- Review paper

Traditional uses, Phytoconstituents and Pharmacological Activities of *Carica papaya* L.: A Comprehensive Review

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(Received: November 11, 2025; Accepted: February 29, 2026; Published (web): June 25, 2026)

ABSTRACT: *Carica papaya* L., family Caricaceae, is well-known for its various nutritional values and pharmacological activities. Several parts of the *Carica papaya*, such as the leaves, fruits and seeds are being used for their potential health benefits in the traditional system. The prime objective of this review work is to explore traditional uses, phytoconstituents and pharmacological activities of *Carica papaya*. Using electronic sources such as PubMed, Google Scholar, and Science Direct, an entire literature search was conducted to compile information and data. In this review work, the findings show that *Carica papaya* contains various bioactive compounds such as flavonoids, alkaloids, tannins and saponins exhibiting the pharmacological activities including anti-inflammatory, antimicrobial and antioxidant properties. *Carica papaya* shows potential in treating notable health conditions, including digestive, inflammation, and infections. But the importance of the identification of molecular targets and toxicological aspects should be considered for new drug discovery and development.

Key words: *Carica Papaya*, phytoconstituents, traditional uses, pharmacological activities.

INTRODUCTION

Throughout the ages, medicinal plants have played a significant role in meeting human health needs, and their current status as a source of therapeutics is widely accepted. It has been asserted that plants' secondary metabolites contain medicinal qualities and the potential to be developed into novel medicinal products.[1] Natural products or molecules extracted from plants have demonstrated significant advantages over synthetic medicines, including being easily accessible, affordable, and having hardly any adverse effects.[2] *Carica papaya* L., commonly known as papaya, is an evergreen tree belonging to the family Caricaceae, which comprises about 31 species. It is a fast-growing herbaceous plant that can reach 10 m in height and the leaves of it are large (50-60 cm in diameter) and spirally arranged up to the top stem. It is commonly grown in the subtropical and tropical regions and cultivated in many countries for its fruits, for its high nutritional and medicinal value.[3-7] Leaves, roots, and seeds of *C. papaya* are thoroughly used in traditional medicine for treating various illnesses.[8] In addition, ethnomedicinal plants have contributed significantly in new drug discovery and development.[9] Many pharmacological activities including anti-inflammatory, anticancer, anti-protozoal, anti-microbial, anti-diabetic, antifungal, anti-hyperlipidemic, anti- thrombocytopenic, anti-viral, anti-gout, antihypertensive, analgesic and hepatoprotective activities have been reported for *C. papaya* owing to the presence of numerous secondary metabolites including flavonoids, tannins, sterols, alkaloids, triterpenoids, isothiocyanates, and other phenolic compounds.[10-22] Hence, the main purpose of this study is to compile extensive and up-

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Dhaka Univ. J. Pharm. Sci. **25**(1): 81-91, 2026 (June)
DOI: https://doi.org/10.3329/dujps.v25i1.91131

to-date information on the ethnomedicinal uses, phytoconstituents, and pharmacological activities of *C. Papaya*, offering valuable insights for researchers involved in drug discovery and development.

