Review
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Ethnobotanical, Phytochemical, and Pharmacological Aspects of Mountain Papaya (*Vasconcellea pubescens* A.DC.)

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Abstract: Mountain papaya (*Vasconcellea pubescens* A.DC.) is a high-altitude species with significant potential as a wild nutritious food source and a therapeutic agent. This review examines the ethnobotanical significance, phytochemical profile, and pharmacological activities of this plant. Specifically, this review contextualises the phytochemical and pharmacological data for the Wonosobo cultivar from the Dieng Plateau within the broader global dataset for this species, including data from Chile and Saudi Arabia. Traditionally, mountain papaya is used as a folk remedy to treat digestive disorders such as diarrhea and dyspepsia, as a topical agent to promote skin tissue repair, and as a natural dewormer for gastrointestinal parasites. The therapeutic properties of mountain papaya are primarily driven by phenolic acids, flavonoids, carpaine alkaloids, and proteolytic enzymes. Pharmacological evaluations highlight the plant's potent antioxidant activity, antiglycation effects, inhibition of alpha-glucosidase and alpha-amylase, broad-spectrum antimicrobial activity, and thrombolytic properties, all of which are relevant to wound healing and the treatment of diabetes, diarrhea, and inflammatory diseases. The traditional uses of mountain papaya are corroborated by pharmacological activity evaluations attributed to related metabolites. This review highlights the need for further standardization and pharmacological validation before mountain papaya-derived products can advance into interventional clinical trials or regulatory approval of phytopharmaceuticals, nutraceuticals, or functional foods.

Introduction

Mountain *Papaya* (*Vasconcellea pubescens* A. DC., Caricaceae) is a nutritionally and therapeutically significant species (1). Native to South America, this species has been introduced to various regions worldwide, including Indonesia and Saudi Arabia, where it is valued for its distinctive fruit characteristics and biochemical properties (2). In Indonesia, mountain *Papaya* has a limited distribution, found primarily in high-altitude volcanic regions such as the Dieng Plateau in Central Java, as well as Bromo and Cangar-Batu in East Java (3).

The medicinal utilization of mountain *Papaya* is part of the local knowledge systems of highland communities, particularly on the Dieng Plateau. Ethnobotanical research indicates that while there is an exceptionally high community appreciation for preserving the plant in its environment (97.3%), specialized local knowledge of its use in treating specific diseases is less widespread, with an appreciation rate of approximately 38%. This traditional use is most prominent among the elderly in the local population (4). Beyond its cultural value, mountain *Papaya* is increasingly recognized for its potential as a functional food and a source of bioactive compounds (2).

Phytochemical investigations have revealed that mountain *Papaya* is rich in secondary metabolites. The fruit extracts are particularly rich in phenolics, flavonoids, and tannins. Comprehensive profiling using gas chromatography-mass spectrometry (GC-MS) has tentatively identified 49 compounds, many of which exhibit drug-likeness and favorable pharmacokinetic properties. These bioactive constituents contribute to a broad range of biological activities, including significant antioxidant potential, notable thrombolytic effects (88.75%), and moderate antibacterial activity against various strains. Furthermore, the plant demonstrates the ability to inhibit clinically relevant enzymes such as urease (78.26%) and tyrosinase (89.85%), suggesting its potential role in the development of future nutraceuticals and preventive therapies (2).

Several recent reviews have covered multiple aspects of mountain *Papaya*. For instance, previous reports about the antibacterial compounds, health-promoting properties, industrial applications, nutritional composition,

physiology of fruit development and ripening, and the ripening process (5 – 7). However, a comprehensive review linking the botanical characteristics, traditional medicine systems, phytochemical complexity, and bioactivities of mountain *Papaya* is not yet available. The existing literature is heavily biased toward cultivars from South America, particularly Chile, and Saudi Arabia, while the Dieng Plateau cultivar remains understudied. This is a significant gap because environmental factors such as altitude, soil composition, and climate, which vary markedly between the Dieng Plateau and other growing regions, strongly influence the qualitative and quantitative profiles of bioactive compounds in mountain *Papaya*. Moreover, the Wonosobo cultivar possesses distinct cultural significance as a plant identity of the Dieng Plateau community, yet its unique ethnobotanical context and potential chemical variations relative to better-studied global cultivars have not been systematically examined. Therefore, while global data on mountain *Papaya* provide a valuable foundation, they cannot be assumed to fully represent the characteristics of the Wonosobo cultivar. This review addresses this gap by contextualising the available global phytochemical and pharmacological data within the framework of Wonosobo's plant identity, identifying both region-specific variations and commonalities that inform future research priorities for this understudied cultivar. This article aims to provide an integrated review of these domains, with particular emphasis on the relationships between the plant's chemical constituents and their pharmacological mechanisms.

Methodology

This review was conducted by systematically searching PubMed, Scopus, SpringerLink, and Google Scholar databases. The search was performed using keywords and Boolean operators, including "mountain *Papaya*" OR "*V. pubescens*" OR "*Vasconcellea cundinamarcensis*" OR "*Carica candamarcensis*" AND ("botany" OR "morphology" OR "taxonomy") AND ("traditional uses" OR "ethnobotany" OR "folk medicine") AND ("phytochemistry" OR "secondary metabolites" OR "phenolic compounds" OR "flavonoids" OR "alkaloids" OR "enzymes") AND ("pharmacology" OR "biological activity" OR "antioxidant" OR "antidiabetic" OR "antimicrobial" OR "wound healing" OR "anthelmintic"). The search was not restricted by publication date to ensure comprehensive coverage of both historical and contemporary literature on the subject.

All retrieved articles from the literature search were screened by title and abstract for relevance. Studies were included if they met the following criteria: original research articles or reviews focusing on mountain *Papaya*; publications containing ethnobotanical information, phytochemical characterisation, or pharmacological evaluation of the plant; articles published in peer-reviewed journals or conference proceedings; and studies available in English or with English abstracts. Exclusion criteria were: studies not directly related to mountain *Papaya*; articles lacking sufficient methodological detail; conference abstracts without full-text availability; and non-English publications without English abstracts. Botanical characteristics, traditional medicinal applications, phytochemical composition, pharmacological activities, and geographical variations in plant composition were extracted. Total flavonoid content (TFC), total phenolic content (TPC), antioxidant activities, and known secondary metabolites, along with their distribution across plant parts, were compiled and analyzed.

