

A Comprehensive Review on Phytochemistry and Pharmacological Activities of *Carica papaya* L.

Author Name

Shravani Vilas Matkar¹, Pandurang Arjun Gambhire², Rutuja Jadhav^{3*}

Affiliation

^{1,2}UG Research group, KCT's Krishna College of Pharmacy, Karad-415110, Maharashtra, India.

³Department of Pharmacology, KCT's Krishna College of Pharmacy, Karad-415110, Maharashtra, India.

Corresponding Author:

Ms. Rutuja Jadhav*

Assistant Professor,

Department of Pharmacology,

KCT's, Krishna College of Pharmacy,

Malkapur, Karad-415110, Maharashtra, India

ABSTRACT

Carica papaya L. has emerged as a pharmacologically versatile plant owing to its diverse phytoconstituents, including alkaloids, flavonoids, phenolics, and proteolytic enzymes. With a focus on antioxidant, anti-inflammatory, antibacterial, antihypertensive, antidiabetic, anticancer, and anti-dengue effects, this review summarises the most recent research on its diverse biological activities. Redox modification, suppression of inflammatory transmission pathways, and immune response regulation are the main fundamental mechanisms. Particular attention is given to the therapeutic potential of papaya leaf extract in dengue-associated thrombocytopenia, where it demonstrates platelet-enhancing and immunomodulatory effects. However, heterogeneity in experimental design, lack of phytochemical standardisation, and limited clinical validation remain critical challenges. Future research should prioritise mechanistic clarity and well-controlled clinical studies to facilitate its translation into evidence-based therapeutics.

KEYWORDS

Carica papaya Linn, Phytochemistry, Antimicrobial activity, plant bioactive compounds, Herbal medicine, dengue management.

Introduction

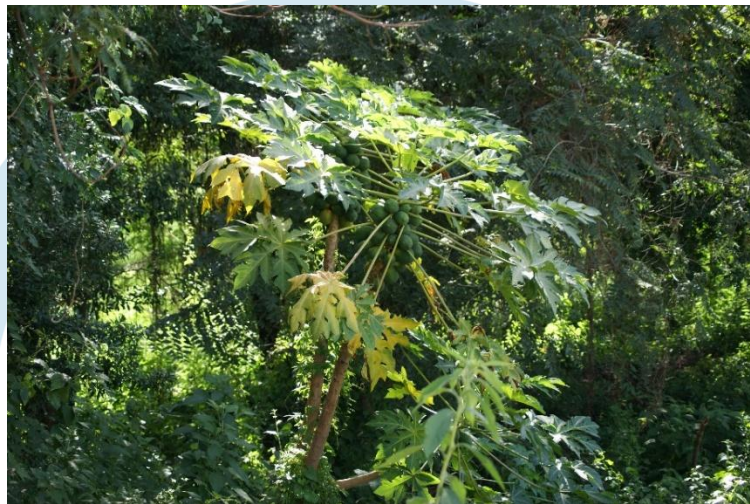
Carica papaya L., a member of the Caricaceae family, is a well-known tropical plant valued for its nutritional as well as medicinal importance [1]. It is extensively grown in India and other tropical and subtropical regions of the world. The plant is widely recognised for its quick development and capacity to adjust to various environmental circumstances. It was previously utilised for the treatment of several illnesses, which has recently drawn a lot of scientific attention.

Numerous phytochemical components, such as alkaloids, flavonoids, glycosides, phenolic compounds, enzymes, vitamins, and minerals, are abundant in the plant. Their various pharmacological actions are caused by these chemicals. Its therapeutic usefulness is further enhanced by the presence of proteolytic enzymes like papain and chymopapain, especially in digestive and anti-inflammatory applications.

In traditional medicine, the plant's various parts, including its leaves, fruits, seeds, latex, and roots—have traditionally been employed to treat diseases like skin problems, infections, inflammation, and digestive issues. Many of these conventional assertions have been validated by recent scientific research, which has shown a variety of biological activities, such as antioxidant, antibacterial, antihypertensive, antidiabetic, and anticancer benefits [3,8].

Besides that, *Carica papaya* has drawn interest for its possible use in handling dengue, especially because of its capacity to boost immunity and increase platelet count. Its bioactive components, which function through a variety of methods like lowering oxidative stress, regulating enzyme activity, and regulating inflammatory mediators, are primarily responsible for these medicinal properties.

In order to emphasise *Carica papaya*'s potential as a natural source for the synthesis of novel therapeutic medicines, the current review attempts to give a thorough overview of the phytochemical profile and pharmacological activity of the plant.



