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REVIEW ARTICLE

A Review on Botanical, Geographical, and Nutritional Properties of the Underutilized Tropical Species *Limonia acidissima* L.

Majedul Hoque*, Mt Farzana Yasmin

Department of Pharmacy, Jahangirnagar University, Dhaka, Bangladesh

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Abstract: *Limonia acidissima* L. (Rutaceae), also called as the wood apple, is a highly resilient, drought-tolerant tropical tree species indigenous to the arid and semi-arid plains of the Indian subcontinent and Southeast Asia. The highly aromatic acidic pulp inside the heavily lignified, stony pericarp, serves as a rich repository of macronutrients, micronutrients, and functional secondary metabolites. The tree has high concentrations of dietary fibers, carbohydrates, pectin, and proteins within the pulp, alongside significant mineral densities predominantly potassium, calcium, and phosphorus and essential vitamins such as ascorbic acid, thiamine, and riboflavin. Phytochemical composition shows rich volatile terpenes, furanocoumarins, alkaloids, flavonoids, phytosterols, and organic acids distributed across the fruit pulp, seeds, leaves, and bark tissues. Traditional healthcare systems, including Ayurveda, Siddha, and Unani, have historically used various parts of this tree species to manage gastrointestinal disturbances, hepatobiliary disorders, metabolic anomalies, respiratory infections, and cardiovascular weakness. Modern pharmacological assays substantiate these ethnobotanical applications, indicating robust antioxidant, anti-hyperglycemic, hepatoprotective, antimicrobial, gastroprotective, and cytotoxic behaviors both *in vitro* and *in vivo*. Although having high-value therapeutic and nutritional characteristics, the crop remains largely neglected by commercial industries due to a lack of standardized processing methodologies, clinical validation, and genetic optimization.

Keywords: *Limonia acidissima*; Nutritional composition; Mineral density; Underutilized crops; Ethnobotanical systems.

1. Introduction

Traditional medicine across the globe continue to rely on herbs and plants as primary therapeutic agents [1]. Modern drug discovery frequently utilize these natural products due to their structural complexity, lower relative toxicity profiles, and multi-target pharmacological mechanisms [2]. Secondary metabolites including alkaloids, phenolics, saponins, steroids, flavonoids, glycosides, terpenoids, and condensed tannins constitute the primary bioactive engine driving these therapeutic applications [3]. Volatile essential oils derived from these botanical frameworks find utility as food preservatives, aromatic enhancers, and industrial antimicrobial agents [4]. *Limonia acidissima* L. (syn. *Feronia limonia* (L.) Swingle, *Feronia elephantum* Correa), a prominent member of the Rutaceae family, represents a highly adaptable, slow-growing tropical tree species native to the subtropical plains and arid regions of India, Bangladesh, Sri Lanka, and Pakistan [5, 6].

Locally designated as *kathbel*, curd fruit, monkey fruit, or elephant apple, this species shows exceptional environmental resilience, thriving in drought-prone, marginal soils where conventional commercial citrus species fail to survive [7]. The tree exhibits an extensive productive lifespan, typically ranging from 12 to 70 years [8]. In the deltaic and semi-arid tracts of Bangladesh, fruit maturation occurs primarily between March and October. Traditional harvesting rely on distinct mechanical and physical indicators of ripeness. A primary field-level diagnostic test involves dropping the fruit from a height of approximately 1 foot (30 cm) onto a compacted horizontal surface; mature fruits exhibit minimal or no rebound because the highly softened, mealy density of the inner pulp absorbs the kinetic impact, whereas immature fruits bounce significantly due to high internal turgidity and water-retaining cellular structures. Post-harvest, fruits are cured in direct sunlight for approximately two weeks to facilitate the metabolic hydrolysis of starches into simple sugars, thereby optimizing the sweet-sour organoleptic profile [9].

The mature pulp has a distinct sour-sweet balance, rendering it suitable for raw consumption and processing into specialized culinary products, including sherbets, preserves, jams, jellies, and spicy chutneys [10, 11]. Structurally, the fruit pulp contains a complex chemical array consisting of polyphenolic fractions, vitamins, amino acids, triterpenoids, phytosterols, and specialized tyramine derivatives [12]. Preliminary phytochemical evaluations have identified major steroidal compounds, acidic glycosides, and distinct furanocoumarins in the fruit, alongside specialized alkaloids, resins, and mucilage in the foliar tissues [13, 14]. Ethnomedicinally, *L.*

* Corresponding author: Majedul Hoque

acidissima is highly regarded for its therapeutic action against chronic diarrhea, bacillary dysentery, asthma, external wounds, inflammatory tumors, and hepatic congestion [15]. The pulp is exceptionally rich in metabolic cofactors, containing significant concentrations of thiamine (B1), riboflavin (B2), niacin (B3), vitamin A, and ascorbic acid (C) [16]. This monograph compiles and evaluates the botanical classification, geographic distribution, nutritional value, phytochemistry, pharmacology, traditional applications, and toxicological thresholds of *L. acidissima*.

2. Literature Sourcing

To obtain a rigorous and updated scientific profile of *L. acidissima*, we established a systematic narrative sourcing strategy. High-throughput electronic search engines including the National Institutes of Health (NIH) repository, PubMed, ScienceDirect, Google Scholar, Scopus, and EBSCOwere searched. Literature search strings combined boolean operators with specific keywords, including "*Limonia acidissima*" OR "*Feronia limonia*" OR "Feronia elephantum", "phytochemical composition" OR "bioactive compounds" OR "furanocoumarins", "nutritional profile" OR "proximate analysis" OR "mineral content", "pharmacological activity" OR "antidiabetic" OR "hepatoprotective" OR "antimicrobial", "traditional medicine" OR "ethnobotanical uses" The selection criteria restricted inclusion to peer-reviewed English-language journal articles, scientific reference book chapters, and authoritative botanical monographs. Studies selected for analysis were required to offer quantitative nutritional data, validated structural characterizations of secondary metabolites, or controlled *In vitro/In vivo* pharmacological evaluations with defined dosing and statistical thresholds. Non-peer-reviewed white papers, preprints, conference abstracts, and articles lacking authenticated taxonomic verification of the plant material were excluded.