Botanical Profile of Mountain *Papaya*

The species is highly adapted to the highlands between 1,000 and 3,000 meters above sea level. It thrives in moderate temperatures (10 °C–25 °C) and cannot tolerate frost or extreme heat above 30 °C. Historically, the species has been subject to nomenclatural confusion, with many synonyms (8, 9). The brief classification of the plant is presented in **Table 1**.

The morphological characters of mountain *Papaya* are depicted in **Figure 1**. It is an arborescent, dicotyledonous plant that reaches heights of 3 to 10 meters. The stem is stout, succulent, and medullose, often exhibiting branching. The stem colour is typically greenish or light grey. The leaves are large, broad, and five-lobed, clustering at the terminal ends of branches to form a dense crown. A defining botanical feature is the dense layer of trichomes on the underside of the leaves, which gives the species its name, pubescens, meaning feathers (9). Trichomes vary by sex, with considerable differences observed in micro-morphological characteristics between female and monoecious plants (10). The male flowers are slender with long, pubescent peduncles and are produced in abundant inflorescences. The female flowers are larger, yellow to white, and arise directly in leaf axils with very

Table 1. Taxonomic rank of mountain *Papaya*.

No.	Rank	Details
1	Kingdom	Plantae Haeckel
2	Phylum	Angiosperms
3	Order	Brassicales Bromhead
4	Family	Caricaceae Dumort.
5	Genus	*Vasconcellea* A. St. -Hil.
6	Species	*V. pubescens* A. DC.
7	Synonyms	*C. candamarcensis* Hook. f. , *Carica pubescens* Solms, *Papaya pubescens* (Lenné & K. Koch) Kuntze, *Vasconcellea cestriflora* A. DC. , among others
8	Vernacular names	Chilean *Papaya*, highland *Papaya*, mountain *Papaya*, mountain pawpaw, pawpaw (general); carikaya, karika, pepaya gunung (in Indonesia); and ababai, bonete, chamburo, chichuacacón, papayuela, siglalón, tapaculo, titi-ish (in South America), among others

short peduncles. The fruits are characterized by their pentagonal or five-sided shape. When ripe, the fruit turns from green to a brilliant yellow or yellow-orange, typically measuring 6–15 cm in length and weighing an average of 200 g. The pulp is juicy and yellow, emitting an intense, acidic aroma. The central cavity contains approximately 150 reddish-brown, glossy seeds. These seeds are known for their spicy or pungent flavour. Seeds from female and monoecious plants differ in macro and micro-morphological characters (6, 9, 10).

Mountain *Papaya* Traditional Uses

Traditionally, mountain *Papaya* has been utilized for its diverse therapeutic properties, particularly in its native Andean regions. It is also used for medicinal purposes in the areas where it was introduced, such as Indonesia. The plant is recognized in folk medicine for treating various digestive ailments, including diarrhea, dyspepsia, and hemorrhoids. The leaves and seeds are used to treat diarrheal diseases due to their antibacterial properties, as well as to reduce intestinal secretion and peristaltic movement. It is also used to alleviate symptoms of indigestion and general stomach discomfort. Latex is used to facilitate protein breakdown and support overall digestion (11). However, the use of raw mountain *Papaya* latex, which contains highly concentrated proteolytic enzymes, poses significant risks of tissue damage and immune system activation. These enzymes may disrupt epithelial barriers by degrading tight junction proteins that normally regulate the passage of molecules through tissue layers. By compromising physical barriers, these enzymes facilitate the entry of allergens into the body, which can lead to sensitization or trigger severe allergic responses (12). Consequently, raw latex consumption is strongly discouraged without proper processing, purification, and standardisation of dosage to mitigate these safety hazards.

Mountain *Papaya* is also frequently used as a topical agent for skin-related conditions. The fruit and latex are applied as topical dressings for diabetic foot ulcers and

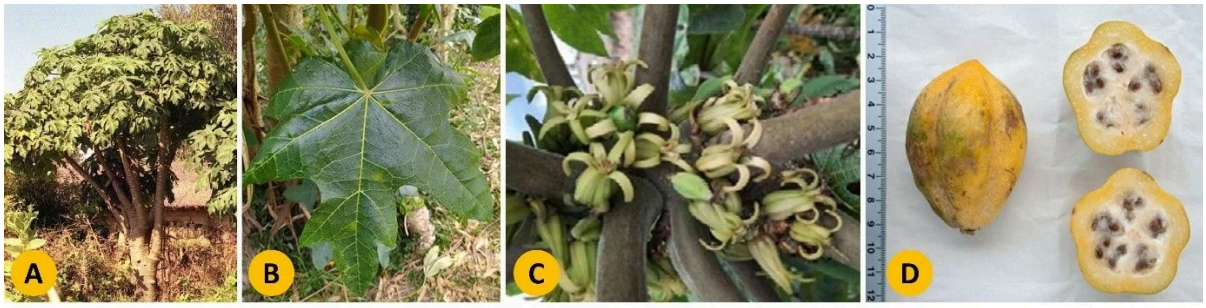


Figure 1. Morphological characters of mountain *Papaya* showing arborescent habit (A), leaf (B), flower (C), and fruits (D) (6).