Carica papaya plant

Botanical Classification

Domain	Flowering plant
Kingdom	Plantae
Subkingdom	Tracheophyta
Class	Magnoliopsida
Subclass	Dilleniidae
Division	Magnoliophyta
Subdivision	Spermatophyta
Phylum	Streptophyta
Order	Brassicales
Family	Caricaceae
Genus	<i>Carica</i>
Botanical name	<i>Carica papaya</i> Linn.

Botanical classification ^[12]

Plant taxonomy involves the discovery, identification, description, classification, and naming of plants. Linnaeus named the genus *Carica* after the leaves of these plants, which are similar to those of *Ficus carica*, or the common fig. The popular name

comes from the Taino word called papáia, which changed slightly in Spanish to become papaya, the most commonly used word worldwide. The fruit is known as papaw or pawpaw in Australia and in many Caribbean nations.

Morphology Description

The papaya is a polygamous plant that can grow up to ten meters in height. The broad, oval-shaped leaves are connected to thin branches that grow in a spiral pattern, one over the other, but obtain a diameter of around 20 to 28 inches. It is challenging to differentiate between male, female, and female papaya plants. A white, milky latex is released when any part of the plant is removed.

The papaya *Carica* species flower has two distinct types with five-parted, white, light-pale petals that combine with the male and female flowers. The petals have a loose connection at the base of the female flower, which also has an ovary below.



Carica papaya flower and fruit

On the axillary section of the main stem, the plant produces a single or a cluster of green fruits that eventually turn yellowish-orange to red. The fleshy edible portion of the ripened fruit is yellowish-orange to pinkish in its appearance, while the inner hollow is loaded with seeds. Temperature and cultivation conditions determine the fruit's freshness. Plants usually start to produce fruit between six and twelve months, and the fruits reach maturity in five to nine months.

Papaya leaves- Papaya leaves, which range in colour from green to yellow, have several advantages, including the potential to treat dengue, malaria, and other viral diseases.

Papaya bark: The outer surface is smooth and green to light brown in young plants. Older plants develop thin, soft, corky layers, but do not form true, hard bark. Because the stem is herbaceous, the bark remains thin, flexible, and easily damaged by external factors. Contains latex canals that release white, milky latex when they are injured.



Carica papaya bark

Geographical source of *Carica papaya*

Carica papaya Linn. is a tropical plant native to Mesoamerica, particularly southern Mexico and Central America. It is widely distributed and cultivated in tropical and subtropical regions worldwide. Papaya is extensively grown in countries such as India, Brazil, Indonesia, Nigeria, Mexico, and the Philippines, with India being the largest producer.

The plant thrives in warm climates with adequate sunlight and well-drained soil. It is commonly cultivated in regions with temperatures ranging from 21-33°C. owing to its adaptability and economic importance, papaya is grown in parts of Africa, Southeast Asia, and South America [16].

Chemical constituents of *Carica papaya*

Carica papaya contains a wide variety of phytochemicals, enzymes, alkaloids, vitamins, and minerals in its leaves, fruits, seeds, latex, and roots. These constituents contribute to the therapeutic and nutritional properties of the plants.

Part	Constituents
Fruits	Protein, fat, fibre, carbohydrates, minerals: calcium, phosphorus, iron, vitamin C, thiamine, riboflavin, niacin, and carotene, amino acids, citric and malic acids (green fruits), volatile compounds: linalool, cis and trans 2, 6-dimethyl-3,6 epoxy-7 octen-2-ol, Alkaloid, α ; carpaine, benzyl- β -D-glucoside, 2-phenylethyl - β -D-glucoside, 4-hydroxy phenyl-2 ethyl- β -D-glucoside and four isomeric malonated benzyl- β -D-glucosides.
Juice	N-butyric, n-hexanoic, and n-octanoic acids; lipids; myristic, palmitic, stearic, linoleic, linolenic, cis-vaccenic, and oleic acids.
Seed	Papaya oil, fatty acids, crude protein, crude fibre, carpaine, benzylisothiocyanate, benzylglucosinolate, glucotropacolin, benzylthiourea, hentriacontane, β -sitosterol, caricin.
Root	Carposide and myrosin are present in the leaves.
Leaves	Alkaloids carpain, pseudocarpain, and dehydrocarpaine I and II, choline, carposide, and vitamins C and E.
Bark	β -Sitosterol, glucose, fructose, sucrose, galactose and xylitol.
Latex	Proteolytic enzymes, papain and chemopapain, glutamine cyclotransferase, chymopapains A, B, and C, peptidase A and B, and lysozymes.