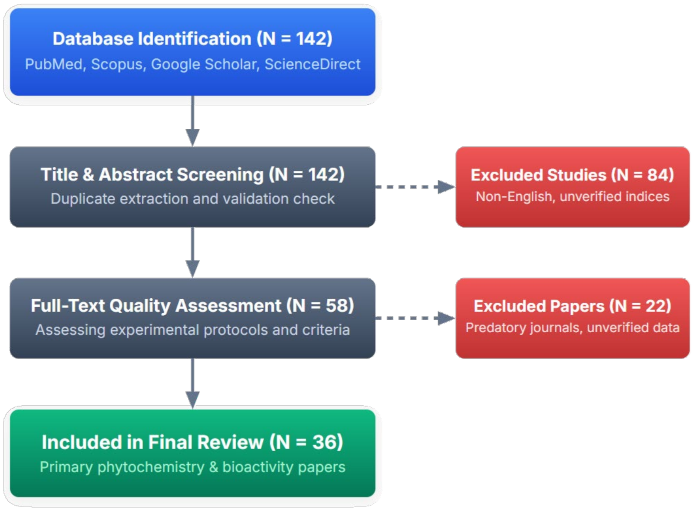

Figure 1. Literature Sourcing and Selection

3. Taxonomy and Morphology

3.1. Nomenclature

Limonia acidissima is belongs to the family Rutaceae (commonly designated as the citrus family), which is characterized by the presence of pellucid glandular cavities containing volatile essential oils. The formal taxonomic hierarchy of the species is organized as follows:

Kingdom: Plantae (Plants)
Sub-kingdom: Tracheobionta (Vascular plants)
Super-division: Spermatophyta (Seed plants)
Division: Magnoliophyta (Flowering plants)
Class: Magnoliopsida (Dicotyledons)
Subclass: Rosidae
Order: Sapindales
Family: Rutaceae (Citrus family)
Genus: *Limonia*
Species: *L. acidissima* L.

3.2. Morphology

Limonia acidissima is a slow-growing, medium-sized, deciduous tree that typically reaches heights of 6 to 10 meters under favorable environmental conditions [17]. The trunk is characterized by its rugged, deeply fissured, greyish-brown bark, which cracks and scales significantly as the tree matures, providing a distinctive textured surface. The branchlet architecture is armed with sharp, rigid, axillary spines measuring 1.5 to 4.0 cm in length, serving as a primary morphological defense mechanism. The younger twigs are finely pubescent and flexible, transitioning into highly lignified, glabrous, and thorny structures over successive growing seasons [18].

The foliage is alternate, pinnately compound, and typically features 5 to 7 leaflets arranged along a narrowly winged or margins-flattened petiole. Each leaflet is obovate or elliptic, measuring 2.0 to 5.0 cm in length, with an entire or slightly crenulate margin and a cuneate base. The foliar surface is coriaceous, exhibiting a lustrous, dark-green coloration on the adaxial surface and a paler green on the abaxial side. Crushing the leaves releases a sharp, citrus-like aroma, indicating the presence of lysigenous oil glands filled with volatile terpenes [17].

The inflorescences consist of small, loose, terminal or axillary panicles. The individual flowers are pentamerous, bisexual, and measure approximately 1.0 to 1.2 cm in diameter. The calyx contains five small, triangular, deciduous sepals, while the corolla is composed of five spreading, greenish-white or dull-red petals. The male reproductive apparatus contains 10 to 12 stamens inserted at the base of an annular disc, surrounding a central, unilocular ovary with a sessile, oblong stigma. This structural configuration supports both insect-mediated cross-pollination and self-pollination [17].

Figure 2. Flowers and Fruits of *Limonia acidissima* L.

The mature fruit is a globose berry measuring 5 to 10 cm in diameter, enclosed in an extremely hard, woody, grayish-white pericarp (rind) approximately 6 mm thick. The fruit interior consists of a dense, highly aromatic, sticky pulp that transitions from pale greenish-yellow in the unripe state to a dark reddish-brown, mealy, and resinous mass upon ripening. Embedded within this acidic pulp are numerous small, white, compressed, non-endospermic seeds covered in a mucilaginous, woolly outer coat [19].

4. Geographical Distribution and Cultivation

Limonia acidissima is indigenous to the dry, arid, and semi-arid plains of the Indian subcontinent, with extensive wild populations distributed across India, Bangladesh, Sri Lanka, and Pakistan [5]. In Sri Lanka, the species is widely distributed in dry-zone forests, particularly in the northern and eastern provinces. The geographical range extends eastward through Myanmar, Thailand, Cambodia, Laos, and Vietnam, and it is cultivated on a limited scale in southern China (Yunnan province) and parts of Malaysia and Indonesia.

Ecologically, the species displays high tolerance to environmental extremes, allowing it to survive in conditions where commercial citrus crops fail. It thrives in warm, dry climates characterized by distinct dry and wet seasons, with annual rainfall limits ranging between 500 mm and 1500 mm. The tree grows from sea level up to an altitude of approximately 1500 meters above mean sea level.

The species is highly adaptable to poor soil profiles, including shallow, rocky, sandy loam, and highly alkaline soils, and it can grow in lateritic formations. Its robust, deep taproot system enables the extraction of moisture from deep geological strata, allowing mature trees to survive prolonged drought periods. However, the species is highly sensitive to waterlogging and excessive soil moisture, which can cause hypoxic conditions in the root zone, promoting root-rot pathogens and limiting overall growth.

5. Nutritional Composition

5.1. Fruit Pulp

The edible pulp of *L. acidissima* is highly valued for its dense concentration of energy, carbohydrates, and dietary fiber, which make it an excellent functional food candidate. Proximate analyses indicate that the pulp contains a low moisture content (64.0 g to 70.0 g per 100 g of fresh weight) compared to other tropical fruits, which accounts for its dense, mealy texture [9, 20]. The dry-matter fraction consists primarily of carbohydrates (25.0 g to 30.0 g per 100 g), which provide an energy yield ranging between 140 kcal and 180 kcal [21]. The carbohydrate profile is characterized by a high pectin content, a complex structural polysaccharide highly valued in the food processing industry for its gelling properties. Dietary fiber is also abundant (3.0 g to 5.0 g per 100 g), which helps regulate bowel movements and prevent gastrointestinal disorders [22]. The protein content of the pulp is relatively high for a fruit crop, ranging between 6.0 g and 7.0 g per 100 g, and it contains essential amino acids like aspartic acid, glutamic acid, and alanine [9]. Conversely, lipids represent a minor fraction (0.5 g to 1.0 g per 100 g), consisting primarily of beneficial unsaturated fatty acids.