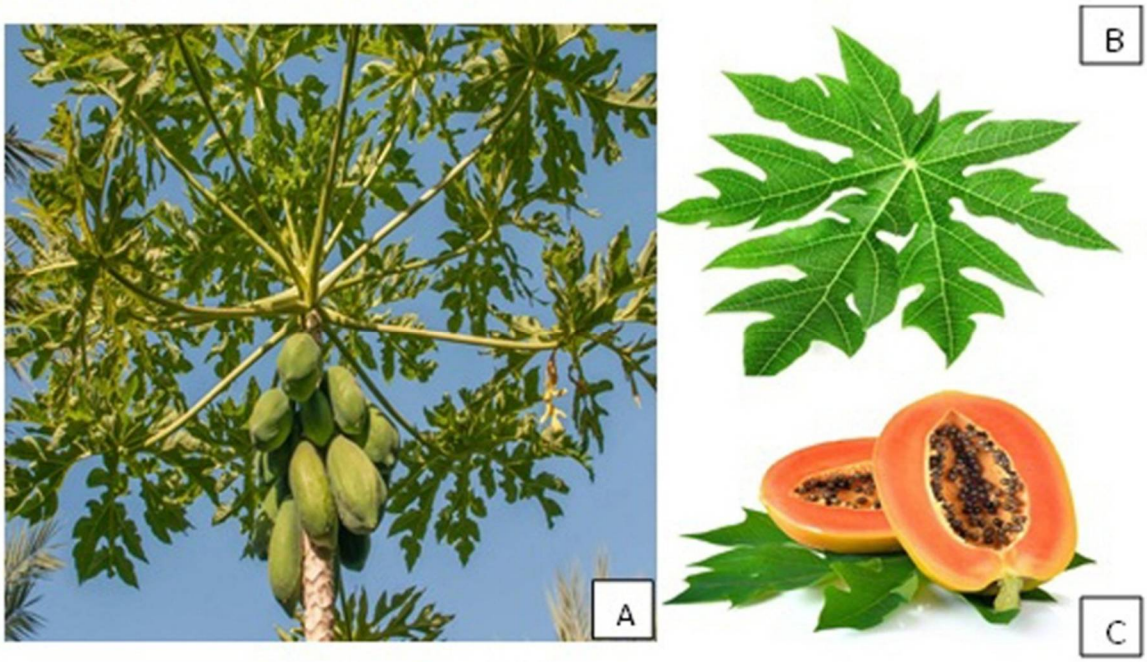

Figure 1. A) Whole plant; B) Leaf; C) Fruit of *Carica papaya*.

MATERIALS AND METHODS

The keywords such as "*Carica papaya*", "Pharmacological activity of *Carica papaya* ", "Phytoconstituents of *Carica papaya*" "traditional uses of *Carica papaya*" and other relevant terms found in the title, abstract, or full-text were used to search the literature. Online scientific databases, namely Google Scholar, PubMed, and Science Direct were used for conducting an extensive literature search. The chemical structures of the phytoconstituents were drawn using Chem. Draw (version 12.0.2) after being searched in the PubChem database. Articles published between 2000 to 2025 were retrieved, containing 189 records through database searching and cross-referencing. After the elimination of duplicate articles and excluding studies, a total of 89 articles were retained for this review.

Inclusion criteria were:

1) Articles written in English.

2) Studies reporting original research or reviews on the ethnopharmacology, phytochemistry, or pharmacological properties of *Carica papaya*.

3) Experimental studies both in vitro and in vivo on the plant's bioactive constituents.

Exclusion criteria included:

1) Articles not in English language;

2) Duplicated publications or studies with redundant data.

3) Studies with insufficient pharmacological data.

Relevant data extracted from the selected articles comprised plant parts used, pharmacological properties, and identified phytochemicals, as well as experimental design, dosage, and results. The findings are systematically presented in tables and figures and also discussed comprehensively, with the selection process illustrated in Figure 2.

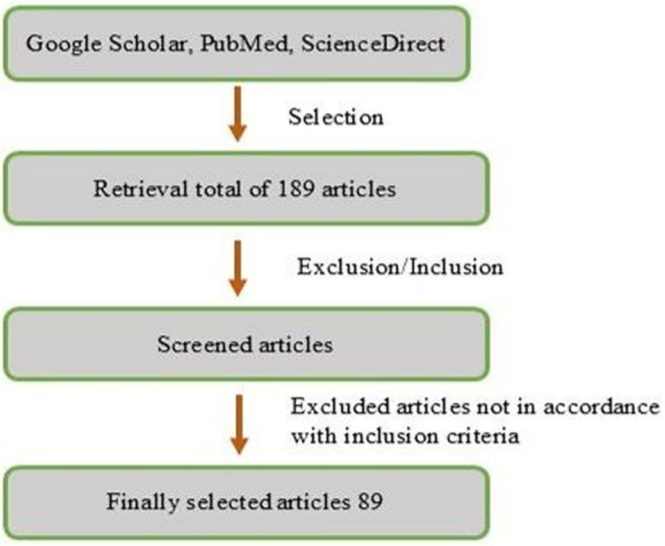

Figure 2. Flow diagram depicting the selection and screening process of retrieved articles.