Chemical composition of various parts of Papaya plants [16]

Medicinal uses of papaya plants

Part	Medicinal uses
Latex	Anthelmintic, relieves dyspepsia, cures diarrhoea, pain of burns and topical use, bleeding haemorrhoids, stomachic, whooping cough
Ripe fruits	It is stomachic, digestive, carminative, diuretics, dysentery and chronic diarrhoea, expectorant, sedative and tonic, relieves obesity, bleeding piles, wounds of the urinary tract, ringworm and skin diseases, such as psoriasis.
Unripe fruit	Laxatives, diuretics, and dried fruits reduce enlarged spleen and liver, are used in snakebites to remove poison, abortifacient, anti-implantation activity, and antibacterial activity.
Seeds	It is carminative, emmenagogue, vermifuge, abortifacient, counter irritant, and used as a paste in the treatment of ringworm and psoriasis. It is also an anti-fertility agent in males.
Seed juice	Bleeding piles, and enlarged liver and spleen.
Root	It is an abortifacient and diuretic, checks irregular bleeding from the uterus, piles, and has anti-fungal activity.
Leaves	Young leaves as a vegetable, jaundice (fine paste), urinary complaints & gonorrhoea (infusion), dressing wounds (fresh leaves), antibacterial activity, vermifuge, in colic, fever, beriberi, abortion (infusion), asthma (smoke).
Flowers	Jaundice, emmenagogue, febrifuge, and pectoral properties.
Stem bark	Jaundice, anti-haemolytic activity, STD, sore teeth (inner bark), anti-fungal activity

Medicinal uses of papaya plants ^[10]

Pharmacological activities of *Carica papaya*

Antihypertensive activity

According to studies, the extract of *Carica papaya* significantly lowers systolic and diastolic blood pressure (BP) in experimental models via relaxing vascular smooth muscles ^[1]. Bioactive alkaloids and phenolic chemicals found in papaya seeds reduce vasoconstriction and blood pressure by decreasing the activity of the angiotensin-converting enzyme (ACE) ^[2].

Furthermore, polyphenols, including flavonoids and vitamin C, prevent oxidative stress in blood vessels and improve endothelial function ^[3]. The mild diuretic effect of leaf extracts promotes sodium excretion, which aids in regulating blood pressure ^[4].

In addition, fermented papaya preparations have demonstrated improved vascular elasticity and reduced arterial stiffness in human studies, supporting their antihypertensive potential ^[5]. The saponins and flavonoids present in papaya leaves also contribute to lipid-lowering effects and improved circulation, further enhancing cardiovascular health.