5.2. Vitamin and Mineral Composition

In addition to macronutrients, the pulp of *L. acidissima* serves as an excellent source of essential vitamins and minerals required for metabolic homeostasis. The vitamin profile is dominated by ascorbic acid (Vitamin C), with concentrations ranging from 2.0 mg to 4.0 mg per 100 g of edible portion [20]. Although this is lower than in some commercial citrus species, its antioxidant capacity is enhanced by the presence of beta-carotene (Vitamin A), which ranges between 80.0 IU and 100.0 IU per 100 g [21]. The fruit also contains significant levels of water-soluble B-complex vitamins, including thiamine (0.03 to 0.05 mg), riboflavin (0.05 to 0.08 mg), and niacin (0.5 to 1.0 mg), which act as crucial coenzymes in cellular energy pathways [22]. The mineral profile of the pulp is exceptional, particularly regarding calcium and potassium, which are crucial for muscular contraction, skeletal health, and cardiovascular function. Calcium levels range between 150.0 mg and 200.0 mg per 100 g, while potassium concentrations are recorded at 400.0 mg to 500.0 mg per 100 g [9]. Phosphorus (80.0 to 120.0 mg per 100 g) and magnesium (40.0 to 60.0 mg per 100 g) are also present in significant quantities, maintaining an optimal electrolyte balance. Iron (0.5 to 2.0 mg per 100 g), sodium (50.0 to 70.0 mg per 100 g), and zinc (35.0 to 40.0 mg per 100 g) round out the mineral profile, supporting erythropoiesis and immune function [20].

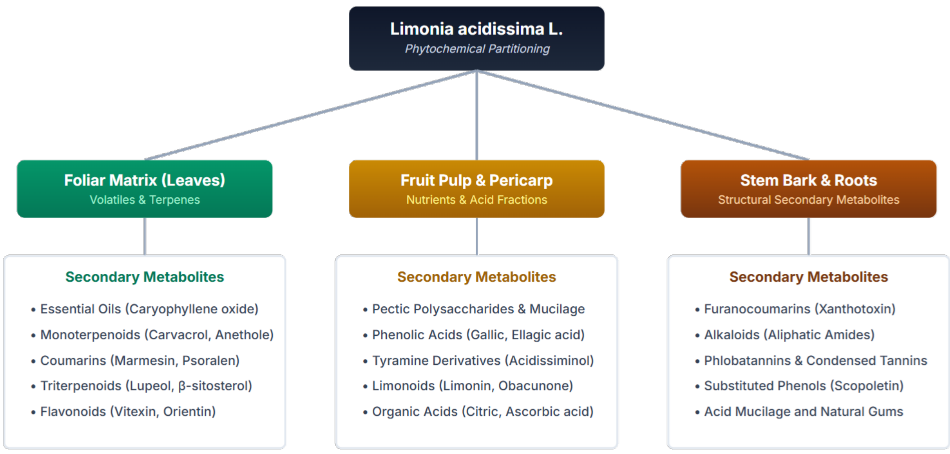

Figure 3. Tissue-Specific Phytochemical Distribution

Table 1. Nutritional composition of *Limonia acidissima* fruit pulp.

Proximate Component	Concentration (per 100 g edible pulp)
Moisture	64.0 - 70.0 g
Carbohydrates	25.0 - 30.0 g
Proteins	6.0 - 7.0 g
Crude Fat	0.5 - 1.0 g
Dietary Fiber	3.0 - 5.0 g
Crude Ash	2.0 - 3.0 g
Energy Value	140.0 - 180.0 kcal

Table 2. Vitamin, and mineral composition of *Limonia acidissima* fruit pulp

Vitamin/Mineral	Concentration (per 100 g edible pulp)
Vitamin C	2.0 - 4.0 mg
Vitamin A (β-carotene)	80.0 - 100.0 IU
Thiamine (B1)	0.03 - 0.05 mg
Riboflavin (B2)	0.05 - 0.08 mg
Niacin (B3)	0.5 - 1.0 mg
Calcium (Ca)	150.0 - 200.0 mg
Phosphorus (P)	80.0 - 120.0 mg
Potassium (K)	400.0 - 500.0 mg
Magnesium (Mg)	40.0 - 60.0 mg
Sodium (Na)	50.0 - 70.0 mg
Iron (Fe)	0.5 - 2.0 mg
Zinc (Zn)	35.0 - 40.0 mg

5.3. Nutritional Profile of the Seeds

The seeds of *L. acidissima*, which are often discarded as agricultural waste during processing, contain a high concentration of nutrients, particularly proteins and lipids. On a dry-weight basis, the seeds exhibit a moisture content of 5.0 g to 8.0 g per 100 g, indicating high physical stability and resistance to microbial spoilage [22]. The protein fraction is remarkably high, ranging between 20.0 g and 25.0 g per 100 g of dry seed weight, which makes them a potential source of plant-based protein isolates.

The lipid content (oil fraction) of the seeds is also significant, ranging from 15.0 g to 20.0 g per 100 g. Gas chromatography reveals that this oil is rich in unsaturated fatty acids, particularly oleic and linoleic acids, which have cardioprotective properties. Carbohydrates account for 35.0 g to 40 g per 100 g, while the crude fiber fraction ranges from 5.0 g to 8.0 g per 100 g. Consequently, the seeds possess a high energy density, yielding between 400.0 kcal and 450.0 kcal per 100 g, suggesting potential applications in livestock feed or fortified human foods.

Table 3. Nutritional composition and significance of *Limonia acidissima* seeds.

