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ETHNOMEDICINAL RELEVANCE AND BIOACTIVE POTENTIAL OF MANILA TAMARIND: AN EVIDENCE-BASED ASSESSMENT

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ABSTRACT

Background: *Pithecellobium dulce* (Roxb.) Benth., commonly known as Manila tamarind, is a leguminous tree traditionally used in indigenous medicine, nutrition, and agroecological practices. Despite its wide ethnomedicinal usage, its comprehensive bioactive and functional potential remains underexplored in mainstream scientific literature. **Methodology:** This review systematically compiles and critically analyzes published data from peer-reviewed journals, ethnobotanical records, and experimental studies focusing on the botanical features, phytochemical composition, nutritional attributes, pharmacological activities, and ecological significance of *P. dulce*. **Results and Discussion:** The species is rich in phenolics, flavonoids, alkaloids, saponins, and essential nutrients, which collectively contribute to its broad pharmacological spectrum. Reported biological activities include antidiabetic, antihyperlipidemic, anti-inflammatory, antioxidant, antimicrobial, wound-healing, analgesic, and antipyretic effects. Mechanistic evidence suggests modulation of oxidative stress, inflammatory mediators, and metabolic pathways. *P. dulce* plays a vital environmental role through nitrogen fixation, soil enrichment, carbon sequestration, and biodiversity support. Beyond its medicinal value, the plant shows strong potential for use in food products, animal feed, herbal formulations, and agroforestry systems. However, limitations such as variability in extraction methods, incomplete toxicity profiling, and insufficient clinical validation restrict its translational applications. **Conclusion:** *Pithecellobium dulce* represents a promising yet underutilized bioresource with multifaceted therapeutic, nutritional, and ecological benefits. Future research should prioritize standardization, advanced phytochemical characterization, safety evaluation, and clinical studies to support its development into functional foods, phytopharmaceuticals, and sustainable industrial products.

INTRODUCTION

Pithecellobium dulce (Roxb.) Benth., commonly referred to as Manila tamarind, Vilayati Imli, Madras Thorn, or Camachile, is a multipurpose evergreen leguminous tree belonging to the

family Fabaceae and subfamily Mimosoideae. The species is believed to have originated in the tropical regions of Mexico and Central America, after which it gradually disseminated and naturalized across South and Southeast Asia, particularly India,

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Thailand, Sri Lanka, and the Philippines [1]. Its adaptability to arid, semi-arid, and nutrient-poor soils has contributed to its widespread cultivation as a shade tree, a fodder species, a living fence, and an agroforestry component in rural landscapes. Traditionally, *P. dulce* has been valued for its edible fruit pulp, which possesses a unique sweet–tangy flavor and is consumed fresh or used in beverages and confectionery. Beyond its nutritional uses, various parts of the plant, including the leaves, bark, seeds, pulp, and pods, have been employed in indigenous systems of medicine for treating ailments such as gastrointestinal disturbances, inflammatory disorders, toothache, skin infections, ulcers, and fever [2]. These traditional applications have stimulated scientific interest in recent decades, particularly as natural plant-based therapeutics gain prominence in the global search for safer alternatives to synthetic drugs.

Modern phytochemical research has revealed that *P. dulce* is rich in diverse classes of bioactive molecules such as flavonoids, phenolic acids, tannins, saponins, terpenoids, alkaloids, & polysaccharides [3]. The presence of quercetin, kaempferol, gallic acid, chlorogenic acid, ferulic acid, epicatechin, tartaric acid & multiple phenolic polymers is believed to contribute to the plant's robust antioxidant capacity & its therapeutic potential. In vitro and in vivo studies have demonstrated several pharmacological activities associated with *P. dulce*, including antidiabetic, antihyperlipidemic, anti-inflammatory, antimicrobial, wound-healing, hepatoprotective, analgesic & antipyretic effects [4–7].

The plant also has significant environmental importance due to its nitrogen-fixing ability, drought tolerance, and capacity to improve soil structure and fertility. Its extensive root system provides strong soil-binding properties, making it suitable for controlling erosion on degraded lands, embankments, and arid zones [8]. Additionally, *P. dulce* supports ecological biodiversity by serving as a habitat and food source for pollinators, birds, and small mammals [9]. Despite these promising attributes, scientific data on the plant's standardization parameters, toxicity profile, pharmacokinetics, and clinical efficacy remain fragmented. The commercial utilization of *P. dulce* as a source of nutraceuticals, phytopharmaceuticals, functional foods, and bio-based industrial products is still in a nascent stage. Comprehensive review articles that synthesize the botanical, phytochemical, nutritional, pharmacological, environmental, and industrial aspects of *P. dulce* are limited. Therefore, the present review

aims to consolidate the available scientific literature on *P. dulce* while adopting a critical and integrative approach. The article provides extensive information on its taxonomy, botanical morphology, chemical composition, nutritional value, medicinal applications, ecological impacts, industrial applications, and prospective research avenues. This study brings together information from several research domains to indicate that *P. dulce* has significant potential as a key asset for environmentally friendly agricultural, medicinal, and bioeconomic growth.

MATERIALS AND METHODS

Literature Search Strategy

A structured literature search was conducted across PubMed, Scopus, Web of Science, and Google Scholar from January 2000 to December 2025. Search terms included “*Pithecellobium dulce*”, “Manila tamarind”, “pharmacological activity”, “phytochemistry”, and “ethnomedicine”. Only peer-reviewed English articles reporting experimental, nutritional, or ethnobotanical data were included. Conference abstracts, duplicated records, and studies lacking primary data were excluded. After screening titles, abstracts, and full texts, 78 relevant publications were retained for qualitative synthesis.

BOTANICAL DESCRIPTION

Taxonomy

The accepted botanical name *Pithecellobium dulce* (Roxb.) Benth. was verified through World Flora Online. Synonyms appearing in earlier literature include *Inga dulcis* and *Mimosa dulcis*. *P. dulce* belongs to the family of Fabaceae, which represents one of the largest groups of flowering plants. It comprises a wide range of legumes that are important for both the environment and the economy. The following is the taxonomic classification [10]:

- **Kingdom:** Plantae
- **Clade:** Angiosperms
- **Clade:** Eudicots
- **Order:** Fabales
- **Family:** Fabaceae
- **Subfamily:** Mimosoideae
- **Genus:** *Pithecellobium*
- **Species:** *Pithecellobium dulce* (Roxb.) Benth.