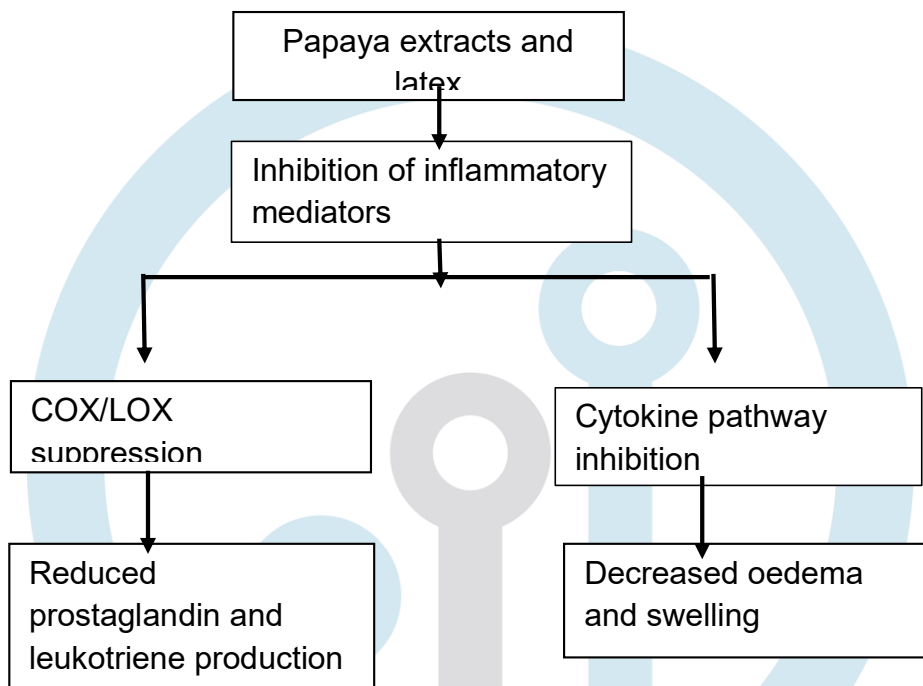
Anti-inflammatory activity

Carrageenan-mediated paw oedema models derived from experimental animals are currently commonly utilised to assess the anti-inflammatory properties of standardised *Carica papaya*. By releasing inflammatory mediators such as histamine, serotonin, and prostaglandins, a substance known as causes acute inflammation that increases vascular permeability and swelling. Because papaya leaf extracts block COX, which stands for other inflammatory pathways, they have been found to have a strong anti-inflammatory impact by significantly reducing paw oedema ^[8]. *Carica papaya* methanol extract from the leaves has been shown to have strong anti-inflammatory properties by dramatically reducing the synthesis of nitric oxide (NO) in RAW 264.7 macrophages stimulated by lipopolysaccharide, also known as LPS ^[9].

The suppression of the cyclooxygenase (COX-2) and lipoxygenase (LOX) enzymes, which reduces prostaglandin and leukotriene synthesis, is the main mechanism responsible for the anti-inflammatory effect ^[11]. Furthermore, research on animals indicates that papain-rich latex possesses anti-edematous and protease-mediated anti-inflammatory properties ^[12]. These bioactive substances work by engaging antioxidant mechanisms, blocking COX/LOX activity, and reducing cytokine pathways for signalling ^[9].

In addition, fruit and leaf extracts' potent antioxidant activity (DPPH and FRAP tests) contributes to anti-inflammatory benefits by reducing tissue harm caused by reactive oxygen species (ROS) ^[14]. Papaya leaves and latex have long been used for the treatment of inflammatory conditions, fever, wounds, and swelling ^[15].

Clinical studies suggest that this enzyme is safe and effective for treating chronic inflammatory illnesses, including inflammatory bowel disease. In experimental studies, papaya extracts from seeds have also shown anti-inflammatory properties. Leaf extracts had dose-dependent effects in carrageenan-triggered inflammatory experiments, with the greatest suppression shown three hours after delivery. But compared to the plant extract, the conventional medication indomethacin had a more apparent effect ^[8].



Antioxidant activity

Carica papaya fruits and leaves are rich sources of antioxidant compounds, including vitamin C, carotenoids, and polyphenols, which act as potent free radical scavengers ^[6]. Ethanolic and aqueous extracts of *Carica papaya* leaves demonstrated significant free radical scavenging activity in DPPH assays, confirming their strong antioxidant potential.

Leaf and seed extracts are particularly rich in total phenolic and flavonoid contents, which show a strong correlation with their antioxidant activity. These compounds protect cells from oxidative damage by reducing malondialdehyde (MDA) levels and inhibiting lipid peroxidation.

Furthermore, supplementation with fermented papaya preparation reportedly increases the levels of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, in humans ^[19]. In vitro studies have also demonstrated that papaya leaf extract reduces DNA fragmentation and oxidative stress-induced cellular damage.

Overall, the antioxidant-rich profile of *Carica papaya* contributes to cellular protection, supports tissue repair, and plays a crucial role in the prevention of oxidative stress-related diseases.

Antibacterial activity

Carica papaya isolates have shown strong antibacterial activity against a variety of Gram-positive as well as Gram-negative bacteria, such as *Proteus* spp., *Escherichia coli* and *Salmonella typhi*, *Pseudomonas aeruginosa* bacterium *Klebsiella pneumoniae*, and *Staphylococcus aureus* ^[20]. Significant zones of inhibition against these pathogens have been proven by ethanolic, methanolic, and aqueous extracts of leaves and seeds.

The antibacterial activity is primarily attributed to bioactive compounds, such as flavonoids, phenolics, tannins, alkaloids, and benzyl isothiocyanate. These compounds exert their effects by disrupting bacterial cell membranes, inhibiting essential metabolic enzymes, and interfering with protein synthesis ^[21].

In addition, the proteolytic enzymes, present in papaya latex, such as papain and chymopapain, contribute to antibacterial activity by degrading bacterial proteins and damaging cell membranes, thereby inhibiting bacterial growth and proliferation. Minimum inhibitory concentration (MIC) values against *S. aureus* and *E. coli* have been reported in the range of 5–20 mg/mL, depending on the type of extract.