Seed Component	Concentration (per 100 g dry weight)	Biological Significance
Moisture	5.0 - 8.0 g	Confers physical stability and resistance to hydrolytic rancidity.
Crude Protein	20.0 - 25.0 g	Rich source of essential amino acids; potential protein isolate.
Crude Oil	15.0 - 20.0 g	Abundant in monounsaturated and polyunsaturated fatty acids.
Carbohydrates	35.0 - 40.0 g	Serves as a major structural and metabolic energy storage pool.
Crude Fiber	5.0 - 8.0 g	Promotes gastrointestinal peristalsis and supports gut microbiota.
Energy Value	400.0 - 450.0 kcal	High caloric density, ideal for dietary enrichment.

6. Phytochemical Composition

6.1. Non-Volatile Bioactive Compounds

Phytochemical screening of the different parts of *Limonia acidissima* reveals a high diversity of secondary metabolites [23]. Qualitative and quantitative evaluations have established the presence of polyphenols, coumarins, alkaloids, flavonoids, phytosterols, triterpenoids, and organic acids across the bark, leaves, fruits, and seeds [13, 14, 24].

6.1.1. Flavonoids and Phenolic Fractions

Flavonoid compounds represent a significant portion of the bioactive matrix within both the foliar tissues and the ripening fruit pulp. Prominent among these is quercetin, a flavonol widely recognized for its high radical-scavenging activity. Additional flavonoids identified in high-performance liquid chromatography investigations include rutin, orientin, and vitexin [25]. These compounds accumulate during maturation, with the outer layers of the fruit pulp displaying higher overall concentrations compared to the central seed-bearing zones. Phenolic acids, most notably gallic acid, ellagic acid, and ferulic acid, are distributed in high densities across the fruit and bark [26]. These phenolic fractions contribute to the astringency of the unripe fruit and serve as key natural antioxidants by stabilizing free radicals through hydrogen atom transfer.

6.1.2. Coumarins and Furanocoumarins

Coumarin derivatives constitute a major chemotaxonomic marker of the family Rutaceae, and *L. acidissima* is particularly rich in these structures. The fruit pericarp, root bark, and leaves contain substantial concentrations of simple coumarins such as umbelliferone and scopoletin, alongside more complex furanocoumarins, including psoralen, bergapten, marmin, and marmesin [26, 27, 28]. These compounds exhibit strong photoreactive and defense properties. Marmesin, in particular, has been isolated in high purity from the root bark and is of significant therapeutic interest due to its organo-protective capabilities.

6.1.3. Triterpenoids and Phytosterols

The structural integrity of the plant membranes and defensive secretions is supported by an array of triterpenoid and phytosterol molecules. The leaves and fruit pulp contain significant fractions of beta-sitosterol, stigmasterol, and gamma-sitosterol, which exhibit high stability and play a role in modulating cellular cholesterol pathways [29]. Among the specialized triterpenoids, the limonoids specifically limonin, acidissimin, acidissiminol, and obacunoneare noted for their highly bitter profiles and potential insecticidal behaviors [30]. Seed matrices are further characterized by highly stable fixed oils rich in unsaturated fatty acids, including oleic and palmitoleic acids, which possess high nutritional value.

Table 4. Distribution and therapeutic relevance of the main phytochemical classes isolated from *Limonia acidissima*.

Chemical Class	Phytochemical Compounds	Plant Tissue Origin	Biological Action	References
Flavonoids	Quercetin, Rutin, Orientin, Vitexin	Fruit pulp, foliar tissues	Antioxidant, anti-inflammatory	[25]
Phenolics & Tannins	Gallic acid, Ellagic acid, Ferulic acid	Fruit, bark, leaves	Antioxidant, astringency, antibacterial	[26]
Furanocoumarins	Psoralen, Bergapten, Marmin, Marmesin	Fruit shell, root bark, leaves	Photoreactive defense, antifungal	[26, 27, 28]
Limonoids	Acidissimin, Acidissiminol, Obacunone	Fruit pericarp, bark	Antimicrobial, insecticidal	[30]
Tyramine Derivatives	Acidissiminol epoxide, Diotamine	Fruit pulp	Antibacterial, cell-wall stabilization	[30]
Phytosterols	Stigmasterol, β-sitosterol, γ-sitosterol	Foliar tissues, pulp	Anti-inflammatory, lipid-modulating	[29]
Saponins & Glycosides	Unspecified triterpene glycosides	Fruit pulp, leaves	Surfactant, expectorant properties	[26]
Benzoquinones	2,6-Dimethoxybenzoquinone	Fruit pericarp	Antifungal, defense signaling	[29]

6.2. Volatile Oil and Terpenes

The distinctive citrus-like, aromatic profile of *L. acidissima* is driven by its complex volatile oil fraction, synthesized within lysigenous oil cavities scattered throughout the leaves, twigs, and pericarp. Gas chromatography-mass spectrometry (GC-MS) characterization of the foliar essential oil has identified up to thirty-two distinct volatile elements, accounting for approximately 98.4% of the total volatile oil content [31, 32].

The volatile profile is dominated by sesquiterpene hydrocarbons, cyclic terpenes, and monoterpenoid phenols. The principal constituent is eudesma-4(14),11-diene, which represents approximately 46.3% of the total volatile fraction. This is accompanied by 1,5-cyclodecandiene (29.6%) and the monoterpenoid phenol carvacrol (13.5%). Other trace but biologically active volatile compounds include caryophyllene oxide, veratraldehyde, germacrene-D, aromadendrene, elemicin, and cis-anethole [24, 32]. This chemical mixture provides the plant with protection against herbivorous predators and fungal infestations.