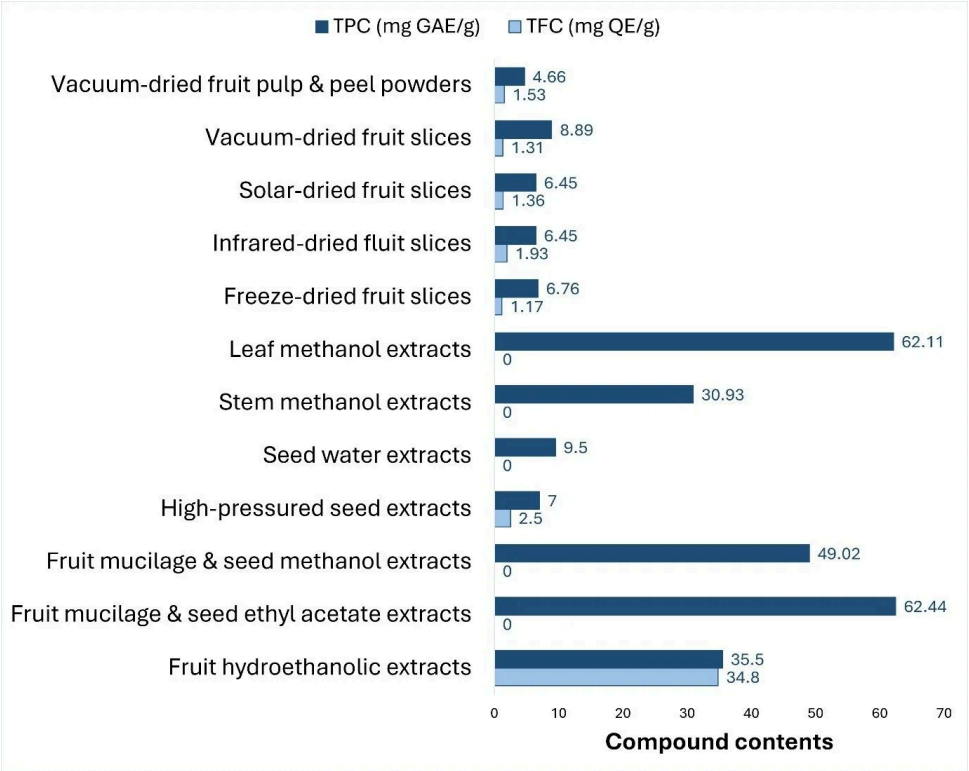


Figure 2. Profile of TFC and TPC of mountain *Papaya*-derived products of different origins (2, 15, 16).

Table 2. Distribution of mountain *Papaya* metabolites in the plant.

Compound class/name	Plant part					
	Leaves	Stems	Fruit - pulps	Fruit - rinds	Seeds	Latex
Phenolic acids						
Gallic acid	✓	✓	✓	✓	✓	-
Chlorogenic acid	✓	✓	✓	✓	-	-
Caffeic acid	✓	✓	✓	-	-	-
Ferulic acid/trans ferulic acid	✓	✓	✓	✓	-	-
p-Coumaric acid	✓	✓	✓	✓	-	-
Protocatechuic acid	✓	✓	-	-	-	-
Flavonoids & glycosides						
Quercetin	✓	✓	✓	✓	✓	-
Rutin	✓	✓	✓	✓	✓	-
Kaempferol	✓	✓	✓	✓	-	-
Naringin	✓	✓	✓	✓	-	-
Manghaslin	-	-	✓	-	-	-
Myricetin	✓	✓	-	-	✓	-
Catechin/epicatechin	-	-	✓	-	✓	-
Procyanidin/prodelphinidin	✓	✓	-	-	✓	-
Isoquercitrin	✓	✓	-	-	-	-
Vitexin/isovitexin	✓	✓	-	-	-	-
Luteolin 7-glucoside	✓	✓	-	-	-	-
Alkaloids						
Carpaine	✓	✓	✓	-	✓	-
Pseudocarpaine	✓	✓	-	-	-	-
Dehydrocarpaine I & II	✓	✓	-	-	-	-
Tetrahydroharman-3-carboxylic acid	-	-	-	-	✓	-
Proteolytic enzymes						
Papain	✓	-	✓	-	-	✓
Chymopapain	-	-	-	-	-	✓
Glycyl endopeptidase	-	-	-	-	-	✓
Terpenes & carotenoids						
beta-Carotene	✓	✓	✓	✓	-	-
Lycopene/beta-cryptoxanthin	✓	✓	✓	-	-	-
Linalool	✓	✓	✓	-	-	-
Ocimene/myrcene/caryophyllene	✓	✓	✓	-	-	-
Lupeol/beta-amyrin/betulinic acid	✓	✓	-	-	-	-
Squalene	-	-	✓	-	-	-
Lipids (fatty acids)						
Oleic acid	-	-	✓	-	✓	-
Palmitic acid	-	-	✓	-	✓	-
Linoleic acid	-	-	✓	-	✓	-
Vitamins & other						
Vitamin C	✓	-	✓	-	-	-
Vitamin B (niacin, folic acid, etc)	✓	-	-	-	-	-
Benzyl glucosinolate	✓	✓	-	✓	-	-
Citric acid	✓	✓	-	✓	-	-
Arbutin	-	-	-	-	✓	-

general skin injuries to accelerate tissue repair and prevent infection. It is used as a folkloric remedy for fungal infections, flat warts, various inflammatory skin conditions, and to stop bleeding from minor wounds. Additionally, in regions where thrombolytic medications are inaccessible, mountain *Papaya* leaves have been used to treat cardiovascular disorders and to prevent blood clot formation (11). In Indonesia's Dieng Plateau, the fruit is widely consumed for its perceived ability to support immunity and overall health (4). The seed is a natural dewormer traditionally used to eradicate gastrointestinal nematodes. This application is highly valued in animal husbandry for controlling infections in livestock (13).

Mountain *Papaya* Chemical Constituents

Phenolic compounds and flavonoids are the most extensively studied compounds in the plant. The fruit and its residues are rich in phenolic acids, particularly caffeic, chlorogenic, ferulic, gallic, and p-coumaric acids. Other phenolic compounds detected in the plants include 4-methoxy-2-nitrophenol, 4-p-coumaroylquinic acid, arbutin, cynarin, ellagic acid, ferulic acid hexosides,