The genus *Pithecellobium* consists of nearly 100 species distributed mainly in tropical and subtropical regions. *P. dulce* constitutes one of the more significant species in this family for both medicine and business (Figure 1). Common vernacular names of the plant include:

- **Manila tamarind** (English)
- **Vilayati Imli** (Hindi)
- **Madras Thorn** (English)
- **Camachile** (Philippines)
- **Seema Chinta / Jungle Jalebi** (India)

These names reflect the plant's widespread cultural integration across continents.



Figure 1: Distinctive coiled (spiral) fruit pods of *Pithecellobium dulce* observed on the mature tree

MORPHOLOGY

The anatomy of *P. dulce* shows adaptations that help it survive in harsh environments while maintaining many ecological processes.

Tree Characteristics

The specimen usually grows to be 10 to 15 meters tall and has a wide, expanding crown that produces thick leaves. The bark is usually gray to brown, not rough, and sometimes has cracks. The plant has paired spines that come from modified stipules. These spines help protect the plant from herbivory [11]. Due to its rapid growth and sturdy structure, it is commonly grown along roadsides, field boundaries, and agroforestry plantations.

Leaves

The leaves are bipinnate and alternately arranged. Each leaf usually consists of a single pair of pinnae, and each pinna bears two opposite, oblong leaflets. The leaflets measure 3–4 cm in length and exhibit a glossy green upper surface and paler underside. The petiole is short and grooved, and stipular spines are often present near the base of the leaves [12]. The leaves are rich in phenolic compounds and flavonoids, contributing to their antioxidant and antimicrobial properties. Traditional medicinal applications include using leaf decoctions as mouthwash for

gingivitis, toothache, and gum inflammation, or applying leaf paste to wounds and ulcers [13].

Flowers

The inflorescences occur as axillary or terminal globular heads. The small, sessile flowers are greenish-white to yellowish-white and possess a tubular corolla with 4–5 lobes. Numerous long stamens extend beyond the corolla, giving the flowers a characteristic feathery appearance [14]. The flowers emit a mild fragrance and produce nectar that attracts insects, particularly bees, making the plant beneficial to pollination networks. Flowering is generally observed between February and May, although timing may vary by geography and climate.

Fruit

The fruit is a distinctive coiled pod, often forming a helix or spiral shape. When immature, the pods appear green and later turn pinkish-red or reddish as they ripen. Each pod contains 4–5 glossy black seeds embedded within a soft, edible pulp that ranges from white to pink depending on the variety [15]. The fruit pulp is rich in:

- simple carbohydrates,
- dietary fiber,
- organic acids (tartaric, citric, malic),
- ascorbic acid (vitamin C),
- phenolics and antioxidants.

The pulp is commonly consumed raw and is an important ingredient in traditional beverages and functional foods.

Seeds

The seeds are ovoid, approximately 1–2 cm in diameter, and encased within the fleshy aril. Although not typically consumed by humans due to their hard testa, seeds possess significant medicinal and nutraceutical value. Extracts from seeds have demonstrated antihyperlipidemic, antidiabetic, and antioxidant activities in experimental studies [16]. When roasted, seeds can be used as a protein-rich flour substitute in certain cultures.

Root System

The plant possesses a deep taproot system accompanied by extensive lateral roots. This root architecture enables efficient absorption of water and nutrients from deeper soil layers, promoting drought tolerance. Additionally, the roots form nodules with nitrogen-fixing bacteria such as *Rhizobium*, contributing to soil fertility and ecological restoration [17]. The robust root system also plays a crucial role in preventing soil erosion on slopes, degraded soils, and high-wind environments.

PHYTOCHEMICAL COMPOSITION

The phytochemical profile of *P. dulce* varies significantly across different plant parts (leaves, bark, pulp, seeds, pods), reflecting the diversity of its biological functions. Advanced techniques such as HPLC, GC–MS, LC–MS/MS, FTIR, and NMR have identified numerous secondary metabolites associated with therapeutic efficacy.

Major Classes of Phytochemicals

The phytochemical profile of *Pithecellobium dulce* comprises several major classes of bioactive constituents, contributing to its broad therapeutic relevance. Among these, flavonoids form an important group, with compounds such as quercetin, kaempferol, rutin, luteolin, and apigenin occurring prominently in different plant parts. These molecules function as potent free-radical scavengers and metal-chelating agents, and they also regulate key inflammatory mediators by modulating signaling pathways, including NF- κ B and COX-2 [18].

Phenolic acids constitute another abundant category, especially in fruit and seed extracts, with gallic acid, chlorogenic acid, ferulic acid, and caffeic acid commonly detected. These constituents participate in antioxidative and antihyperglycemic mechanisms by suppressing α -amylase and α -glucosidase activity and reducing biomolecular oxidative damage [19]. The plant also contains considerable amounts of hydrolyzable and condensed tannins distributed in the bark, leaves, and pods. These compounds possess astringent, antimicrobial, anti-inflammatory, and anti-ulcer properties and additionally support lipid-lowering activity through their effects on cholesterol metabolism (Table 1) [20]. Saponins, primarily isolated from the seeds and pulp, demonstrate notable antidiabetic and antihyperlipidemic actions, attributed to their ability to limit intestinal glucose uptake, promote insulin release, and inhibit lipid absorption [21].

Alkaloids identified in the bark and leaf tissues contribute further to the plant's antimicrobial and analgesic activities. Organic acids such as tartaric, malic, and citric acids are also present and are responsible not only for the characteristic acidic taste of the fruit but also for enhancing digestive function and antioxidant capacity [22]. Volatile constituents, including terpenoids, aldehydes, ketones, and esters identified through GC–MS analysis, impart aroma and exhibit antimicrobial effects. In addition, the plant contains substantial quantities of polysaccharides, pectins & dietary fiber, which support

hypolipidemic effects by promoting bile acid excretion & beneficially modulating gut microbiota composition (Figure 2) [23].

In terms of pharmacologically active preparations, methanolic and ethanolic fruit extracts show strong antioxidant and antidiabetic activities, whereas hydroalcoholic leaf extracts exhibit considerable antimicrobial and anti-inflammatory potential. Aqueous bark decoctions are traditionally recognized for their anti-ulcer and astringent actions. Seed extracts enriched in saponins exert marked antidiabetic and lipid-lowering effects, while tannin-rich pod extracts demonstrate antioxidant, antimicrobial, and anthelmintic activity. Collectively, these diverse extracts act in a complementary manner, contributing to the broad therapeutic efficacy associated with *P. dulce*.