RESULTS

Traditional/ethnomedicinal uses. Several parts of the papaya such as fruits, leaves, bark, seeds, flowers, latex, and roots have been utilized in traditional medicine to treat health conditions like infections, diabetes, cardiovascular diseases, infections and cancer.[23] In Asian nations including India, Sri Lanka, Pakistan, Laos, Cambodia, and Vietnam, *C. papaya* is recognized for its potential use as a contraceptive. The latex from the plant is employed in treating conditions like eczema, psoriasis, and cancer.[24,25] Leaf decoctions are often consumed in the form of tea or juice to treat digestive disorders, jaundice, and dengue fever.[26] Nguyen *et al.*, documented the use of seed extracts as remedies for intestinal worms, thirst relief and pain alleviation in this region.[27] In Cameroon, residents use *C. papaya* leaf extract as an essential component in traditional antimalarial remedies. *C. papaya* extracts are applied for treating malaria and diabetes in Nigeria.[28] The fruits, seeds and leaves of *C. papaya* are used in China to improve the flow of breast milk from nursing women and to treat bacterial infections, inflammations and stomachaches.[29]

Phytoconstituents. Preliminary phytochemical screening of different parts of *Carica papaya* demonstrated the presence of bioactive secondary metabolites including flavonoids, glycosides, alkaloids, saponins, tannins, triterpenoids.[30-35] The hydroethanolic extract of *Carica papaya* leaves disclosed the presence of several compounds such as neophytadiene, palmitic acid, phytol, linolenic acid, ethyl palmitate, bisphenol, cyclohexanone, d-limonene, tetradecamethyl cycloheptasiloxane, nonacosane, eicosane, and carpaine based on GC-MS analysis.[36,37] Nugroho *et al.*[38] isolated and quantified flavonoids compound from *C. papaya* methanolic leaves extract such as myricetin 3-rhamnoside, rutin, kaempferol 3-rutinoside, and kaempferol using HPLC and spectroscopic techniques. Ghosh *et al.*[39] identified chemical constituents of *C. papaya* chloroform seeds extract using GC-MS analysis including phenyl carbamate, palmitic acid, methyl ester, N-Phenyldiethanolamine, 2,4-ditertbutyl, 4-Benzyloxybenzonitrile, oleic acid, (-)-Dibenzoyl-L-tartaric acid, stearic acid, acetate (ester), and 2-hydroxy-1- (hydroxymethyl)ethyl ester. The fruit of the *C. papaya* plant has the highest levels of β-cryptoxanthin, β-carotene, lycopene, rosmarinic acid, and diosmetin-7-O-rutinoside.[26,40–42] Major bioactive compounds of *C. papaya* with their effects are listed in (Table 1).

Table 1. Phytoconstituents of various parts of *Carica papaya* along with effects.

Parts	Phytoconstituents/bioactive compounds	Effects	References
Leaf	Alkaloids	Antithrombocytopenia, antimalarial	14, 43
	Carpaine, carposide, emetine		
	Flavonoids	Platelet production, anti- inflammatory, antioxidant, anti-aging, cardiovascular protection, anti-dengue	44-47
	Quercetin, kaempferol, rutin, apigenin, catechin, gallic acid		
	Coumarins	Antioxidant	48
	p-coumaric acid, o-coumaric acid, 5,7-dimethoxycoumarin		
	Indole derivatives	Anticancer, anticholinesterase, anti-diabetic, and antioxidant	49
	2-(3-methoxyphenyl) methylidene-1H-indol-3-one		
Seed	Carotenoids, β-carotene, and β-cryptoxanthin, hexadecanoic acid, methyl ester, 11-octadecenoic acid, and oleic acid	Anti-inflammatory, antioxidant, antidiabetic	50,51
Fruit	β-cryptoxanthin, β-carotene and lycopene	Osteoblastic bone formation and osteoclastic bone resorption inhibition, prostate cancer	52,53