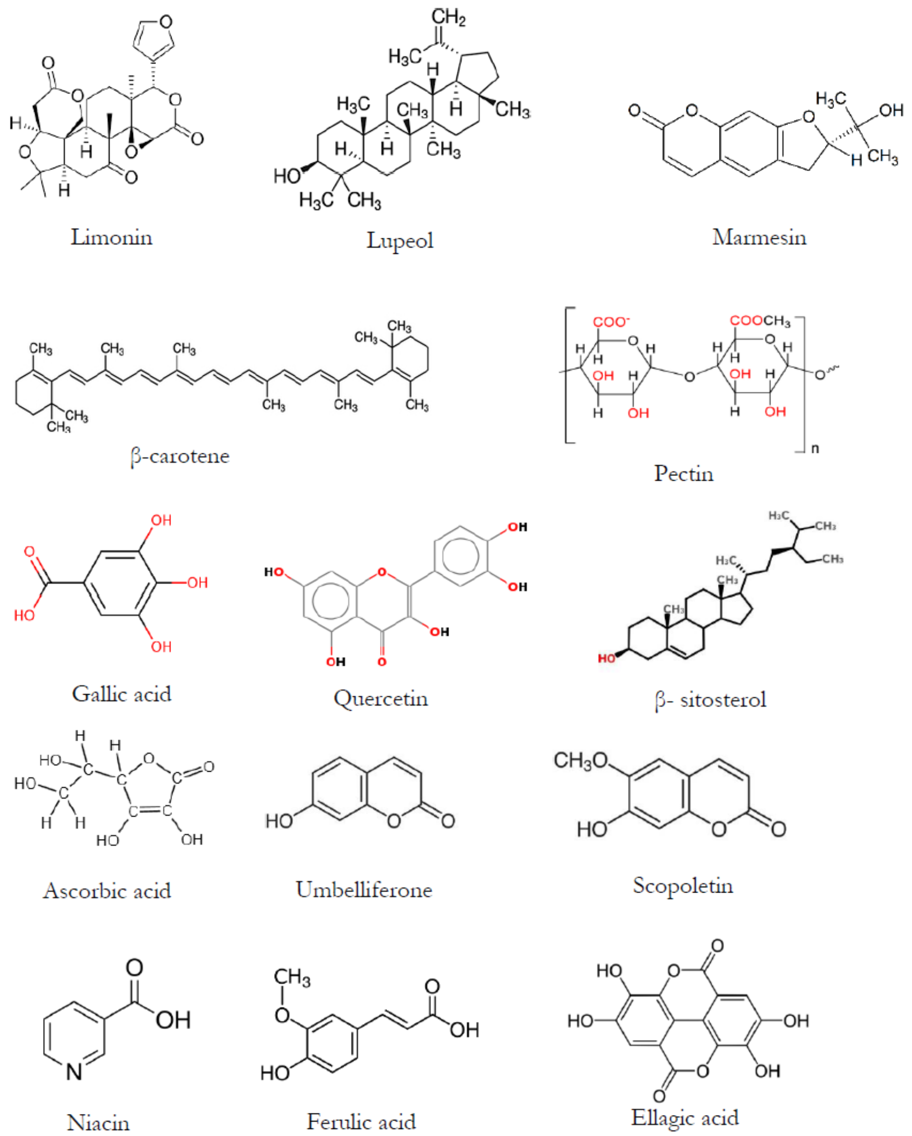

Figure 4. Structures of Important Phytoconstituents in *Limonia acidissima*

Table 4. Gas chromatography-mass spectrometry analysis of the volatile constituents of *Limonia acidissima* leaves [24, 32].

Volatile Compound	Chemical Classification	Composition (% of Volatile Fraction)
Eudesma-4(14),11-diene	Sesquiterpene hydrocarbon	46.3%
1,5-Cyclodecandiene	Cyclic terpene	29.6%
Carvacrol	Monoterpenoid phenol	13.5%
cis-Anethole	Phenylpropanoid	2.8%
Caryophyllene	Sesquiterpene	1.3%
Caryophyllene oxide	Sesquiterpene oxide	1.7%
Germacrene-D	Sesquiterpene hydrocarbon	1.2%
Elemicin	Phenylpropanoid ether	0.9%
Veratraldehyde	Aromatic aldehyde	0.3%
3,4-Dimethylcinnamic alcohol	Phenylpropanoid derivative	0.1%
Aromadendrene	Sesquiterpene	0.1%

7. Pharmacological Activities

Almost all parts of *L. acidissima* have significant therapeutic potential. These activities are supported by pre-clinical *in vitro* and *In vivo* models, showing multiple mechanisms of action.

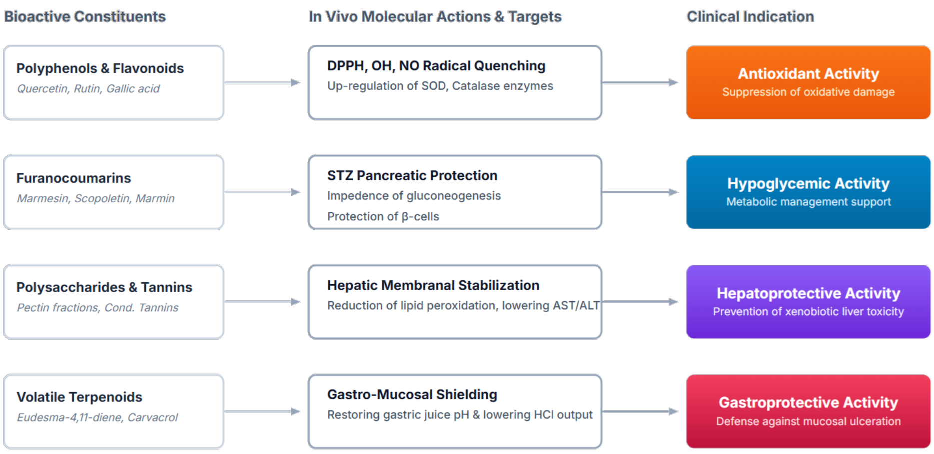

Figure 5. Pharmacological Activities and Molecular Targets

7.1. Antineoplastic and Cytotoxic Activity

Malicious cellular proliferation remains a primary focus of global medical investigation. Highly purified acidic heteropolysaccharides isolated from *L. acidissima* fruit structures have demonstrated marked *In vivo* inhibitory properties against tumor progression in murine biological test models [33]. In comparative evaluations using the potato disk bioassay rapid screening tool for crown gall tumors caused by *Agrobacterium tumefaciens*the crude extract of *L. acidissima* demonstrated an inhibition rate of 16.1%, which fell slightly below the 20.0% threshold required for high-priority antineoplastic categorization [27]. However, methanolic pulp extracts administered at a concentration of 570 mg/kg body weight in mice bearing Dalton's Ascitic Lymphoma (DAL) showed robust anti-tumor activity [34].

The administration of this extract significantly reduced the count of viable tumor cells within the peritoneal cavity while increasing the non-viable cell count. This cytotoxic behavior is believed to be mediated by the activation of peritoneal macrophages or the induction of cellular lysis via localized cytokine release. The treated animal cohorts demonstrated a recovery of red blood cell (RBC) counts and hemoglobin concentrations, suggesting protective effects on the hematopoietic system during tumor challenges.