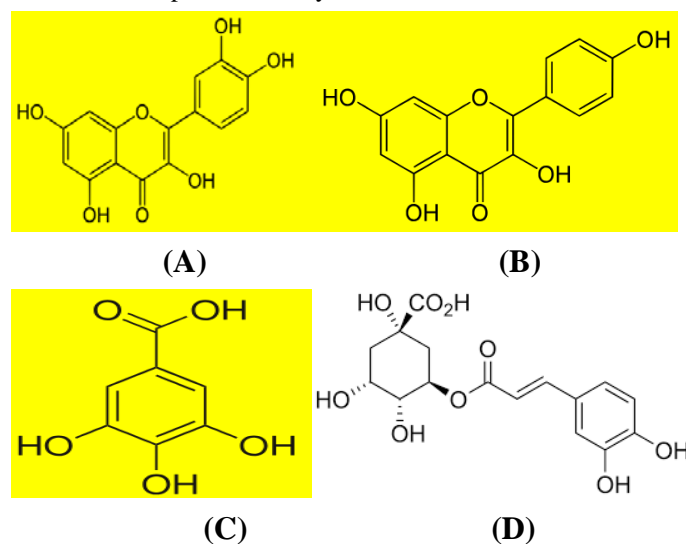


Figure 2: Two-dimensional chemical structures of the major bioactive markers identified in *Pithecellobium dulce*: (A) quercetin, (B) kaempferol, (C) gallic acid, and (D) chlorogenic acid.

NUTRITIONAL COMPOSITION OF PITHECELLOBIUM DULCE

While *P. dulce* has historically been consumed for its palatable fruit pulp, recent analytical studies show that the species is a nutritionally dense plant with significant potential for use in functional foods, nutraceuticals, and therapeutic formulations. Various plant components—particularly the fruit pulp, seeds & pods contain carbohydrates, proteins, essential minerals, fatty acids, vitamins, and health-promoting phytochemicals [24]. The variation in nutritional composition depends on factors such as genotype, geographic origin, season, maturity stage & extraction method. Key nutritional elements are summarized here.

Table 1: Major bioactive marker compounds of *Pithecellobium dulce*, their plant sources, extraction solvents, and reported pharmacological activities

Marker compound	Plant part	Common extraction solvent	Reported biological activity
Quercetin	Leaves, fruit pulp	Methanol / Ethanol	Potent antioxidant; suppresses NF- κ B-mediated inflammation; improves glucose uptake; exhibits antimicrobial and cytoprotective effects
Kaempferol	Leaves, seeds	Ethanol / Hydroalcoholic	Anti-inflammatory; antihyperlipidemic; supports vascular function; contributes to insulin sensitization
Gallic acid	Fruit pulp, bark	Aqueous / Methanol	Strong free-radical scavenging activity; antimicrobial; gastroprotective; inhibits lipid peroxidation
Chlorogenic acid	Fruit pulp, seeds	Methanol / Ethanol	Antidiabetic via α -glucosidase inhibition; antioxidant; modulates lipid metabolism and hepatic glucose output
Rutin	Leaves	Methanol	Antioxidant; capillary-protective; anti-inflammatory
Tannins	Bark, pods	Aqueous / Ethanolic	Astringent; antimicrobial; anti-ulcer; wound-healing
Saponins	Seeds, pulp	Methanol / Hydroalcoholic	Antidiabetic; antihyperlipidemic; enhances insulin secretion; limits intestinal glucose absorption
Phenolic acids (ferulic, caffeic)	Leaves, fruit	Methanol	Antioxidant; neuroprotective; anti-inflammatory

Proximate Nutrient Composition

The proximate nutrient profile of *Pithecellobium dulce* provides essential information on its moisture, ash, lipid, protein, crude fiber, and carbohydrate content, all of which collectively determine its nutritional quality and potential applications in food, nutraceutical, and therapeutic formulations. These parameters also serve as indicators of the plant's physicochemical characteristics and post-harvest behavior, thereby influencing its suitability for processing and storage.

Moisture Content

The fruit pulp of *P. dulce* typically contains 50–70% moisture, which contributes to its soft texture, refreshing taste, and overall digestibility. Moisture content plays a decisive role in determining the sensory properties of the pulp, the stability of the fruit during storage, and its tendency to undergo microbial deterioration under ambient conditions. Increased humidity speeds up the metabolism of enzymes and microbes, shortening shelf life. On the other hand, moderate dehydration makes things more stable and makes long-term storage easier.

This parameter also directly affects how easy it is to turn the pulp into useful products such as drinks, fermented foods, jams & sweets. Also, the method of dehydration used, such as solar drying, hot-air convection, or freeze-drying, has a big effect on how well heat-sensitive phytochemicals, especially phenolic compounds and organic acids, stay stable. These compounds tend to break down at high temperatures [25].

Crude Protein

The pulpy portion of the crop usually has 3–6% protein, while the leaves have 12–18%, and the seeds have a lot more, between 25% and 32%. The protein content of the seed is similar to that of chickpeas and pigeon peas, both legumes. This shows that it could be a sustainable source of plant-based protein for functional foods and dietary supplements [26]. Amino acid analysis shows that the seed contains essential amino acids such as lysine, leucine, valine, isoleucine, and methionine. These amino acids all play a role in the seed's biofunctional relevance. The amino acid spectrum improves the plant's nutritional value and makes it more likely to be added to protein-rich products for people who don't have easy access to animal proteins.

Lipid Content

The pulp and seeds of *P. dulce* have very different amounts of lipids. The pulp contains a fraction of a percent of lipids, but the seeds contain much more, between 8% and 12%. These seed lipids encompass polyunsaturated fatty acids (PUFAs), monounsaturated fatty acids (MUFAs), and comparatively smaller fractions of saturated fatty acids [27].

Among these, linoleic acid and oleic acid are the predominant constituents, both recognized for their beneficial effects on lipid metabolism, cardiovascular health, and anti-inflammatory responses. The presence of such fatty acids positions *P. dulce* seeds as a promising natural ingredient for cardioprotective dietary formulations.