Likewise, when papaya seed extracts are mixed with common antibiotics like amoxicillin and antibiotic ciprofloxacin, synergistic responses have been seen, leading to increased antibacterial activity when compared to crude extracts alone. Also, papaya-mediated silver nanoparticles have shown potent bacteriostatic activity against a number of gastrointestinal diseases [10].

In general, gram-negative microorganisms are more susceptible to the extracts than gram-positive ones, indicating that *Carica papaya* spp. has broad-spectrum antibacterial activity.

Antifungal activity

Carica papaya has demonstrated significant antifungal activity against various pathogenic fungi, including *Candida albicans*, *Aspergillus niger*, and *Trichophyton* species [22]. Methanolic, ethanolic, and aqueous extracts of papaya leaves, seeds, and latex have shown considerable inhibition of fungal growth in several in vitro studies.

The antifungal activity is mainly attributed to the presence of bioactive compounds, such as flavonoids, tannins, phenolic compounds, and benzyl isothiocyanate. These compounds exert their effects by disrupting fungal cell membrane integrity, increasing permeability, and causing the leakage of intracellular components, ultimately leading to fungal cell death.

In addition, proteolytic enzymes, such as papain, contribute to antifungal action by degrading the structural proteins of fungal cells and inhibiting their growth and proliferation. Studies have reported that methanolic and ethanolic extracts exhibit higher antifungal activity than aqueous extracts because of the better solubility and extraction of active phytoconstituents.

Furthermore, the antifungal effect was dose-dependent, with higher concentrations showing greater inhibition zones against fungal strains. These findings suggest that *Carica papaya* possesses promising antifungal potential and may serve as a natural alternative for the treatment of fungal infections.

Activity against the dengue virus

Carica papaya leaf extract has gained considerable attention for its potential role in dengue fever management. Several clinical and experimental studies have reported that papaya leaf extract significantly increases platelet count (thrombocytes) in patients with dengue, thereby helping to manage thrombocytopenia, a major complication of dengue infection [3,8].

This effect is attributed to the presence of bioactive compounds, such as flavonoids (e.g., quercetin), which exhibit antiviral activity by inhibiting viral replication and protease activity. Papaya leaf extract enhances the expression of genes involved in platelet production, such as ALOX12 and PTAFR, thereby promoting thrombopoiesis.

Moreover, the extract enhanced the immune response by lowering oxidative stress and raising the white blood cell count. Its antioxidant qualities reduce the harm that dengue virus infection causes to cells. Additionally, papaya leaf extract has been identified in clinical research to shorten the length of illness and improve overall recovery.

Overall, *Carica papaya* leaf extract exhibits promising anti-dengue activity and may serve as a supportive therapeutic agent in dengue management, although further large-scale clinical studies are required to establish its efficacy and safety.

Antimalarial activity

In vitro and in vivo, *Carica papaya* has shown significant antimalarial activity against Plasmodium species, especially Plasmodium falciparum [1]. In contaminated experimental models, leaf and seed extracts have been shown to suppress parasite development and lower parasites.

The presence of bioactive substances that disrupt parasite metabolism and replication, such as alkaloids, flavonoids, and phenolic ingredients, is the main cause of the antimalarial activity. These substances may impede the vital enzymatic pathways necessary for parasite reproduction and interact with heme detoxification activities.

Carica papaya extracts have been proven in vivo to significantly lower parasitemia and enhance haematological parameters, suggesting protective effects against problems caused by malaria. Furthermore, the plant's antioxidant qualities aid in lowering the oxidative stress linked to malaria infection. All things considered, *Carica papaya* has encouraging antimalarial potential and could be used as a supportive treatment for malaria. But further research is needed to confirm its safety and effectiveness in humans, especially in clinical trials.

Wound healing activity

Although its latex comprises proteolytic enzymes like papain and chymopapain, *Carica papaya* has shown notable wound-healing activity^[12]. By eliminating necrotic tissue and accelerating wound closure and epithelial formation, these enzymes aid in enzymatic cleaning.

Treatment with *Carica papaya* leaf extract dramatically raises the hydroxyproline level in vivo, indicating increased collagen synthesis and higher tension strength of the healing tissue^[22]. In order to avoid secondary infections at the area of the wound, flavonoids, alkaloids, and phenolic compounds also contribute to antibacterial activity against bacteria like *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.

The plant's anti-inflammatory qualities also aid in promoting healthy granulation tissue production while minimising oedema. Additionally, papaya pulp has been shown to promote fibroblast proliferation and angiogenesis, accelerating the healing process. The plant's antioxidant action of vitamins A and C promotes tissue regeneration and lessens oxidative stress.

