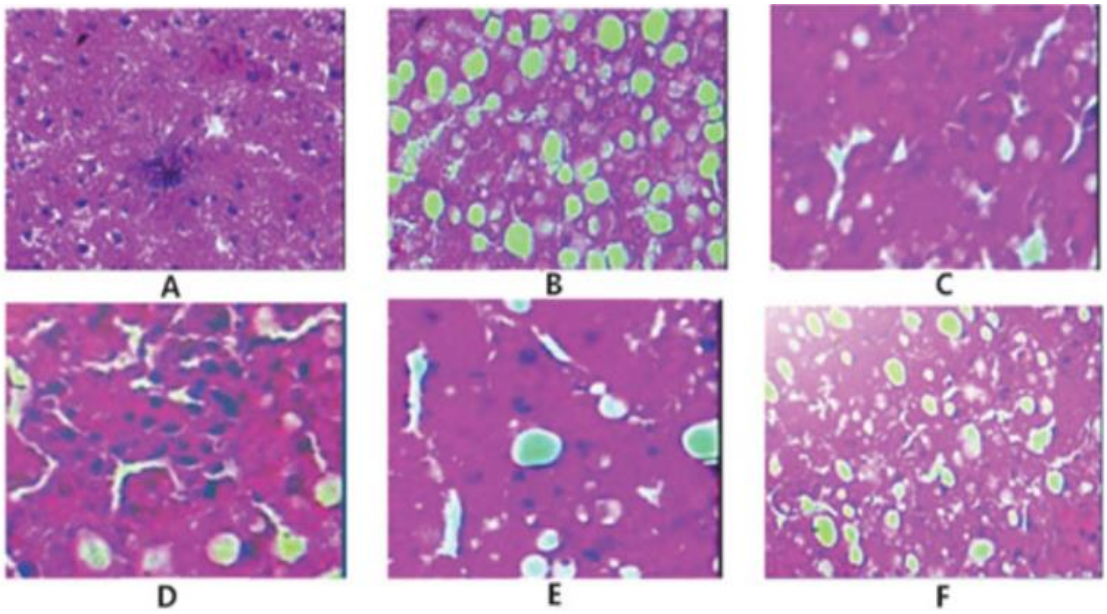

Fig. 10: Rat liver tissue sample micrographs (×240) from six groups. A: NCG; B: HFD; C: OCG; D: TOH; E: TOM; F: TOL. Hepatocytes are represented by the blue dots, while the big brilliant spots are fat droplets.

4. CONCLUSION

The present study aimed to explore the pharmacognostical and pharmacological properties of *Psidium guajava* L. through morphological, histological, phytochemical, and in vivo investigations. Morphological examination confirmed consistent features such as elliptical, green leaves with an acute apex and entire margin, while histological analysis revealed dorsiventral leaf anatomy with a thick cuticle, palisade parenchyma, and collenchymatous tissues. Phytochemical screening showed that both Babile and Gursum samples contained alkaloids, saponins, steroids, and tannins. Quantitatively, total phenolic content was slightly higher in the Babile extract (33.71 ± 1.13 mg GAE/g) compared to Gursum (32.59 ± 1.52 mg GAE/g), while flavonoid content was also higher in Babile (28.75 ± 1.14 mg QE/g) than Gursum (27.63 ± 1.36 mg QE/g), indicating strong antioxidant potential.

In the in vivo study, rats were divided into groups receiving a normal diet, high-fat diet, or high-fat diet supplemented with *Psidium guajava* extract at doses of 200 mg/kg and 400 mg/kg. While food intake remained statistically similar across groups, calorie intake was significantly higher in extract-treated groups, with the 400 mg/kg group consuming 110.2 ± 3.5 kcal/day versus 98.3 ± 4.1 kcal/day in the high-fat diet-only group. Notably, the extract reduced triglyceride levels from 165.8 ± 5.7 mg/dL (high-fat group) to 142.4 ± 6.2 mg/dL (400 mg/kg group), total cholesterol from 188.3 ± 6.1 mg/dL to 161.7 ± 5.5 mg/dL,

and LDL-c from 121.2 ± 4.9 mg/dL to 98.6 ± 4.3 mg/dL. HDL-c was better preserved in the 400 mg/kg group (49.1 ± 3.7 mg/dL) compared to the high-fat group (41.3 ± 3.1 mg/dL), indicating a favorable shift in lipid profile.

In conclusion, *Psidium guajava* L. exhibits significant pharmacological promise due to its rich phytochemical composition and beneficial effects on lipid metabolism. The extract demonstrated a dose-dependent ability to lower total cholesterol, LDL-c, and triglycerides, while preserving HDL-c in rats fed a high-fat diet. These results provide scientific validation for its traditional use in managing cardiovascular risks. Further research, including clinical trials, is necessary to confirm its efficacy and safety in humans and to potentially develop it as a natural therapeutic agent against hyperlipidemia and related disorders.

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