Carbohydrates

Carbohydrates represent one of the major nutritional components of *P. dulce*, with the fruit pulp being particularly rich in simple sugars such as glucose, fructose, and sucrose. These sugars contribute to the characteristic sweet–acidic flavour of the ripe fruit and serve as readily accessible energy sources. In contrast, the seeds contain more complex carbohydrates and polysaccharides that play functional roles in modulating glycaemic responses, supporting digestive processes, and influencing the growth and composition of the gut microbiota. Quantitatively, carbohydrate content ranges from approximately 45–55% in the seeds and 60–70% in the fruit pulp on a dry-weight basis [28]. Such values highlight the plant's suitability as an energy-dense food source with diverse physiological benefits.

Dietary Fiber

Both soluble and insoluble dietary fiber fractions are present in considerable amounts in the pods and seeds of *P. dulce*, with total dietary fiber levels reported at 8–22%. These fiber components contribute significantly to gastrointestinal health by promoting bowel motility, reducing intestinal transit time, and supporting a balanced gut environment. Additionally, the fibrous components can help decrease cholesterol absorption, exert prebiotic effects by selectively stimulating beneficial gut microbiota, and help regulate postprandial blood glucose levels [29]. Such characteristics make the plant a valuable candidate for the formulation of fiber-rich therapeutic foods.

Ash and Mineral Content

Ash content serves as an indicator of the plant's total mineral composition, and *P. dulce* is recognized for its richness in essential minerals, including calcium, magnesium, iron, potassium, manganese, and zinc. These micronutrients play critical roles in bone mineralization, enzymatic functions, cellular metabolism, and immune regulation. The high mineral density enhances the plant's nutritional value and supports its potential use as a complementary dietary source for populations at risk of mineral deficiencies [30].

Vitamin Composition

Biochemical tests consistently demonstrate that *P. dulce* contains several important vitamins, especially vitamin C (ascorbic acid), a carotenoid-based form of vitamin A, and smaller amounts of B-complex vitamins. Vitamin C, which is

one of the most common vitamins in the fruit pulp, is a strong antioxidant that helps make collagen, boosts immune function, gets rid of reactive oxygen compounds, and stops signs of absence that are similar to scurvy [31]. The carotenoid content makes the fruit even more antioxidant-rich and beneficial for your eyes and skin, adding to its potential as a functional food.

Organic Acids and Sugars

The pulp from fruits contains many organic acids, such as malic, tartaric, citric, and succinic. These natural acids not only give the fruit its unique taste, but they also play a role in many physiological and biochemical processes. They affect how the body absorbs minerals, especially calcium and iron, help keep the stomach's pH level stable, improve digestion, and kill harmful bacteria by making the environment less hospitable for them [32]. Along with organic acids, the presence of reducing sugars provides a quick energy boost and improves the fruit's overall taste and smell. This makes it good for both fresh eating and use in processed foods.

Mineral Composition

Pithecellobium dulce's mineral profile underscores its nutritional importance because different parts of the plant, especially the fruit, pulp, leaves, and seeds, contain many macro- and microelements. The flesh of the fruit has 60–120 mg of calcium per 100 g, the leaves have 90–140 mg of calcium per 100 g, and the seeds have the most calcium, with 150–190 mg per 100 g. Calcium is very important for bone health, controlling enzymes, and neuromuscular activity. The fact that it is found in every component of the plant shows how important it is as a food source of important minerals. Iron content also varies across tissues, with 1.5–4.0 mg/100 g in the fruit pulp, 5.5–7.2 mg/100 g in the leaves, and 6–10 mg/100 g in the seeds, indicating significant potential to support haemoglobin synthesis and prevent iron-deficiency disorders, especially in populations with limited access to animal-based iron sources.

Potassium, a mineral essential for electrolyte balance and cardiovascular health, is also present in considerable concentrations, ranging from 250–480 mg/100 g in the pulp, 400–600 mg/100 g in leaves, and 450–700 mg/100 g in seeds. Magnesium, another critical nutrient involved in biochemical reactions and energy metabolism, occurs at 30–45 mg/100 g in pulp, 45–70 mg/100 g in leaves, and 40–65 mg/100 g in seeds. Additionally, zinc is found in measurable amounts, ranging

between 0.5–1.2 mg/100 g in the fruit pulp, 1.2–2.4 mg/100 g in leaves, and 1.0–2.0 mg/100 g in seeds, contributing to immune function, antioxidant defense, and cellular repair mechanisms. Collectively, these mineral values demonstrate that *P. dulce* possesses a nutrient composition comparable to, and in some cases exceeding, that of many commonly consumed fruits and legumes, underscoring its potential as a functional food resource and an accessible source of essential micronutrients for nutritional intervention programs, as shown in Table 2 [33].

Table 2: Comparative proximate and mineral composition of *Pithecellobium dulce* seeds relative to commonly consumed legumes (chickpea and pigeon pea)

Parameter	<i>P. dulce</i> seed	Chick pea	Pigeon pea
Protein (%)	25–32	~19	~21
Fiber (%)	8–22	12	15
Iron (mg/100g)	6–10	6.2	5.0
Calcium (mg/100g)	150–190	105	130

Antioxidant Capacity

The antioxidant potential of *Pithecellobium dulce* has been extensively documented and is largely attributed to its rich phytochemical profile, including flavonoids such as quercetin and rutin, phenolic acids such as gallic and chlorogenic acids, tannins, saponins, and a spectrum of natural organic pigments. These bioactive compounds act synergistically to enhance the plant's capacity to neutralize reactive oxygen species and mitigate oxidative stress, a central mechanism involved in various chronic and degenerative diseases.

The antioxidant properties of *P. dulce* extracts have been assessed using multiple standardized analytical assays, including the DPPH radical scavenging test, ABTS assay, Ferric Reducing Antioxidant Power (FRAP) assay, and Oxygen Radical Absorbance Capacity (ORAC) assay, each offering insights into distinct aspects of free-radical quenching [34]. Across published studies, extracts consistently demonstrate high total phenolic content (TPC) and elevated total flavonoid content (TFC), both of which directly correlate with potent antioxidant activity. The results of this study collectively demonstrate that *P. dulce* possesses significant free-radical-scavenging properties, thereby underscoring its therapeutic potential in conditions marked by oxidative damage, including inflammation-related illnesses, metabolic diseases such as diabetes, and neurological disorders in which oxidative stress is a critical pathological factor. The plant's high levels of antioxidants not only support its traditional

use but also make it an excellent option for producing natural antioxidant products, nutraceuticals, and drugs.