isoferulic acid hexosides, neochlorogenic acid, protocatechuic acid, pyrogallol, sinapic acid-hexosides, trans-ferulic acid, and tyrosol (1, 2, 14). Quercetin and kaempferol derivatives are the major flavonoid constituents. The free and glycosidic flavonoids identified in the mountain *Papaya* are 3''-O-L-rhamnopyranosylastragalin, 5-deoxykaempferol, 6''-O-p-coumaroyltrifolin, apigenin, catechin, epicatechin, epigallocatechin, eupatorine, gallocatechin, isoquercitrin, isorhamnetin-3-O-robinobioside, isorhamnetin-3-O-rutinoside, isovitexin, kaempferol 3-O-D-glucoside, kaempferol 3-rhamnoside, kaempferol 7-O-β-glucoside, kaempferol-3-O-glucoside-3''-rhamnoside, luteolin 7-glucoside, luteolinidin 5-glucoside, manghaslin, myricetin, naringin, nicotiflorin, proanthocyanidin, procyanidin B1, procyanidin B2, prodelphinidin B, quercetin, quercetin 3-(2-glucosylrhamnoside), quercetin 3-O-(2'-caffeoyl)-rutinoside, quercetin 3-O-(2'-coumaroyl)-rutinoside-7-O-hexoside, quercetin 3-O-(2'-hexo)-hexosyl-7-O-hexoside, quercetin 3-O-(2'-rhamno)-rutinoside-7-O-hexoside, quercetin 3-O-(di)-rhamnosyl-hexoside, quercetin 3-O-rutinoside-7-O-hexoside, quercetin-3-O-(2'-coumaroyl)-rutinoside, quercetin-3-O-sophoroside, quercituron, rutin, tiliroside, vicenin II, and vitexin (1, 2, 14). The quantitative phenolic compound and flavonoid profile of the plant products is summarized in **Figure 2**.

Condensed tannins are commonly found in the seeds, while other organs also contain both condensed and hydrolyzed tannins. Untargeted metabolic profiling using liquid chromatography-mass spectrometry (LC-MS) analysis has tentatively identified catechin, epicatechin, epigallocatechin, gallocatechin, procyanidin B1, procyanidin B2, and prodelphinidin B (14). Alkaloids are commonly detected in leaf, seed, and fruit residues. Carpaine is identified as the principal alkaloid in the leaves and seeds. Pseudocarpaine and dehydrocarpaine I and II are tentatively identified in the leaves. Tetrahydroharman-3-carboxylic acid, an aromatic β-carboline alkaloid, was detected in fruit residues (14). Qualitative tests have confirmed the presence of saponins in the fruit pulp, seeds, leaves, and stems. The triterpenes such as betulinic acid, lupeol, squalene, and β-amyrin are identified in the plant's leaves. The bright yellow colour of the fruit is due to tetraterpenes such as β-carotene, lycopene, and β-cryptoxanthin (1, 2, 13, 16, 17).

Mountain *Papaya* contains a high content of proteolytic enzymes. The plant's latex contains approximately 40% enzymes, 80% of which are cysteine endopeptidases, such as papain, chymopapain, glycyl endopeptidase, and caricain (6). The fruit is a dense source of essential nutrients that complement its secondary metabolite profile. The fruit is high in vitamins C, A, B1, B2, and E, as well as minerals such as calcium, iron, potassium, and magnesium. The seeds are rich in monounsaturated fatty acids, particularly oleic acid (16).

The qualitative and quantitative profiles of these compounds in mountain *Papaya* vary with plant organ, plant sex, geographical origin, and the processing applied to the samples. The leaves contain the highest diversity of active compounds. By contrast, seeds contained high levels of lipids and tannins, as well as a minor amount of benzyl isothiocyanate. The distribution of major metabolites in the organs is presented in **Table 2**.

The sex of the plant, whether female, male, or monoecious, affects the phytochemical diversity of the leaves. Monoecious plants show the widest range among the others (18). Different cultivars of mountain *Papaya* exhibit variations in biochemical properties. This might be due to differences in soil composition and altitude, as reported from the Dieng Plateau in Indonesia or the Coquimbo valleys in Chile (19). Processing fruits using methods such as vacuum and infrared drying can yield dried products with distinct phytochemical profiles. The difference is likely due to the release of phenolic compounds from the fruit matrix during heat treatment, while degrading heat-sensitive vitamins like vitamin C (16, 20).

There are 62 compounds identified in the leaves and stalks, which can be grouped by the extraction solvent. Forty compounds are detected in methanol, chloroform, and ethyl acetate extracts. These include major flavonoids such as quercetin and kaempferol, the principal alkaloids

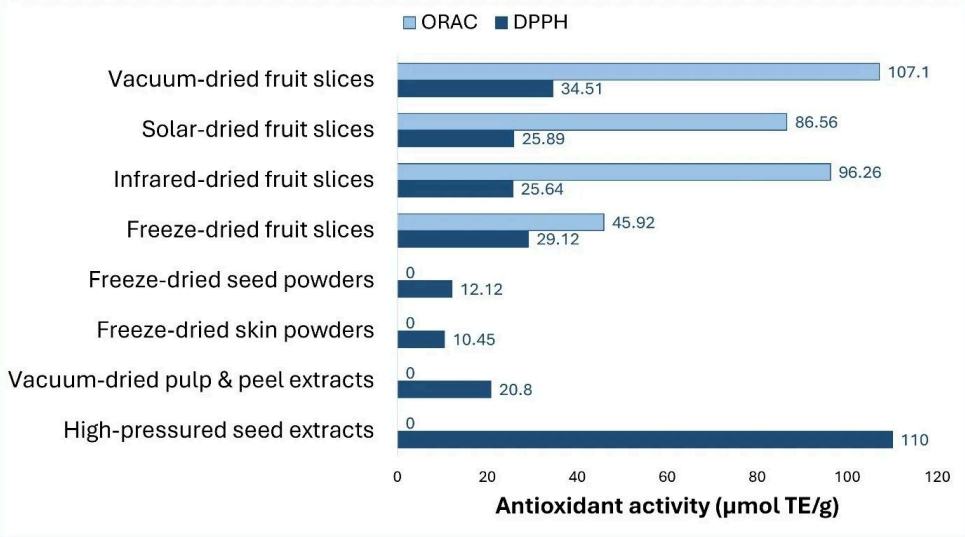


Figure 3. Comparison of the antioxidant activity of products derived from mountain *Papaya* of different origins (16, 20).

carpaine and pseudocarpaine, and other markers such as β-carotene, chlorogenic acid, ferulic acid, and benzyl glucosinolate. B-complex vitamins (such as niacin, pantothenic acid, thiamin, riboflavin, and folic acid), sugars (glucose and galactose), and tannins (procyanidin and prodelphinidin B) were identified only in the methanolic extract. On the other hand, linalool oxide was identified solely in the chloroform extract. Terpenes and carotenoids were detected in ethyl acetate and chloroform extracts but were absent in methanol extracts. These include ocimene, myrcene, caryophyllene, cryptoxanthin, and antheraxanthin. Hence, methanol is considered the best solvent for extracting phenolic compounds and their glycosidic derivatives.