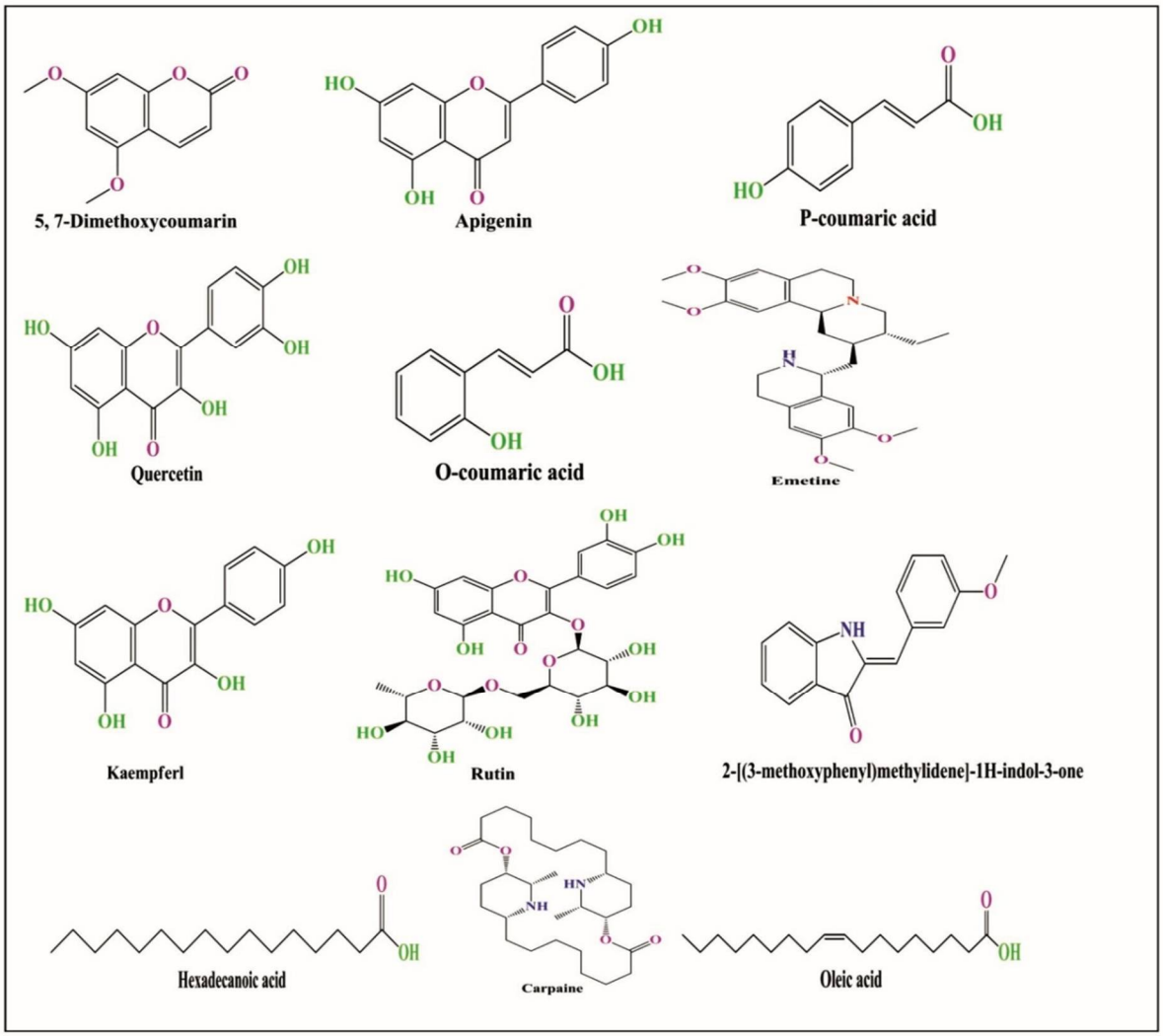

Figure 3. Phytoconstituents from several parts of *Carica papaya*.[14,26,43-51]

Pharmacological activity

Nephroprotective effect: Several studies have proved the nephroprotective effect of *Carica papaya*. Naggayi *et al.*[54] showed the nephroprotective effects of *Carica papaya* aqueous seed extract against paracetamol-induced kidney damage in male Wistar rats pretreated with *Carica papaya* seed extract at doses of 750 mg/kg daily and 500 mg/kg daily for 7 days. Mag *et al.*[55] revealed the nephroprotective effects of *Carica papaya* ethanolic leaves extract administered orally at a dose of 600 mg/kg and 300 mg/kg against mercuric chloride ($HgCl_2$) induced nephrotoxicity in female Wistar rats.