Influence of Extraction Solvents on Bioactive Yield and Pharmacological Activity

Comparative studies demonstrate that methanolic and ethanolic extracts consistently yield higher concentrations of flavonoids and phenolic acids than aqueous preparations, resulting in superior antioxidant and antidiabetic efficacy. Conversely, aqueous extracts retain polysaccharides and tannins responsible for gastroprotective and anti-ulcer effects. This solvent-dependent phytochemical selectivity explains variability in reported pharmacological outcomes and highlights the need for standardized extraction protocols.

PHARMACOLOGICAL ACTIVITIES OF *PITHECELLOBIUM DULCE*

A lot of preclinical research indicates that *Pithecellobium dulce* exhibits a wide range of pharmacological effects. For example, it has been shown to be an antioxidant, anti-inflammatory, antidiabetic, anti-ulcer, lipid-lowering, antimicrobial, analgesic, antipyretic, hepatoprotective, wound-healing, anticancer, and safe substance. These effects are mostly due to the plant's many phytochemical compounds, such as flavonoids, phenolic acids, tannins, saponins, and terpenoids, which together alter multiple molecular pathways. The pharmacological attributes and underlying mechanisms reported in the literature are summarized below in a detailed narrative form.

Antioxidant Activity

One of the most common biological effects of *P. dulce* is its antioxidant properties. Its extracts are known to combat oxidative stress in various ways. The plant itself contains naturally occurring flavonoids, such as quercetin and kaempferol, that directly neutralize reactive oxygen species (ROS). These compounds have been shown to neutralize deleterious radicals, including superoxide anions ($O_2^{\bullet-}$), hydroxyl radicals ($\bullet OH$), and nitric oxide radicals ($NO\bullet$), thereby averting cellular oxidative damage [35]. In addition to removing free radicals, the phenolic acids in the plant can also bind to metals, especially Fe^{2+} and Cu^{2+} . This stops Fenton-type reactions from making highly reactive free radicals [36]. Extracts from seeds and leaves have exhibited substantial inhibition of lipid peroxidation, as indicated by reduced malondialdehyde (MDA) levels in experimental liver and brain

homogenates [37]. Furthermore, administration of *P. dulce* extracts enhances endogenous antioxidant defenses by stimulating key enzymes, including superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and glutathione peroxidase (GPx), thereby improving the overall cellular redox balance [38].

Anti-inflammatory Activity

The anti-inflammatory properties of *P. dulce* are mediated through its ability to modulate inflammatory enzymes, cytokines, transcription factors, and cell-membrane stability. Extracts from leaves, seeds, and bark have been reported to inhibit pro-inflammatory enzymes such as cyclooxygenase-2 (COX-2) and lipoxygenase (LOX), both of which are central regulators of prostaglandin and leukotriene synthesis during inflammation [39]. The plant also reduces the expression of key inflammatory cytokines, including TNF- α , IL-1 β , IL-6, and C-reactive protein (CRP), which collectively contribute to the suppression of acute and chronic inflammatory responses [40]. One of the important molecular pathways influenced by the plant is the NF- κ B signaling cascade. Flavonoids present in the plant prevent I κ B α degradation, thereby inhibiting NF- κ B nuclear translocation and blocking transcription of inflammation-related genes [41]. Additional studies indicate that seed extracts stabilize lysosomal membranes, thereby reducing the release of histamine and other inflammatory mediators, thereby further contributing to their anti-inflammatory effects.

Antidiabetic Activity

Numerous studies suggest that *P. dulce* possesses notable antidiabetic and antihyperglycemic properties, with both seed and fruit extracts demonstrating beneficial effects on glucose homeostasis. A primary mechanism involves inhibiting key carbohydrate-digesting enzymes, such as α -amylase and α -glucosidase, which slow the breakdown of complex sugars and delay glucose absorption, thereby minimizing postprandial glucose spikes [42]. Most antidiabetic evaluations employed streptozotocin (STZ)-induced diabetic rat models, while some studies utilized alloxan-induced hyperglycaemia. Seed extracts significantly reduced fasting glucose, HbA1c, and lipid markers in STZ-induced models, indicating β -cell-protective mechanisms. Saponins and related phytochemicals are also implicated in enhancing pancreatic β -cell responsiveness, promoting insulin secretion, and facilitating GLUT-4 translocation to peripheral tissues, which improves glucose

uptake in skeletal muscle [43]. Moreover, seed extracts have been shown to significantly ameliorate metabolic parameters by lowering serum glucose, HbA1c, triglycerides, and total cholesterol levels while simultaneously increasing HDL cholesterol and adiponectin, an adipokine associated with increased insulin sensitivity [44]. The plant's antioxidant potential also protects pancreatic tissues from oxidative damage, helping preserve β -cell integrity and function.

Antihyperlipidemic Activity

The lipid-lowering activity of *P. dulce* is well documented and appears to involve several complementary biochemical pathways. Saponins present in the seeds bind to intestinal bile acids, forming complexes that are excreted in feces. This loss of bile acids compels the liver to convert more endogenous cholesterol into bile acids, thereby lowering circulating cholesterol levels [45]. Flavonoids such as quercetin and rutin also contribute to lipid reduction by upregulating hepatic LDL receptors, enhancing the clearance of LDL and VLDL particles from the bloodstream [46]. Animal studies reveal increased fatty acid β -oxidation, reduced hepatic triglyceride accumulation, and elevated expression of genes involved in fat metabolism, including PPAR- α and CPT-1, suggesting improved lipid catabolism [47]. In addition, extracts inhibit de novo lipogenesis by downregulating SREBP-1c, acetyl-CoA carboxylase (ACC), and fatty acid synthase (FAS), key mediators of lipid synthesis [48]. The plant's antioxidant components further support cardiometabolic health by preventing LDL oxidation & limiting foam cell formation, which are critical events in the development of atherosclerotic lesions [49].

Antimicrobial Activity

Several extracts of *P. dulce* exhibit broad-spectrum antibacterial activity against both Gram-positive and Gram-negative bacteria. Leaf and bark extracts have been shown to inhibit species such as *Staphylococcus aureus*, *Bacillus subtilis*, and *Streptococcus pyogenes*, with methanolic extracts demonstrating substantial zones of inhibition, attributed to their flavonoids, tannins, and terpenoids that disrupt microbial cell-wall integrity [50]. Against Gram-negative pathogens, such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, and *Klebsiella pneumoniae*, the fruit and seed extracts act through mechanisms including alteration of membrane permeability, disruption of bacterial electron transport chains, and inhibition of efflux pumps, thereby significantly impairing bacterial survival [51].