7.2. Antimicrobial and Antifungal Activity

Extracts of the fruit pericarp and leaves exhibit broad-spectrum activity against clinically relevant bacterial pathogens. Methanolic and acetonic shell extracts administered at 250 mg/kg body weight produced moderate inhibition zones against *Klebsiella oxytoca* (34.45% inhibition) and *Vibrio metschnikovii* (35.63%), alongside observable inhibitory profiles against *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus* [35]. Foliar ethanolic extracts display clear bactericidal efficacy against dysentery-causing strains, including *Shigella boydii*, *Shigella dysenteriae*, and *Shigella flexneri*, helping to reduce the severity and frequency of bacterial diarrheal episodes [36].

The foliar volatile oil displays moderate to high antibacterial activity against both Gram-positive and Gram-negative targets, with minimum inhibitory concentrations (MIC) ranging from 125 mug/mL to 500 mug/mL [32]. This antibacterial action is attributed to the hydrophobic nature of its major components, eudesma-4(14),11-diene and carvacrol, which can insert into the bacterial lipid bilayer, disrupt membrane integrity, leak intracellular ions, and collapse the proton motive force. For fungal pathogens, cup-plate diffusion assays have validated the antidermatophytic potential of these leaf extracts, showing dose-dependent inhibition against *Microsporum gypseum*, *Trichophyton mentagrophytes*, *Candida albicans*, and *Trichophyton rubrum* [37].

7.3. Antidiabetic and Antihyperglycemic Activities

Management of diabetes mellitus via natural plant matrices is supported by several studies on *L. acidissima*. The administration of a 95% ethanolic extract of unripe fruits at 250 mg/kg body weight to streptozotocin (STZ)-induced diabetic rats produced a significant, sustained reduction in both fasting and postprandial blood glucose levels [38]. Additionally, methanolic pulp extracts administered at 1.75 g/kg body weight effectively prevented systemic hyperglycemic spikes in oral glucose tolerance tests [39]. Longer-term evaluations of the bark extracts are also promising; a 21-day intervention with methanolic bark extracts at doses of 200 mg/kg and 400 mg/kg body weight reduced blood glucose levels by 39.0% and 54.5%, respectively [40].

Further work on the fruit pericarp (shell) indicates that its methanolic fractions provide notable protection against diabetic nephropathy [41]. This protective effect is linked to a reduction in lipid peroxidation within renal tissues and the preservation of glomerular structures, driven by the antioxidant profile of the extract.

7.4. Antioxidant and Free Radical Scavenging Activity

Oxidative stress is a primary driver in the development of chronic diseases. Aqueous, methanolic, and ethyl acetate extracts of *L. acidissima* pulp display high radical-scavenging activity across several *in vitro* assay designs, including DPPH, hydroxyl radical scavenging, FRAP, and nitric oxide assays [42, 43]. The total phenolic content of the ripe pulp was quantified at 229.0 mg/g gallic acid equivalents (GAE) within the glycosidic fraction, compared to 37.5 mg/g in phenolic esters and 11.0 mg/g in free phenolics [44].

The DPPH radical-scavenging efficiency of this phenolic glycoside extract reached 88.7%, which compares favorably to commercial reference standards such as Trolox (64.6%) and butylated hydroxytoluene (BHT, 83.2%). This high antioxidant activity is attributed to the presence of multiple hydroxyl groups on the aromatic rings of the phenolic glycosides, which can donate hydrogen atoms to neutralize reactive oxygen species [44].

7.5. Gastroprotective and Antiulcer Activity

The gastroprotective properties of *L. acidissima* pulp have been demonstrated in models of acute gastric mucosal injury. In rats subjected to indomethacin-induced gastric ulcers, oral administration of the pulp extract at 500 mg/kg body weight reduced ulceration [45]. This protective effect was mediated by a significant reduction in free gastric hydrochloric acid (HCl) levels and an increase in overall gastric pH, helping to protect the delicate mucosal lining. In excision wound models, a methanolic fruit extract at 400 mg/kg body weight accelerated wound healing [15]. This was evidenced by increased wound contraction rates, a shorter epithelization period, and elevated hydroxyproline levels in the granulation tissue, which indicate active collagen synthesis.

Additionally, leaf extracts administered at 400 mg/kg body weight provided protection against ethanol-induced gastric mucosal lesions by preventing the infiltration of inflammatory polymorphonuclear leukocytes into the submucosal layers [13].

7.6. Hepatoprotective and Organoprotective Activities

The hepatoprotective effects of a methanolic extract of *L. acidissima* root bark and its isolated furanocoumarins, such as marmesin, have been evaluated using carbon tetrachloride (CCl4)-induced hepatic damage models in HepG2 cell lines and animal subjects [46]. *In vitro*, co-supplementation of the extract with CCl4 significantly improved cell viability and reduced the leakage of intracellular marker enzymes, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT). *In vivo*, oral administration of both the extract and purified marmesin prevented the CCl_4-induced rise in plasma AST and ALT levels, while reducing hepatic lipid peroxidation. Histopathological analysis confirmed these protective effects, showing minimal structural alterations in the liver parenchyma of treated cohorts compared to the severe necrosis observed in untreated controls.

7.7. Neuroprotective Properties

Ischemic brain injury involves complex oxidative cascades and neuronal death. In rat models of 30-minute global cerebral ischemia followed by reperfusion, treatment with a methanolic extract of *L. acidissima* fruit at 250 mg/kg and 500 mg/kg body weight produced clear neuroprotective effects [47]. Treated animals showed significant improvements in motor performance and sensory coordination compared to ischemic control groups.

Biochemical analysis of brain tissue indicated a significant reduction in lipid peroxidation and total nitrite levels ($P < 0.01$). This was accompanied by a significant recovery in the activity of key endogenous antioxidant enzymes, including catalase ($P < 0.01$) and superoxide dismutase (SOD, $P < 0.05$), indicating the potential of the extract to limit ischemic oxidative injury.