Anti-hyperlipidemic activity: *Carica papaya* seed aqueous extract administered at a dose of 200 mg/kg/day in high-fat diet induced Wister rats reduced total cholesterols, glyceroids and LDL levels, indicating anti-hyperlipidemic activity.[56] According to Ademuyiwa *et al.*[36] the *Carica papaya* leaf extract showed anticholesterolemic activities, given in egg yolk induced Wistar rats at doses of 100, 250, 500 mg/kg for 14 days. Abdel-Halim *et al.*[57] also evaluated hypolipidemic activity of *Carica papaya* aqueous leaf extract administered at a dose of 200 mg/kg body weight in hyperlipidemic rats. Matsuane *at el.*[21] found the hypolipidemic effects of papaya juice extract, given for 6 weeks in fructose and high-fat diet induced male Wistar rats at a dose of 500 mg. Another study also demonstrated the hypolipidemic effects of pulp of *Carica papaya* against alloxan induced diabetic rats by reducing the levels of TC, TG, VLDL and LDL.[58]

Antianemia: Adewuyi established anti-anemic effects of *Carica papaya* extracts in his research. This study exhibited the strongest anti-anemic effects of *Carica papaya* seeds and leaves extracts administered in aluminum chloride-induced anemic rats at doses of 75 and 150 mg/kg.[59]

Table 2. Several parts of *Carica papaya* with their effects.

Plant parts	Extract	Methods/Tests	Effects	Reference
Seed	Aqueous	MTT test, Real-time RT-PCR	Anticancer/ colorectal cancer treatment	60
	Aqueous	Histopathological examination (Albino Wistar Rats)	Nephroprotective activity	54
	Ethanolic	Wistar rats, 2,2-Diphenyl-1 picrylhydrazyl (DPPH) assay	Non-toxicity, antioxidant activity	61
	Ethanolic	Sprague Dawley rats	Anti-hepatocellular carcinoma effect	62
	Methanolic	Rats, hematological parameters were tested	Hematopoietic	59
Leaf	Methanolic	Rats, hematological Parameters were tested	Anti-anemic	59
	Ethanolic	Wistar rats, biochemical and Hematological Assays	Anticholesterolemic activities	36
		Alloxan induced diabetic mice	Antidiabetic	63
	DMSO and PBS	FFU quantitative RT-PCR and immuno- fluorescence assay	Antiviral activity against chikungunya virus and Dengue virus type 2	64
	Hydroethanolic	Mice, antioxidant activity test, DPPH assay	Antimalarial and Antioxidant activity	65
	Hydromethanolic	MTT cytotoxicity assay	cytotoxic activity against breast cancer	4
	Hexane Dichloromethane	DPPH and BSL bioassays	Antioxidant, Cytotoxic activity	66
Pulp	Ethanolic	DPPH assay	Antioxidant	67
Root	Ethanolic and Aqueous	Antibiotic Susceptibility Test	Antibacterial	68
	Aqueous	Alloxan induced diabetic rats	Antidiabetic, recuperation of hepatic tissues and renal dysfunction	69
Fruit	Methanolic	DPPH assay and the FRAP assay	Antioxidant,	70
Flower	Methanolic	*DPPH• radical scavenging activity*	Antioxidant	71

Antimicrobial: It was reported that *Carica papaya* leaf extract reduced parasitemia in Plasmodium berghei-infected mice, showing antimicrobial properties.[65] According to Baskaran *et al.*, different solvent extracts of *Carica papaya* leaf showed antimicrobial activity against bacteria and fungus. The chloroform extract showed more activity against *Micrococcus luteus* (zone of diameter 15.17 ± 0.29 mm) compared to other solvent extracts.[72] Another study revealed the antimicrobial activity, tested by agar well diffusion. In this study, the papaya methanolic leaf extract showed the strongest antimicrobial activity, especially against *Candida albicans* (26 mm inhibition).[73] According to Gupta *et al.*[74] the protein content of *Carica papaya* aqueous leaf extract has antimicrobial activity tested using gram-positive (*Bacillus subtilis*) and gram-negative (*E. coli*, *Salmonella typhi*, and *pseudomonas fluorescens*) bacterial strains. Seed extract of *Carica papaya* was found to exhibit antibacterial activity when tested on *Salmonella Enteritidis* and *Bacillus cereus*.[75]