Antifungal Activity

Ethanol and aqueous extracts of *P. dulce* have displayed considerable antifungal activity against dermatophytes and yeasts, including *Candida albicans*, *Aspergillus niger*, and *Trichophyton mentagrophytes*. The antifungal effects are largely linked to steroidal saponins and phenolic compounds that disrupt fungal cell membranes, bind to ergosterol, impair mitochondrial function, and ultimately cause cell death [52].

Antiviral Properties

Emerging in vitro studies indicate that extracts from *P. dulce* may inhibit various viruses, including influenza viruses, herpes simplex virus (HSV-1), and dengue virus [53]. Proposed mechanisms include interference with viral entry, inhibition of viral replication enzymes, and stimulation of host antiviral immune responses. While these findings are promising, further animal-based and clinical investigations are needed to establish therapeutic relevance.

Analgesic Effects

Both seed & leaf extracts have demonstrated analgesic potential in preclinical models, acting through peripheral and central pathways. The analgesic effects are partly attributed to the suppression of prostaglandin synthesis by inhibiting COX-1 & COX-2 enzymes [54]. Additionally, certain phytoconstituents may interact with opioid receptors, raising pain thresholds in hot plate & tail immersion assays, indicating central analgesic activity [55]. The reduction of local inflammatory mediators also contributes to the overall pain-relieving effects.

Antipyretic Activity

Methanolic leaf extracts have shown significant antipyretic activity in yeast-induced pyrexia models, reducing elevated body temperature through suppression of prostaglandin E₂ (PGE₂) synthesis in the hypothalamus [56]. This effect may be complemented by antioxidant activity and cytokine-modulating actions that stabilize thermoregulatory mechanisms.

Anti-ulcer Activity

Extracts from the fruit, leaves, and bark of *P. dulce* have been widely investigated for their gastroprotective effects. One of the key mechanisms involves enhancement of gastric mucosal defense, including increased mucus content, mucin secretion, and bicarbonate production, which collectively reinforce the gastric mucosal barrier [57]. Aqueous extracts inhibit the H⁺/K⁺

ATPase enzyme in gastric parietal cells, resulting in reduced gastric acid secretion and improved ulcer healing [58]. Antioxidant actions also contribute significantly to gastroprotection by reducing lipid peroxidation and increasing antioxidant enzyme levels, such as SOD and CAT, thereby attenuating damage caused by ethanol- or NSAID-induced gastric ulcers [59]. Furthermore, tannin-rich extracts have demonstrated activity against *Helicobacter pylori*, a major etiological agent of peptic ulcers, facilitating additional protection and recovery [60].

Hepatoprotective Activity

Experimental studies provide strong evidence for the hepatoprotective potential of *P. dulce*. The extracts enhance detoxification mechanisms by elevating endogenous antioxidants, including glutathione (GSH), glutathione-S-transferase (GST), and catalase (CAT), thereby mitigating oxidative stress-induced liver damage [61]. Saponins help stabilize hepatocellular membranes, reducing leakage of intracellular enzymes and preserving organ integrity. Additionally, the plant exhibits anti-fibrotic effects by inhibiting TGF-β1 expression, reducing collagen deposition, and suppressing α-SMA, key markers of hepatic fibrosis [62]. Improvements in serum biomarkers, including ALT, AST, ALP, and bilirubin, further confirm its liver-protective effects.

Wound-Healing Activity

The wound-healing potential of *P. dulce* is linked to its ability to modulate collagen synthesis, fibroblast proliferation, microbial control, and angiogenesis. Extracts significantly increase hydroxyproline content, an indicator of enhanced collagen deposition and improved structural integrity of newly formed tissues [63]. Flavonoid-rich fractions stimulate rapid fibroblast multiplication, accelerating the formation of granulation tissue essential for wound repair. The plant's antimicrobial constituents prevent colonization by pathogenic bacteria such as *S. aureus* and *E. coli*, maintaining a clean wound environment conducive to healing. Moreover, the extracts promote angiogenesis by stimulating vascular endothelial growth factor (VEGF), facilitating nutrient delivery & tissue regeneration [64].

Cytotoxic and Anticancer Potential

Preliminary studies indicate that *P. dulce* possesses selective cytotoxic activity against several cancer cell lines, including MCF-7 (breast), HepG2 (liver), A549 (lung), and HCT-116

(colon) [65]. The anticancer mechanisms involve induction of apoptosis via caspase-3 activation, disruption of mitochondrial membrane potential, downregulation of the anti-apoptotic protein Bcl-2, and cell-cycle arrest at the G2/M phase. While these findings are promising, additional studies are needed to establish safety, specificity, and therapeutic applicability in clinical settings.

TOXICOLOGICAL STUDIES

Twenty-eight-day oral administration (500 mg/kg) showed no histopathological abnormalities in liver, kidney, or heart tissues. Serum ALT, AST, ALP, creatinine, and urea remained within physiological ranges, confirming systemic safety.

Acute Toxicity

Acute toxicity assessments reveal a high margin of safety, with LD₅₀ values exceeding 2,000 mg/kg for leaf and fruit extracts. No significant behavioral abnormalities or mortality have been observed at these doses, indicating low acute toxicity [66].

Sub-chronic Toxicity

Sub-chronic administration for up to 28 days at a dose of 500 mg/kg has shown no significant alterations in hematological parameters, liver function markers, or histopathology of the vital organs, including the kidney, liver, heart, and lungs [67].

Cytotoxicity

Extracts demonstrate selective cytotoxicity, with normal fibroblasts showing minimal toxicity at concentrations that effectively inhibit cancer cells. This suggests a potentially favorable therapeutic window for anticancer applications.

Translational Barriers and Clinical Research Needs

Despite extensive preclinical evidence, clinical validation remains lacking due to variability in extraction, lack of standardized dosing, and limited pharmacokinetic data. Phase I safety trials followed by pilot nutraceutical studies are urgently required to establish human tolerability and bioefficacy.

MOLECULAR MECHANISMS OF ACTION

Although the ethnomedicinal relevance of *Pithecellobium dulce* has been recognized for generations, recent advances in molecular pharmacology have begun to elucidate how its bioactive constituents act at the cellular and biochemical levels. The major phytochemical groups present in the plant, such as

phenolic acids, flavonoids, tannins, and saponins, engage with a wide array of intracellular signaling pathways that modulate oxidative balance, inflammatory cascades, glucose homeostasis, lipid regulation, antimicrobial defense, and tissue repair. These phytoconstituents do not act through a single mechanism; instead, they target multiple molecular nodes simultaneously, contributing to the plant's broad therapeutic profile.