Mountain *Papaya* Biological Activity

Mountain *Papaya* is a potent source of exogenous antioxidants. The plant's antioxidant capacity is primarily attributed to its high concentrations of flavonoids and phenolic compounds (**Figure 3**). The *in vitro* antioxidant evaluations were performed by using the 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS), 2,2-diphenyl-1-picryl-hydrazyl (DPPH) scavenging activity, ferric reducing antioxidant power (FRAP), nitric oxide scavenging (NOS), oxygen radical absorbance capacity (ORAC), and total antioxidant capacity (TAC) (1, 16). In addition, flavonoids activate the nuclear factor erythroid 2-related factor 2 pathway, which increases the expression of endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. Ethanolic extracts of fruits have demonstrated significant protection against lipid peroxidation in rat liver tissues by reducing malondialdehyde levels in both *in vitro* and *in vivo* models (17). Key antioxidant components of mountain *Papaya* are phenolics and flavonoids, which are abundant in both the fruit and the leaves. The typical phenolic compounds include rutin, mangiferin, and hydroxycinnamic acids. Vitamins C, A, B, and E, which are stored in the pulp, also contributed to the activity. The antioxidant activity of the fruits is also attributable to carotenoids, such as β-carotene, lycopene, and β-cryptoxanthin (16).

Mountain *Papaya* shows potential for the management of metabolic syndrome and type 2 diabetes. Fruit extracts suppress alpha-glucosidase activity in a dose-dependent manner, with their effect significantly influenced by industrial conditions. For example, infrared-dried fruits showed increased alpha-glucosidase inhibition, up to 24-fold, compared to fresh fruit. This is attributed to improved retention of phenolic acids, such as chlorogenic, p-coumaric, and trans-ferulic acids, after processing (16). Fruit extracts of Saudi origin exhibited alpha-amylase inhibitory activity as evaluated using the 3, 5-dinitrosalicylic acid (DNSA) *in vitro* model. Betulinaldehyde and 9, 19-cyclolanost-24-en-3-ol were predicted to exhibit the strongest inhibitory activity, and their binding affinities are comparable to those of acarbose, which was evaluated using molecular docking with PyRx and AutoDock Vina (2). These sugar-metabolism enzyme-inhibitory activities support the use of fruit extracts to slow carbohydrate digestion and reduce blood-sugar spikes. The *in vivo* studies showed that the fruit juices increased superoxide dismutase and high-density lipoprotein levels and significantly decreased triglyceride levels in high-fat diet-streptozotocin-induced diabetic Wistar rats (21). In addition, the antihyperglycemic effect of the combination of mountain *Papaya* and *Momordica charantia* L. fruit extract on alloxan-induced diabetic rats was comparable to that of each used individually (22). Chronic hyperglycemia leads to the formation of advanced glycation end products, which are linked to serious diabetic complications and metabolic syndrome. Seeds and mucilage from fruits decrease the formation of advanced glycation end products and oxidative modifications in proteins. Antiglycation activity is strongly correlated with phenolic and catechin content, with the ethyl acetate extract being more potent than the methanol extract (14). Diabetic conditions often cause excessive lipid peroxidation and pancreatic β-cell death. The high antioxidant capacity of mountain *Papaya* fruits neutralizes reactive oxygen species, providing a mechanistic defense against oxidative stress that drives diabetic progression.

Mountain *Papaya* exhibits broad-spectrum activity against various pathogens. Extracts from the fruit, rind, and seeds are effective against bacteria such as *Escherichia coli, Staphylococcus aureus, Bacillus cereus,* and *Salmonella* sp. The P1G10 proteolytic fraction from the plant's latex has been shown to inhibit the growth and cell wall integrity of the plant pathogen *Botrytis cinerea* (16, 23, 24). Ethyl acetate fractions exhibit greater antibacterial potency than n-hexane or water fractions, suggesting that semipolar flavonoids and phenolic compounds are likely responsible for the antimicrobial activity. The effectiveness of the fractions also depended on the specific bacterial strain. *Shigella flexneri* was sensitive to both ethyl acetate and n-hexane fractions, but *E. coli* was only sensitive to the ethyl acetate fraction. In addition, none of the fractions from either the rind or the seeds showed any inhibitory activity against *Bacillus cereus* (24). Compared to other organs, seeds appear to possess the strongest antimicrobial properties, particularly against *Staphylococcus aureus* (16).

The high concentration of papain in the latex supports tissue repair. P1G10 accelerated the resolution of skin lesions by modulating inflammatory mediators. The fraction's proteolytic activity accelerated excisional wound closure in rodent models by upregulating VEGF and modulating inflammatory markers, thereby mitigating early inflammation and promoting rapid tissue regeneration (25). In addition, topical application of P1G10 stimulated tissue repair following acute exposure to Ultraviolet B radiation in mice and reduced UVB-induced erythema and hyperplasia. The fraction also inhibited the degradation of collagen fibres, resulting in increased collagen abundance and improved fibre alignment compared with untreated irradiated skin. These effects simultaneously reversed the depletion of endogenous antioxidants like glutathione, glutathione peroxidase, and superoxide dismutase, while reducing lipid peroxidation (26). Mountain *Papaya* proteases also act as protective agents against gastric ulcers and exhibit anti-inflammatory effects in models of acute colitis. The anti-colitis effects of mountain *Papaya* were evaluated using a murine model of acute colitis induced by the 2,4,6-trinitrobenzenesulfonic acid (TNBS). It effectively prevented the treated animals'body weight loss, typically associated with colitis, and reduced colon macroscopic damage scores and

increased goblet cell density. This leads to the restoration of the mucus layer, a vital primary barrier for protecting the colonic tissue (27). P1G10 displays healing activity against gastric ulcers induced by indomethacin or acetic acid, which were mediated by increasing mucus content and secreting prostaglandin E2. However, the proteolytic activity of the fraction was not essential for its gastroprotective action (28). Additionally, fruit extracts have been shown to increase gingival fibroblast numbers, thereby aiding the healing of oral mucosal wounds (29).