Antidiabetic: In a study investigated by Juárez-Rojop, *Carica papaya* leaf chloroform extract administered at doses of 31, 62 and 125 mg/kg over 20 days in streptozotocin-induced diabetic rats decreased serum glucose, triglycerides and transaminases.[76] Another study evaluated antidiabetic activity of *Carica papaya* leaf extract given to streptozotocin-induced diabetic rats intraperitoneally at doses of 1.0 g/100 mL and 3.0 g/100 ml for six weeks reduced fasting blood sugar levels, indicating antidiabetic activity.[77] *Carica papaya* seed extract controls diabetes by stimulating insulin production by pancreatic ß-cells, inhibiting both α-glucosidase and α-amylase activities.[51] Solikhah *et al.*, reported that leaf extract of *Carica papaya* administered intraperitoneally in alloxan induced diabetic Wistar mice at a dose of 250, 500 and 1000 mg/kg body weight for 14 days, significantly reduced serum glucose level.[63]

Anti-dengue and chikungunya: Patil *et al.*[64] has reported that *Carica papaya* leaf extract showed antiviral activity against chikungunya virus (CHIKV) and dengue virus type-2 (DENV-2) infection in in vitro. According to another report, *Carica papaya* aqueous leaf extract has anti-dengue effect, as tested on DENV-infected THP-1 cells.[15] A study showed that the methanol extract silver synthesized nanoparticles of *C. papaya* leaf highly inhibited DENV-2 replication in an in vitro system, as demonstrated by a focus reduction neutralization test using Vero E6 kidney cell lines.[78]

Antiulcer: A study evaluated the antiulcer effect of hydroalcoholic extract of *Carica papaya* fruits on a pyloric ligation-induced gastric ulcer model and demonstrated a dose-dependent reduction in ulcer index at 500 mg/kg.[79] Pinto *et al.*[35] observed gastroprotective activity of methanolic extract of *Carica papaya* seeds given at doses of 125, 250, and 500 mg/kg in indomethacin and ethanol induced acute gastric ulcer model through reducing gastric lesions.

Anticancer: The treatment of colorectal cancer (Caco-2) cells with *Carica papaya* seed extract enhanced the expression of p53, Caspase3, and Cycs resulting in cell cycle arrest, apoptosis and inhibition of the growth and proliferation of colon cancer cells.[60] Another study investigated the anti-proliferative effects of leaf juice of *Carica papaya* against prostate cancer.[80] Sianipar *et al.*[81] showed the anticancer potential on colon cancer cell (WiDr cell) of the hexane fraction of *Carica papaya* flower. Leaf extract of *Carica papaya* inhibited tumor cell growth and enhanced cytotoxicity of human peripheral blood mononuclear cells (PBMC) against K562 cells along with inhibited pancreatic cancer cell proliferation.[11,25]

Anti-inflammatory activity: The anti-inflammatory properties of *Carica papaya* leaf extract administered at doses of 25 to 200 mg/kg in formaldehyde-induced arthritis rats decreased the formation of granulomas and oedema.[10] According to Jeon *et al.*, papaya ripe seed extracts suppressed nitric oxide production and NF-κB signaling pathways in a variety of cell types.[82] Amazu *et al.*[34] reported anti-inflammatory activity of *Carica papaya*

seed extract administered intraperitoneally at doses of 50-200 mg/kg in fresh egg albumin induced inflammatory adult white Wistar rats by inhibiting the action of inflammatory mediators (histamine, prostaglandin, cytokines, and so on).