Bioavailability Considerations

Although polyphenols exhibit strong in vitro bioactivity, their oral bioavailability is limited by intestinal degradation and rapid metabolism. Encapsulation strategies and food-matrix integration may enhance systemic absorption.

ANTIOXIDANT SIGNALING PATHWAYS

Activation of the Nrf2–ARE Signaling Axis

Extracts of *P. dulce* have been shown to activate Nuclear Factor Erythroid 2–Related Factor 2 (Nrf2), a transcription factor considered the central coordinator of cellular antioxidant defense [68]. Under normal conditions, Nrf2 remains sequestered in the cytoplasm by its repressor protein Keap1. The phytochemicals present in the plant induce subtle redox signals that modify key cysteine residues on Keap1, thereby dissociating Keap1 from Nrf2. Once released, Nrf2 accumulates and translocates into the nucleus, where it binds to Antioxidant Response Elements (ARE) located in the promoter regions of numerous cytoprotective genes. This interaction upregulates crucial antioxidant enzymes such as heme oxygenase-1 (HO-1), NADPH quinone oxidoreductase (NQO1), superoxide dismutase (SOD), catalase (CAT) & glutathione peroxidase (GPx). Collectively, this cascade strengthens the cell's intrinsic defense systems, contributing to cytoprotection, mitigation of oxidative damage & attenuation of aging-related cellular decline.

Suppression of ROS-Generating Enzymes

In addition to enhancing antioxidant defenses, *P. dulce* extracts also exert inhibitory effects on major enzymatic sources of reactive oxygen and nitrogen species. Studies indicate that the plant downregulates NADPH oxidase (NOX), xanthine oxidase, and inducible nitric oxide synthase (iNOS), thereby limiting excessive ROS and RNS production [69]. The combined effects of promoting antioxidant gene expression while suppressing ROS-generating enzymes help maintain redox homeostasis and prevent oxidative tissue injury.

ANTI-INFLAMMATORY PATHWAYS

Modulation of the NF- κ B Pathway

The flavonoids and tannins of *P. dulce* exhibit strong anti-inflammatory potential by targeting the nuclear factor kappa-B (NF- κ B) pathway, a master regulator of pro-inflammatory gene expression. These compounds inhibit the phosphorylation and degradation of I κ B α , the inhibitory protein that retains NF- κ B in the cytosol [70].

By preventing I κ B α degradation, nuclear translocation of the NF- κ B p65 subunit is effectively blocked. Consequently, the transcription of inflammatory mediators such as TNF- α , IL-1 β , and IL-6 is substantially reduced, thereby dampening inflammatory signaling and alleviating tissue inflammation.

Modulation of COX and LOX Pathways

Phenolic constituents further regulate inflammation by modulating both the cyclooxygenase (COX) and lipoxygenase (LOX) pathways. These compounds inhibit COX-2, which reduces prostaglandin synthesis & similarly block 5-lipoxygenase (5-LOX), thereby decreasing leukotriene formation [71]. This dual inhibition significantly contributes to the plant's analgesic and anti-inflammatory activity, making it effective in conditions involving pain, swelling, and inflammatory tissue damage.

ANTIDIABETIC MECHANISMS

AMPK Pathway Activation

Extracts from *P. dulce* seeds have been reported to activate AMP-activated protein kinase (AMPK), a metabolic sensor that enhances insulin sensitivity and regulates energy balance [72]. Activation of AMPK stimulates cellular glucose uptake, promotes fatty acid oxidation, and suppresses hepatic gluconeogenesis. Through these mechanisms, AMPK activation improves glycaemic control and reduces metabolic dysregulation in diabetes.

Enhancement of Insulin Signalling

Flavonoids found in the plant also enhance insulin signalling at multiple molecular checkpoints. These compounds promote phosphorylation of insulin receptor substrate-1 (IRS-1), activate the PI3K/AKT pathway, and facilitate the translocation of GLUT-4 transporters to skeletal muscle cell membranes [73]. By enhancing these critical steps, *P. dulce* mimics mechanisms associated with established antidiabetic drugs such as

metformin, thereby improving glucose utilization and peripheral insulin responsiveness.

LIPID-LOWERING MECHANISMS

Downregulation of SREBP-1 and Fatty Acid Synthase

The lipid-modulating effects of *P. dulce* are partly mediated through downregulation of sterol regulatory element-binding protein-1 (SREBP-1) and fatty acid synthase (FAS), two key regulators of lipogenesis [74]. Suppression of these genes reduces hepatic fatty acid synthesis and prevents triglyceride accumulation, thereby improving lipid profiles.

Activation of PPAR- α

Another important mechanism involves the activation of peroxisome proliferator-activated receptor- α (PPAR- α). Activation of this nuclear receptor enhances mitochondrial β -oxidation and accelerates the clearance of plasma lipids [75]. Through these actions, *P. dulce* supports lipid normalization and helps prevent metabolic disorders associated with dyslipidaemia.

ANTIMICROBIAL PATHWAYS

Membrane Disruption

Tannins and saponins from *P. dulce* exhibit strong antimicrobial activity by directly interacting with microbial cell membranes. These compounds increase membrane permeability, induce pore formation, and cause leakage of essential intracellular contents, leading to microbial lysis and cell death [76]. The mechanism is broad-spectrum, affecting both Gram-positive and Gram-negative organisms.

Inhibition of Nucleic Acid Replication

Flavonoids in the plant further contribute to antimicrobial defense by binding to bacterial DNA gyrase and topoisomerase IV—enzymes essential for DNA replication and supercoiling [77]. Inhibiting these enzymes disrupts nucleic acid synthesis, preventing bacterial proliferation and aiding in infection control.

WOUND-HEALING MECHANISMS

Activation of TGF- β /Smad Signaling

The wound-healing efficacy of *P. dulce* is associated with the modulation of the Transforming Growth Factor- β (TGF- β)/Smad signaling pathway. Plant extracts enhance TGF- β 1 expression and increase Smad2/3 activation, thereby promoting fibroblast proliferation & extracellular matrix deposition [78].

This acceleration of cellular repair processes supports faster wound closure.