Fruit and seed extracts of mountain *Papaya* reduced fever in animal models (30). In addition, the plant's notable thrombolytic effect suggests potential for cardiovascular health applications (2). Mountain *Papaya* seed extracts reduce egg counts of gastrointestinal nematodes, such as *Haemonchus contortus*, in sheep. This is attributed to compounds like benzyl isothiocyanate and tannins, which damage the parasite's cuticle (13). Seed extracts also act as repellents and larvicides against *Aedes aegypti*, the mosquito vector for dengue fever (31).

Relationship Between Traditional Uses, Phytochemical Profile, and Evaluated Bioactivities

A unique feature of mountain *Papaya* is its high papain content, which is up to 5 times higher than that of *Carica papaya* L. This is central to its traditional use as a digestive aid and to its modern use in wound debridement (6). In the traditional management of diabetes and other degenerative diseases, the antioxidant mechanism plays a significant role (32). The mechanism is driven by phenolic compounds, which underpin the management of diabetic complications and pancreatic protection in diabetic models (2, 14, 16, 22). Nevertheless, the plant's effectiveness often stems from the synergistic action of its bioactive compounds, such as flavonoids and tannins, rather than from any single molecule. The detailed matrix correlating the plant's traditional uses, phytochemistry, and pharmacological activity is proposed in **Figure 4**.

Limitations

This narrative review is subject to several limitations. Ethnobotanical data is limited by the decline of traditional knowledge among younger generations in native and introduced regions, which may lead to an incomplete picture of historical medicinal uses. Much of the pharmacological activity is attributed to crude extracts rather than to isolated bioactive compounds. This limits the selection of specific compounds for development into modern medicine or as marker compounds for standardization. The detection capacity of the LC-MS and GC-MS techniques used to analyze metabolites in the cited literature was limited. Hence, the full spectrum of the metabolites cannot be displayed. The vast majority of pharmacological evidence in the cited literature is derived from *in vitro* assays or animal models, with no evidence from human clinical trials. This limits the therapeutic claims of the mountain *Papaya*-derived products. Also, the available literature is largely concentrated on specific cultivars from Chile, Indonesia, and Saudi Arabia. Different soil compositions, environmental conditions, and altitudes strongly influence biochemical properties and metabolite profiles. Hence, findings from one region may not generalize to other regions.

Conclusion and Future Perspective

Mountain *Papaya* represents an underutilized but highly valuable highland fruit with a distinctive botanical and therapeutic profile. It is a rich reservoir of bioactive secondary metabolites, most notably phenolic acids (such as gallic and chlorogenic acids), flavonoids (such as rutin and quercetin), alkaloids (such as carpaine and pseudocarpaine), and the proteolytic enzyme papain. The documented traditional medicinal uses of the plant are widely varied. The plant is used to treat gastrointestinal disorders and diarrhea, as well as diabetes, wound healing, and parasitic infections. The proven biological activities include antioxidant capacity, antimicrobial activity against

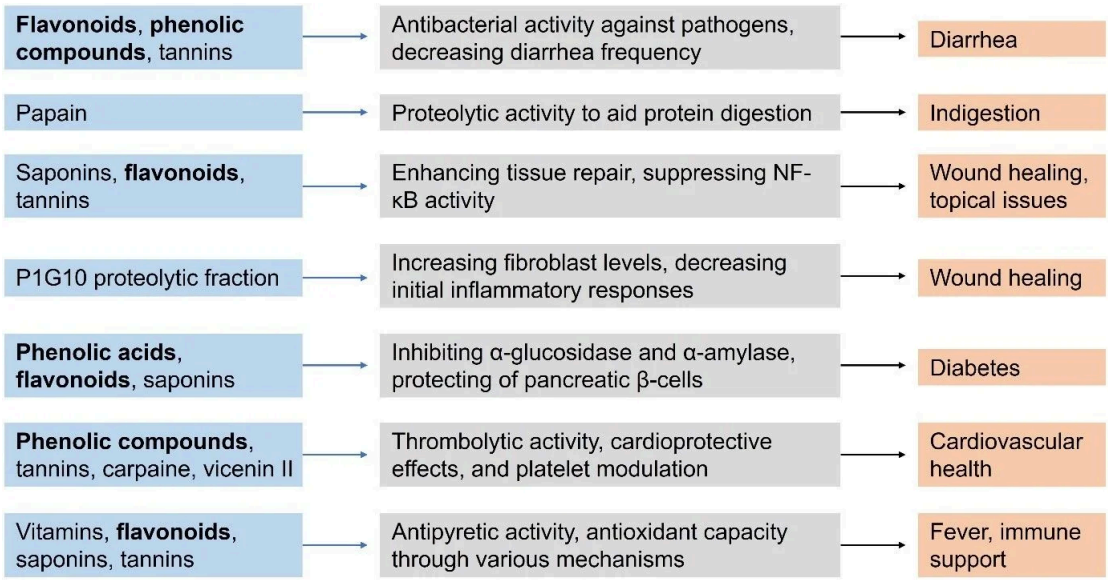


Figure 4. Relationship between bioactive compounds, the corresponding pharmacological activities, and the relevant traditional uses.

various human and plant pathogens, and inhibition of alpha-glucosidase and alpha-amylase. Furthermore, its use as a natural anthelmintic in livestock and its thrombolytic properties suggest broad applications in both veterinary and human cardiovascular health. Collectively, these findings underscore mountain *Papaya* as a promising candidate for the development of high-value phytopharmaceuticals, nutraceuticals, and functional food products. Moving forward, prioritising comprehensive chemical fingerprinting and quality control protocols for the local Dieng cultivar will be essential to bridge the gap between its traditional heritage and the production of globally reproducible, commercially viable products.