7.8. Analgesic, Antipyretic, and Anti-inflammatory Activities

Peripheral analgesic activity was evaluated using the acetic acid-induced abdominal writhing assay in mice. Methanolic and acetonic extracts of the fruit peel administered orally produced a significant reduction in writhes, with inhibition rates of 60.53% and 59.65%, respectively [35]. While these values were lower than that of the reference drug diclofenac sodium (78.07% inhibition at standard clinical equivalent dosages), they confirm the presence of compounds capable of modulating peripheral nociceptive pathways, likely through the inhibition of localized prostaglandin synthesis.

7.9. Antidiarrheal and Gastrointestinal Effects

Traditional applications of the bark and unripe fruit in managing acute gastrointestinal distress have been validated in animal models. The administration of an aqueous bark extract produced a significant reduction in overall fecal output and a decrease in gastrointestinal transit velocity in charcoal meal tests [48]. This antidiarrheal action is attributed to the presence of condensed tannins and polar phenolic fractions, which can bind to mucosal proteins, forming a protective layer that reduces secretion and slows intestinal peristalsis.

7.10. Antimalarial, Larvicidal, and Vector-Control Effects

Vector-control strategies are essential for limiting the transmission of mosquito-borne pathogens. Volatile fractions and crude organic extracts of *L. acidissima* leaves display larvicidal and ovicidal activity against mosquito vectors. Hexane extracts of the foliar tissues produced high ovicidal action against the eggs of *Culex quinquefasciatus* and *Aedes aegypti*, achieving egg mortality rates of 79.2% and 60.0% at a concentration of 500 ppm [49]. This indicates potential for the development of natural vector-control agents with lower environmental persistence than synthetic organophosphates

8. Ethnobotanical Applications and Traditional Medicine

8.1. Systems of Traditional Medicine

Historically, *Limonia acidissima* has occupied a central role in several traditional healthcare paradigms of South Asia, including Ayurveda, Siddha, Unani, and various indigenous folk networks [50, 51]. The therapeutic application of its morphological parts is documented in early classical Sanskrit treatises, where the plant is classified as an agent capable of stabilizing metabolic processes and alleviating gastrointestinal distress.

8.1.1. Ayurvedic and Siddha Practices

In Ayurvedic medicine, different tissues of *L. acidissima* are categorized based on their distinct energetic and physiological effects. The unripe fruit is classified as an astringent (*grahi*) due to its high concentration of condensed tannins, rendering it a preferred intervention for acute diarrheal episodes, dysentery, and internal hemorrhoids [51].

Table 5. Ethnobotanical formulations and regional medicinal applications of *Limonia acidissima*

Plant Tissue	Traditional Form of Preparation	Therapeutic Purpose	Folklore Medicine
Fruit Pulp (Unripe)	Dehydrated powder, aqueous suspension	Mitigation of acute diarrhea and bacillary dysentery	Ayurveda, Siddha (India, Sri Lanka) [51]
Fruit Pulp (Ripe)	Fresh beverage, sweet paste	Gastroprotection, cooling tonic, hepatoprotective agent	Ayurveda, Sri Lankan folk medicine [51]
Foliar Tissue	Fresh crushed paste, decoction	Acceleration of wound healing, treatment of skin infections	Folk medicine (Bangladesh, East India) [51]
Stem Bark	Concentrated aqueous decoction	Healing of mucosal ulcers, systemic astringent	Unani, tribal healthcare networks [52]
Seed Matrix	Cold-pressed oil, crushed flour	Hair tonic, expelling intestinal parasites, joint pain	Traditional Unani, folk medicine [51, 52]
Root System	Boiled root decoction	Alleviation of severe abdominal colic and flatulence	Tribal medicine (Chittagong Hill Tracts) [52]

Conversely, the fully ripened fruit pulp is recognized as a cooling cardiotonic and hepatoprotective agent (*pitta-shamaka*). It is commonly administered alongside natural sweeteners like honey or unrefined sugar to balance gastric acidity, quench thirst, and counteract systemic heat syndromes [51]. In the Siddha system of medicine, preparations of the root bark are utilized to alleviate chronic fever, clear respiratory congestion, and address internal digestive colic.

8.1.2. Unani and Folk Formulations

The Unani system values the seeds and seed-derived fixed oils of *L. acidissima* as powerful anthelmintics and anti-inflammatory agents. Folk medicine networks across Bangladesh and India utilize fresh leaf paste as a topical dressing to accelerate wound healing on infected dermal lesions, boil eruptions, and localized skin infections [51]. Decoctions prepared from the dried tree bark are consumed orally to manage oral sores, throat infections, and peptic ulcers [52, 53].

8.2. Tissue-Specific Therapeutic Classifications

The traditional distribution of *L. acidissima* formulations across different regions highlights the versatile therapeutic utility of its anatomical components.

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9. Safety Evaluation and Toxicological Thresholds

9.1. *In vitro* Cytotoxicity and Cellular Effects

While *L. acidissima* is globally recognized as an edible and therapeutic crop, modern toxicological profiling remains essential to establish safe consumption limits. *In vitro* cellular assays have investigated the potential cytotoxic behaviors of highly concentrated extracts. In evaluations using human breast cancer (MCF-7) cell lines, purified volatile fractions and organic pulp extracts demonstrated a dose-dependent induction of cellular apoptosis and DNA fragmentation [54]. This apoptotic response suggests a therapeutic window for oncology research but also emphasizes the need for careful dose monitoring, as non-targeted healthy cell lines can exhibit minor morphological alterations at elevated exposure levels.

9.2. *In vivo* Safety Margins and Overdosage Effects

Animal model evaluations indicate that oral administration of aqueous and methanolic pulp extracts is highly tolerated, with no mortality observed in acute toxicity studies at doses up to 2000 mg/kg body weight in rodent models [52]. However, the volatile oil fractions scattered within the foliage and unripe pericarp display a more complex toxicity profile. At high concentrations, these essential oils exhibit significant larvicidal, pupicidal, and developmental toxicity against insect vectors, such as *Aedes aegypti*, driven by the high density of photoreactive coumarins and volatile terpenes [53].

Excessive oral consumption of the mature fruit pulp can lead to localized gastrointestinal disturbances. Because of its extremely high pectin and active tannin content, overconsumption may slow down intestinal peristalsis, resulting in severe constipation, abdominal bloating, flatulence, and transient gastric irritation.