Antioxidant activity: Jeon *et al.*[82] used ABTS (2, 2'-Azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) radical scavenging activity and FRAP (ferric reducing antioxidant power) assay to find out the antioxidative activity of *Carica papaya* seed extract. The results of this investigation revealed the antioxidant properties of seed extracts. Using the DPPH assay method, Alorkpa *et al.*[83] showed that *C. papaya* leaf extract exhibited antioxidant activity. Antioxidant potential of *Carica papaya* leaf extract was established by cell-free DPPH and FRAP and cell-based hydrogen peroxide (H_2O_2) assay.[84,85]

Wound-healing activity: The ethanolic seed extract of *Carica papaya* administered at 50 mg/kg in wounded rats exhibited wound healing activity.[86] It was revealed that 1.0% and 2.5% papaya latex hydrogels significantly improved wound healing in burn models in mice.[87] Additionally, Ahlawat *et al.*[88] exhibited the wound healing activity of *C. papaya* aqueous root extract in a research study. According to Anuar *et al.*[89] epicarp extract of *C. papaya* has potential wound healing effects.

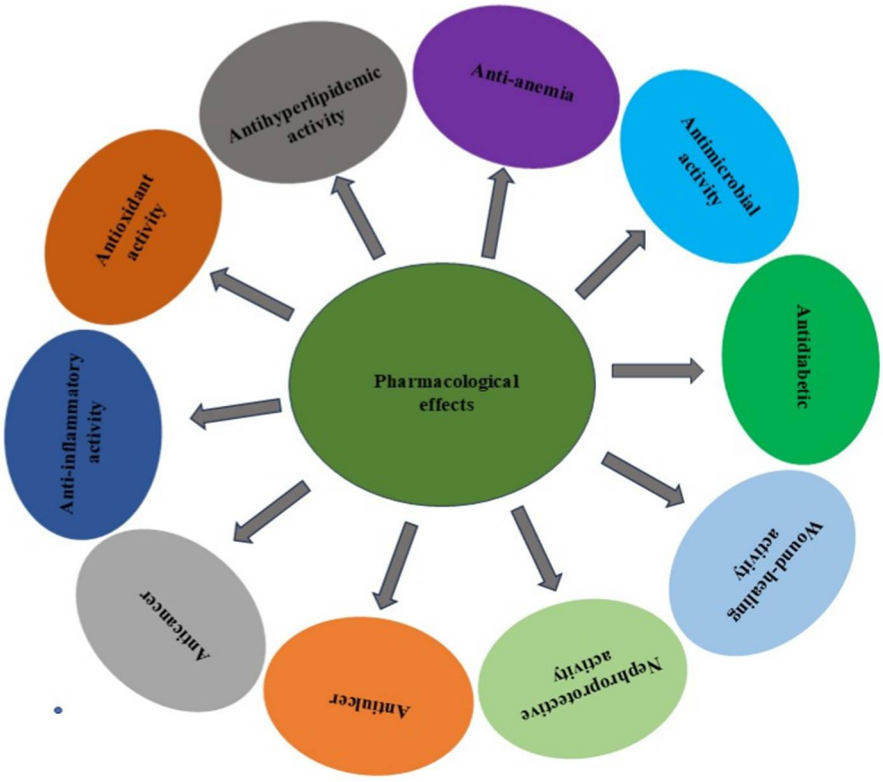

Figure 4. Pharmacological activities of *Carica papaya*.[34,54,56,59,60,72,76,79,82,86]

CONCLUSIONS

In this review, we thoroughly endeavored to provide a critical analysis of the phytoconstituents, traditional applications, and pharmacological properties of *C. papaya*, a valuable plant species frequently used as both a component of folk medicine and a food source. The leaves, seeds, and fruits of *C. papaya* are the most traditionally used and scientifically studied parts of the plant, whereas investigations on the pulp, latex, flower, and bark are comparatively scarce. Many of the pharmacological activities of *C. papaya* extracts highlighted in this review have not been reported by clinical studies. In addition, the precise identification,

mechanism of action, and toxicological studies of bioactive compounds of *C. papaya* remain underexplored. It is necessary to emphasize further scientific investigations of isolated and evaluated compounds from *C. papaya* for the development of novel therapeutic agents. Further scientific investigations, including in vitro and in vivo studies, are needed to fully comprehend the therapeutic potential of *C. papaya*. Moreover, it is expected that after sufficient clinical research and scientific investigations about potential toxicity, the use of standardized crude formulation of different parts of *C. papaya* may be able in managing and preventing various human ailments.

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