Future research for mountain *Papaya* should shift from preliminary *in vitro* characterization to advanced clinical and industrial applications. While *in vitro* results for antidiabetic and antioxidant activities are promising, rigorous *in vivo* and clinical trials are necessary to validate their therapeutic potential for diabetes and other metabolic disorders. In addition, the acute and chronic toxicological investigations are required to establish safety profiles for human use. Further standardization should be applied to the selected mountain *Papaya*-derived preparations or nutraceuticals. Qualitative and quantitative identification of specific compounds, such as gallic acid, chlorogenic acid, rutin, or quercetin, whether as bioactive or marker compounds for standardization, should be prioritized beyond crude extract evaluation. Further, sustainable extraction methods using "green solvents" should be developed to minimize environmental impact and toxicity. Also, comparative studies across different altitudes, climates, and soil types are needed to understand how environmental factors influence the qualitative and quantitative profile of bioactive compounds.

Abbreviations

ABTS = 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); DNSA = 3,5-dinitrosalicylic acid; DPPH = 2,2-diphenyl-1-picryl-hydrazyl; FRAP = ferric reducing antioxidant power; GC-MS = Gas Chromatography-Mass Spectrometry; LC-MS = Liquid Chromatography-Mass Spectrometry; NOS = nitric oxide scavenging; ORAC = oxygen radical absorbance capacity; TAC = total antioxidant capacity; TNBS = 2,4, 6-trinitrobenzenesulfonic acid

Declaration

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

Not applicable.

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References

1. Ery Rahayu S, Sulisetijono, Lestari U. Phytochemical Screening, Antioxidant Activity, and Total Phenol Profile of *Carica pubescens* Leaves from Cangar, Batu-East Java, Indonesia. IOP Conf. Ser.: Earth Environ. Sci. 2019;276(1):012022. doi: https://doi.org/10.1088/1755-1315/276/1/012022

2. Khan KUR, Aati HY, Khan MA, Ovatlarnporn C, Arshad MA, Rauf A, *et al*. Unveiling the biochemical properties of Saudi mountain papaya (*Vasconcellea pubescens*): A wild nutritious food source with therapeutic relevance. Journal of Agriculture and Food Research. 2025;24:102451. doi: https://doi.org/10.1016/j.jafr.2025.102451

3. Laily A, Purnomo P, Daryono B, Purwantoro A. Local Knowledge: Sex Determination on *V. pubescens* A.DC in Java, Indonesia. Proceedings of the 1st International Conference on Education, Humanities, Health and Agriculture, ICEHHA 2021, 3-4 June 2021, Ruteng, Flores, Indonesia. 2021. doi: https://doi.org/10.4108/eai.3-6-2021.2310676

4. Adelisa SN, Indah NK, Ningrum LW. Appreciation of the Ethnobotany of *Carica* (*V. pubescens* A.DC.) by the Dieng Plateau Local Community. J. Ris. Biol. dan Apl. 2024;6(2):109-115. doi:

https://doi.org/10.26740/jrba.v6n2.p109-115

5. Méndez T, Jara-Villacura V, Parra-Palma C, Morales-Quintana L. Postharvest Biology and Quality Preservation of *V. pubescens*: Challenges and Opportunities for Reducing Fruit Losses. Horticulturae. 2025;11(10):1165. doi: https://doi.org/10.3390/horticulturae11101165

6. Lemus-Mondaca R, Puente-Díaz L, Cifuentes A, Lizama K, González P. Chilean Papaya (*V. pubescens*): A Native Fruit with a High Health-Promoting Functional Potential. Antioxidants. 2024;13(12):1521. doi: https://doi.org/10.3390/antiox13121521

7. Rahma NA, Diniatik D, Astuti IY. Narrative Review: Kandungan Senyawa Sekunder dan Aktivitas Antibakteri Spesies Pepaya (*Carica papaya*) dan *Carica* (*V. pubescens*). J. Pharm. Sci. Clin. Res. 2025;10(2):144. doi: https://doi.org/10.20961/jpscr.v10i2.87821

8. WFO. *V. pubescens* A.DC. [Internet]. World Flora Online. 2026. Available from: https://www.worldfloraonline.org/taxon/wfo-0000421667#synonyms

9. Scheldeman X, Kyndt T, D'Eeckenbrugge GC, Ming R, Drew R, Droogenbroeck B Van, *et al*. *Vasconcellea*. In: Wild Crop Relatives: Genomic and Breeding Resources. Berlin: Springer; 2011. p. 213–249.

10. Laily AN, Daryono BS, Purwantoro A, Purnomo P. Various macro and micro-morphological characters of three sex types of highland papaya (*V. pubescens*) in Java, Indonesia. Biodiversitas. 2023;23(12):6238-6246. doi: https://doi.org/10.13057/biodiv/d231219

11. Paniagua-Zambrana NY, Bussmann RW, Romero C. *C. papaya* L. *V. pubescens* A. DC. Caricaceae. Cham: Springer International Publishing; 2020. doi: https://doi.org/10.1007/978-3-319-77093-2_57-1

12. Giangrieco I, Ciardiello MA, Tamburrini M, Tuppo L, Rafaiani C, Mari A, *et al*. Comparative Analysis of the Immune Response and the Clinical Allergic Reaction to Papain-like Cysteine Proteases from Fig, Kiwifruit, Papaya, Pineapple and Mites in an Italian Population. Foods. 2023;12(15):2852. doi: https://doi.org/10.3390/foods12152852

13. Baihaqi ZA, Widiyono I, Angeles AA, Suwignyo B, Nurcahyo W. Anthelmintic activity of *C. pubescens* aqueous seed extract and its effects on rumen fermentation and methane reduction in Indonesian thin-tailed sheep: An *in vitro* study. Vet World. 2023:16(7):1421-1428. doi: https://doi.org/10.14202/vetworld.2023.1421-1428

14. Pino-Ramos LL, Farias DR, Olivares-Caro L, Mitsi C, Mardones C, Echeverria J, *et al*. Chilean papaya (*V. pubescens* A. DC.) residues as a source of bioactive compounds: Chemical composition, antioxidant capacity, and antiglycation effects. Heliyon. 2024;10(19):e38837. doi: https://doi.org/10.1016/j.heliyon.2024.e38837