Due to the potent blood-glucose-lowering properties of the fruit pericarp and leaf extracts, individuals undergoing active pharmacotherapy with synthetic hypoglycemic drugs must exercise caution to prevent synergistic hypoglycemic episodes [52]. Traditional networks also advise against the continuous, daily consumption of concentrated foliar decoctions during pregnancy and lactation, as historical reports suggest potential uterotonic risks associated with high-dose alkaloidal fractions.

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10. Socio-Economic Value

10.1. Nutritional and Processing Economics

Despite its classification as an underutilized crop, *L. acidissima* possesses significant economic potential that can support rural livelihoods and enhance climate-resilient agriculture. In regional markets across Bangladesh, India, and Sri Lanka, the commercialization of fresh wood apples provides a direct source of seasonal income for smallholder farmers. A single mature fruit commands a market value of approximately 40 to 50 BDT (Bangladeshi Taka) in local regional markets, while sorted, high-quality selections can reach up to 250 BDT per kilogram when distributed to urban retail centers or processing hubs [9].

Value-addition through processing represents the most promising economic pathway. Due to the high structural stability of the fruit pulp and its natural acidic profile, it is highly suited for the manufacture of long-shelf-life products including jams, jellies, thick marmalades, spiced chutneys, and dehydrated fruit leathers [11, 51]. Processing the mealy pulp into stable, spray-dried fruit powders also creates raw ingredients for the global functional beverage and nutraceutical industries [16].

10.2. Industrial Byproducts and Rural Livelihoods

Beyond the edible pulp, almost every part of the wood apple tree can be commercialized. The rugged stem bark exudes a clear, highly viscous natural mucilage when wounded. This gum serves as a viable, low-cost alternative to commercial gum arabic, finding applications as an adhesive, stabilizer in printing inks, and binding agent in traditional dye formulations [52].

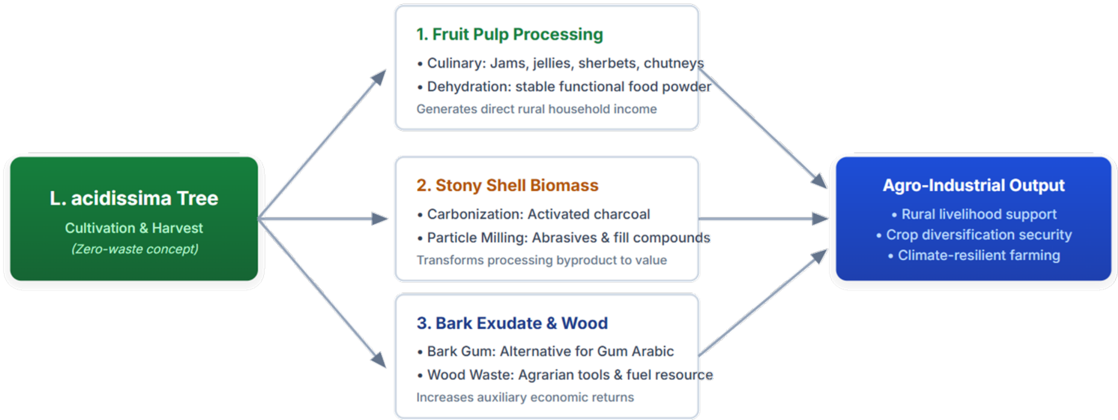

Figure 6. Socio-Economic and Industrial Valorization Cycle

The extremely hard, stony outer shell of the fruit, typically discarded as processing waste, can be carbonized to produce high-grade activated charcoal or crushed into fine abrasive powders for industrial use. Additionally, the dense, yellow-gray wood of mature, non-productive trees is highly valued for manufacturing heavy-duty agricultural implements, textile carvings, and durable handicrafts, thereby creating a multi-layered economic return for rural communities [52].

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11. Future Strategic Directions and Research Gaps

11.1. Phytochemical and Metabolomic Mapping

While baseline screening has identified major chemical classes such as furanocoumarins, flavonoids, and volatile sesquiterpenes in *L. acidissima*, significant knowledge gaps remain. Future research must prioritize high-resolution, untargeted metabolomic profiling using advanced liquid chromatography-mass spectrometry (LC-MS/MS) and nuclear magnetic resonance (NMR) spectroscopy. This mapping is essential to isolate and characterize rare secondary metabolites, particularly the unique tyramine derivatives and specialized limonoids, establishing their exact chemical configurations and stereochemistry.

11.2. Clinical and Pharmacological Validation

A significant portion of the current pharmacological evidence supporting the therapeutic benefits of *L. acidissima* is derived from *in vitro* assays and pre-clinical *In vivo* animal models. To transition this underutilized crop into validated modern therapeutics, well-designed, randomized, double-blind clinical trials are required. The main areas of focus should include evaluating its efficacy in human subjects for blood glucose regulation, lipid management, and gastroprotective activities, accompanied by pharmacokinetic profiling to determine human bioavailability and metabolic clearance pathways.

11.3. Agronomic Breeding and Genetic Optimization

From an agricultural perspective, the slow-growing nature and high phenotypic variability of wild populations present challenges for large-scale industrial cultivation. Horticultural research should focus on implementing molecular marker-assisted breeding and clonal propagation techniques to select high-yielding, thin-shelled, and disease-resistant cultivars. Applying modern biotechnology, such as plant tissue culture and genetic selection, will help establish standardized orchards, ensuring a consistent supply of raw material rich in target bioactive compounds for the global pharmaceutical sector.

12. Conclusion

Limonia acidissima L. is a highly resilient, multi-functional tropical species that bridges the gap between traditional ethnomedicine and modern functional food science. The dense matrix of its pulp is rich in carbohydrates, dietary fibers, essential minerals, and vitamins, along with polyphenols, coumarins, and volatile monoterpenes. Several reported literature have also validated its diverse pharmacological capabilities, including antidiabetic, antimicrobial, hepatoprotective, gastroprotective, and neuroprotective activities. While its socio-economic potential in agro-forestry and value-added food processing is clear, realizing its full potential requires targeted research. High-resolution metabolomic mapping, human clinical validation, and biotechnological crop optimization will help establish this resilient species as a valuable contributor to global nutrition, sustainable agriculture, and natural drug discovery.

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