Enhancement of Collagen Maturation

In addition to stimulating fibroblast activity, *P. dulce* boosts collagen maturation, as evidenced by elevated hydroxyproline levels—an indicator of collagen stabilization and cross-linking [79]. Enhanced collagen organization ensures the formation of stronger, more resilient scar tissue, underscoring the plant's therapeutic potential in wound management.

ETHNOMEDICINAL USES OF *PITHECELLOBIUM DULCE*

Pithecellobium dulce has ethnomedicinal significance across a broad geographical spectrum, encompassing Central America, the Indian subcontinent, Nepal, Sri Lanka, Mexico, and the Philippines, where various plant components, including leaves, bark, pods, fruit pulp, and seeds, are utilized in traditional healing practices. These various applications demonstrate its classification as a versatile species with considerable therapeutic and cultural significance in indigenous and folk medicine traditions across multiple continents [80].

Uses in Indian Traditional Medicine

P. dulce is well-known in India by common names like "Vilayati Imli," "Jungle Jalebi," and "Seema Chinta." It is also an important part of household treatments and local herbal traditions. People really like the fruit pulp because it can help with digestive problems like indigestion, constipation, hyperacidity, and stomach contractions. These benefits come from a mix of tannins, organic acids, and mild laxatives that help keep the intestines moving and bring the gastrointestinal tract back into balance [81]. People often drink leaf decoctions to help with dysentery, diarrhea, and stomach ulcers. This shows that the plant is a traditional way to heal the gut, likely due to its stringent nature and mucosal-protective phytochemicals [82].

Oral and Dental Care

In traditional oral hygiene, the leaves of *P. dulce* are very important. People often use them as a natural mouthwash to treat gingivitis, ease a toothache, and prevent bleeding gums. These applications are supported by the plant's intrinsic antimicrobial and astringent properties, which help reduce the oral microbial load, tighten gum tissue, and lessen inflammatory symptoms in the oral cavity [83].

Skin Disorders

Topical applications of *P. dulce* have long been recognized in traditional Indian medicine for the treatment of dermatological conditions. Fresh leaf paste is applied to the skin to manage rashes, eczema, ringworm infections & wounds that show signs of inflammation or infection. The therapeutic outcomes observed in these treatments are linked to the presence of flavonoids, phenolics, and other bioactive compounds with demonstrated wound-healing, antifungal, and anti-inflammatory effects [84].

Anti-inflammatory and Analgesic Uses

The bark and seeds of *P. dulce* are valued for their traditional use in relieving inflammatory conditions. A poultice prepared from the bark is commonly used by local healers to reduce swelling, mitigate joint pain, and promote recovery from sprains. In addition, powdered seeds are administered to help reduce fever and alleviate general body pain, reflecting the plant's longstanding use as a natural analgesic and antipyretic agent within community-based healing systems [85].

Uses in Central American Traditional Medicine

In regions of Central America, particularly Mexico and Guatemala, *P. dulce* is used as a traditional remedy for respiratory ailments such as cough, sore throat & mild respiratory infections. It is also used in emergency folk treatments such as those administered for snake bites, indicating its perceived detoxifying & protective attributes. Leaf infusions are commonly consumed for their diuretic activity and as a general cleansing preparation intended to remove metabolic impurities from the body, which aligns with the plant's historical use as a natural detoxifying agent in local ethnomedicinal systems [86].

Uses in Traditional Philippine Medicine

In Philippine herbal medicine, where the plant is commonly known as "Camachile," several parts of *P. dulce* are used to treat gastrointestinal and systemic conditions. Young leaves are administered to treat dysentery, while decoctions prepared from the bark are recommended for managing gastrointestinal bleeding. The fruit is routinely consumed as a natural laxative, with traditional practitioners recognizing its mild purgative effect and its ability to promote smooth bowel evacuation without significant irritation [87].

Uses in Ayurvedic and Siddha Traditions

Although *P. dulce* is not formally classified as a classical drug in the principal Ayurvedic pharmacopoeias, it is employed by contemporary practitioners to balance the Pitta and Kapha doshas, mitigate inflammatory conditions, and support detoxification therapies such as Shodhana. In Siddha medicine, references to the plant highlight its use in treating Vatha disorders, chronic ulcerations, and various skin eruptions, reflecting its relevance in longstanding South Indian medical traditions that rely on botanical agents for systemic and dermatological healing [88].

Uses in Unani Medicine

Within the Unani system of medicine, *P. dulce* also occupies an established therapeutic role. The bark is incorporated into traditional Qurs formulations to reduce inflammation and strengthen tissues. Seed extracts are used as expectorants and blood-purifying agents, while the fruit pulp is prescribed to enhance digestive strength and correct disturbances associated with sluggish gastrointestinal function. These uses are consistent with the plant's recognized Unani attributes, including its expectorant, astringent, and stomach-strengthening actions [89].

ROADMAP FOR FUTURE RESEARCH

Future investigations should integrate LC-MS metabolomics, proteomics-based peptide profiling, standardized extract development, pharmacokinetic modeling, and Phase-I clinical trials. These approaches will accelerate translation from ethnomedicine to validated phytopharmaceuticals.

CONCLUSION

Pithecellobium dulce represents a medicinally valuable species at the intersection of ethnomedicine and modern scientific inquiry. Traditional systems across Asia, Central America, and the Philippines have long used its leaves, bark, fruit pulp, and seeds to treat digestive disorders, inflammation, skin diseases, microbial infections, and systemic ailments. Contemporary phytochemical studies substantiate these uses by identifying flavonoids, tannins, alkaloids, phenolic acids, and essential minerals that contribute to its antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and gastroprotective activities.

Despite promising preliminary evidence, significant gaps remain in standardized extraction methods, pharmacokinetics, toxicity evaluation & molecular mechanisms of action. Future research

integrating advanced analytical techniques, in vivo models, and controlled clinical trials is essential to validate its therapeutic potential and support safe, evidence-based applications. Overall, *P. dulce* stands as a versatile botanical resource with considerable promise for the development of novel phytopharmaceuticals and functional health products.

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NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

All authors contributed significantly to the conception and design of the review. Sagar Kamble, Sudir Karpe, Swapnali Raut, Saniya Shaikh, and Pratiksha Devram were involved in literature survey, data collection, and critical analysis of published studies. Manisha Lavate conceptualized the study, supervised the overall work, and critically revised the manuscript for intellectual content. All authors participated in drafting and revising the manuscript, approved the final version, and agree to be accountable for all aspects of the work.

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