15. Fuentes Y, Giovagnoli-Vicuña C, Faúndez M, Giordano A. Microencapsulation of Chilean Papaya Waste Extract and Its Impact on Physicochemical and Bioactive Properties. Antioxidants. 2023;12(10):1900. doi: https://doi.org/10.3390/antiox12101900

16. Vega-Gálvez A, Poblete J, Quispe-Fuentes I, Uribe E, Bilbao-Sainz C, Pastén A. Chemical and bioactive characterization of papaya (*V. pubescens*) under different drying technologies: evaluation of antioxidant and antidiabetic potential. Food Measure. 2019;13(3):1980-1990. doi: https://doi.org/10.1007/s11694-019-00117-4

17. Sasongko H, Efendi NR, Sugiyarto. The ethanolic extract of mountain papaya (*V. pubescens* A.DC.) fruit against lipid peroxidation of rat liver tissues. AIP Conference Proceedings. 2018;2019:050001. doi: https://doi.org/10.1063/1.5061894

18. Laily A. Sex effect on the telomer length, elemental composition, and phytochemical content of highland papaya (*V. pubescens* a.dc.) leaves. Sabraojbg. 2023;55(4):1170-1182. doi: https://doi.org/10.54910/sabrao2023.55.4.13

19. Rifqi MS, Chasani AR. Genetic Diversity and Phylogenetic Relationships of Mountain Papaya (*V. pubescens*) in Dieng Plateau Based on Internal Transcribed Spacer Sequence. Agrivita J Agr Sci. 2023;45(3):600. doi: https://doi.org/10.17503/agrivita.v45i3.4216

20. Vega-Gálvez A, Poblete J, Rojas-Carmona R, Uribe E, Pastén A, Goñi MG. Vacuum drying of Chilean papaya (*V. pubescens*) fruit pulp: effect of drying temperature on kinetics and quality parameters. J Food Sci Technol. 2021;58:3482–3492. doi: https://doi.org/10.1007/s13197-021-05005-8

21. Rachmawati S, Kusuma T, Anjani G, Muniroh M. *C. pubescens* fruit juice improved superoxide dismutase, triglyceride and high-density lipoprotein levels in type 2 diabetes mellitus Wistar rats. Food Res. 2024;8(3):300-307. doi: https://doi.org/10.26656/fr.2017.8(3).255

22. Sasongko H, Lestari RG, Yugatama A, Farida Y, Sugiyarto2 S S. Antidiabetic and Antioxidant Effect Combination *V. pubescens* A.DC. and *Momordica charantia* L. Extract in Alloxan- Induced Diabetic Rats. Pj. 2020;12(2):311-315. doi: https://doi.org/10.5530/pj.2020.12.49

23. Torres-Ossandón MJ, Vega-Gálvez A, Salas CE, Rubio J, Silva-Moreno E, Castillo L. Antifungal activity of proteolytic fraction (P1G10) from (*Vasconcellea cundinamarcensis*) latex inhibit cell growth and cell wall integrity in *Botrytis cinerea*. International Journal of Food Microbiology. 2019;289:7-16. doi: https://doi.org/10.1016/j.ijfoodmicro.2018.08.027

24. Sugiyarto, Novalina D, Susilowati A, Sasongko H. Antibacterial activity of ethyl acetate and n-hexane fractions of *C. pubescens* rind and seeds. AIP Conference Proceedings. 2018;2019:050005. doi:

https://doi.org/10.1063/1.5061898

25. Freitas K, Barcelos L, Caliari M, Salas C, Lopes M. Healing activity of proteolytic fraction (P1G10) from *V. cundinamarcensis* in a cutaneous wound excision model. Biomedicine & Pharmacotherapy. 2017;96:269-278. doi: https://doi.org/10.1016/j.biopha.2017.09.109

26. Freitas KM, Veloso ES, Ferreira Ê, Caliari MV, Salas CE, Lopes MT. Effects of P1G10 against UVB-induced damage: Reduction of antioxidant stress, inflammation and cell proliferation. Journal of Photochemistry and Photobiology. 2025;25:100255. doi: https://doi.org/10.1016/j.jpap.2024.100255

27. Albuquerque RM, Pizzitola MP, Araújo e Silva AC, Dittz D, Freitas KM, Ferreira Ê, *et al*. The Proteolytic Fraction From *V. cundinamarcensis* Latex Displays Anti-Inflammatory Effect in A Mouse Model of Acute TNBS-Induced Colitis. Sci Rep. 2020;10(1):3074. doi: https://doi.org/10.1038/s41598-020-59895-3

28. Araujo e Silva AC, de Oliveira Lemos F, Gomes MTR, Salas CE, Lopes MTP. Role of gastric acid inhibition, prostaglandins and endogenous-free thiol groups on the gastroprotective effect of a proteolytic fraction from *V. cundinamarcensis* latex. Journal of Pharmacy and Pharmacology. 2015;67(1):133-141. doi: https://doi.org/10.1111/jphp.12318

29. Kristanti RA. The Effect of *C. pubescens* Lenne and K. Koch Fruit Extract from Dieng Plateau and Cangar to the Amount of Fibroblasts Cells on the Healing of Oral Mucosal Inflammation. J. Islamic Pharm. 2016;1(1):20. doi: https://doi.org/10.18860/jip.v1i1.3457

30. Sasongko H, Widiasih P, Putri NL. Antipyretic properties of *Carica* (*V. pubescens* A.DC.) fruit and seeds ethanolic extract in experimental animals. IOP Conf. Ser.: Mater. Sci. Eng. 2019;578(1):012044. doi: https://doi.org/10.1088/1757-899x/578/1/012044

31. Anggraeni T, Laela N. The potency of *Carica* (*C. pubescens* Lenne & K. Koch) seed extract as repellent agent against mosquito vector of dengue (*Aedes aegypti* Linn.). IOP Conf. Ser.: Earth Environ. Sci. 2020;468(1):012011. doi: https://doi.org/10.1088/1755-1315/468/1/012011

32. Gerber PA, Rutter GA. The Role of Oxidative Stress and Hypoxia in Pancreatic Beta-Cell Dysfunction in Diabetes Mellitus. Antioxidants & Redox Signaling. 2017;26(10):501-518. doi: https://doi.org/10.1089/ars.2016.6755

Additional Information

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