Overall, *Carica papaya* exhibits effective wound healing properties through a combination of enzymatic, antimicrobial, anti-inflammatory, and antioxidant mechanisms, making it a promising natural therapeutic agent for wound management. Aqueous extracts from the roots of *C. papaya* induced an immediate healing process in albino rats exhibiting similar therapeutic efficacy to that of Framycetin sulphate cream and a faster epithelization process^[8].

Anticancer Activity

Carica papaya has shown promising anticancer activity due to its rich content of bioactive compounds, including flavonoids, phenolic acids, and proteolytic enzymes such as papain^[2,5]. These compounds exhibit antioxidant and immunomodulatory properties, which play a crucial role in the prevention and progression of cancer.

The anticancer mechanism is primarily associated with the reduction of oxidative stress, which is a key factor in carcinogenesis. Antioxidant constituents of *Carica papaya* neutralise reactive oxygen species (ROS), thereby preventing DNA damage, lipid peroxidation, and mutation-induced cellular transformation.

In vitro studies have demonstrated that papaya leaf extracts can inhibit the proliferation of various cancer cell lines and induce apoptosis (programmed cell death). This effect is mediated through activation of caspase pathways and modulation of pro- and anti-apoptotic proteins. Additionally, papaya extracts have been reported to enhance immune responses by stimulating cytokine production in peripheral blood mononuclear cells^[5,6].

Additionally, through improving immune surveillance and preventing tumour development, proteolytic enzymes like papain may have anticancer benefits. Despite these encouraging results, more in vivo and clinical research is needed to completely understand the molecular pathways and validate the therapeutic potential of *Carica papaya* in the treatment of cancer. Papain, an enzyme found in papaya, is an element of the plant and is highly beneficial in the treatment of cancer.

Fibrin breaks down by papain, which coats the tumour cells into amino acids. The pigment lycopene is found inside the papain, which is highly reactive towards free radicals and oxygen. Papaya also contains isothiocyanate, which protects the breast, prostate, pancreas, lung, leukaemia, and colon cancer^[13].

Antidiabetic Activity

In numerous experimental investigations, *Carica papaya* indicates notable antidiabetic efficacy. In animal models of streptozotocin-induced diabetes, leaf extracts, especially ethanolic and aqueous extracts, have been shown to reduce blood glucose levels^[8].

The presence of bioactive substances that increase insulin secretion, improve insulin sensitivity, and control glucose metabolism—such as flavonoids, alkaloids, and phenolic constituents—is largely responsible for the antidiabetic impact. Additionally, these substances contribute to diabetes management by inhibiting important enzymes involved in the synthesis and absorption of glucose.

Treatment with *Carica papaya* leaf extract from has been demonstrated in vivo to significantly lower serum glucose, triglycerides, and liver enzyme levels, suggesting enhanced metabolic function and hepatoprotective benefits. Additionally, the plant's antioxidant qualities aid in preventing issues like damage to tissue and reducing oxidative stress linked to diabetes. The hypoglycaemic advantages associated with extracts from other sections of the plant, such as seeds and unripe fruits, have also been shown, emphasising that the antidiabetic potential of *Carica papaya* as a whole is derived from a variety of parts.

The hypoglycaemic advantages provided by extracts from other sections of the plant, such as seeds and unripe fruits, have also been shown, indicating that the antidiabetic potential of *Carica papaya* is derived from a variety of sections. All things considered, *Carica papaya* shows encouraging anti diabetic activity and could be a useful natural treatment for diabetes. To prove its effectiveness and safety in humans, more clinical research is necessary. In vitro studies evaluated the effects of hexane, ethyl acetate, aqueous, and methanolic seed extracts of *C. papaya* on α -amylase and α -glucosidase enzymes. IC50 values ranged from 76.96 to 93.26 mg/ml, indicating that all tested extracts reduced enzyme activity. In vivo, the assay showed that administering different doses of *C. papaya* extract reduced blood glucose levels in streptozotocin (STZ)-induced diabetic rats^[10].

Conclusion

Carica papaya L. is an important medicinal plant rich in bioactive compounds that contribute to its diverse pharmacological activities. Studies have demonstrated its antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and anti-dengue properties. These effects are mainly attributed to the presence of flavonoids, alkaloids, and phenolic compounds. Although promising results have been reported, further clinical studies are required to establish its safety and therapeutic efficacy. Overall, *Carica papaya* L. has significant potential as a natural source for drug development.

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