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Morphology, phytochemistry and pharmacological aspects of *Carica papaya*, an review

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Abstract

Present review focuses on the Morphology, phytochemistry and pharmacological aspects of *Carica papaya* (Linn). The plant is well known to us since ancient time. The plants are traditionally used to treat several conditions such as stomach disorders, diarrhea, skin diseases, male contraceptives, and home remedies for colds. Phytochemically, the whole plant contains lycopene, carotenoids, alkaloids, monoterpenoids, flavonoids, mineral, vitamins enzyme papain. This nutritious fruits feed the body and immune system. Various medicinal properties attributed to the plant and parts thereof includes antibacterial, anticancer, insecticidal, wound healing etc.

Keywords: *Carica Papaya*, Phytochemistry, Phytoconstituents, Pharmacological Activities

1. Introduction

Since the ancient period, plants have a long history of natural remedy in traditional medicine. Ethno-botanical information on medicinal plants and their usage by indigenous cultures is useful in the conservation of traditional cultures, biodiversity, to promote health care and drug development. WHO focusing attention towards the developing countries to encourage them to use herbal medicine, which they have been traditionally, used for centuries [1-13].

Papaya (*Carica papaya* Linn.) is one of the most cultivated plants in tropical countries and the most popular and economically important species among the caricaceae family [14]. It is a species of the flowering plants that is native to India, Malaysia, Indonesia, Philippines and Sri Lanka including Oman. Several Asian countries have cultivated the papaya on commercial basis. In some tropical countries, papaya is also cultivated as garden plant. The plant is a medium and a thinly branched tree with a single stem.

The average height is about 5 to 10 m. The leaves of the plant are spirally arranged up to the top stem. Normally, the leaves are big with oval shape with about 20–28 in. diameter. All parts of the plant contain white latex. The flowers are 5-parted pale white color petals and highly dimorphic. Both the male and female flowers are fused to the petals. The female flowers contain ovary and its five petals twisted loosely connected at the base. All parts of papaya have medicinal values and have been used traditionally for the treatment number of diseases globally.

Traditionally, it is used mainly to treat several conditions such as stomach disorders, diarrhea, skin diseases, male contraceptives, and home remedies for colds. Good numbers of studies have indicated that papaya possesses significant anticancer activities for colorectal, prostate, cervical and breast cancers. The extracts from the fruit, seeds, and leaves of the selected plant have also been shown to have significant cytotoxic activities against cancer cell lines including

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breast, liver and cancer of hematopoietic cell lines [15]. *Carica papaya* is cultivated for its fruits, it is favored by the people of the tropics, as breakfast, and as ingredients in jellies, preserves, or cooked in various ways. Papain, the proteolytic enzyme has a wealth of industrial uses. It is used for meat-tenderizers and chewing gums [16]. This known by various names across various regions (see Table 1).

Table 1 Popular names of plant in various countries

Region/ Country	Name
Southern Asia and East Indies	Kapaya, kepaya, lapaya and tapaya
Australia and West Indies	Papaw or paw paw
Brazil	Mamao (big breast) or tree melon
Spain	Melon zapote, lechosa, papaya (<i>the fruit</i>), papyo @ papyero(<i>the plant</i>), frutabomba, mammon and mamona
France	Papaya (<i>the fruit</i>), papayer(<i>the plant</i>) or “figuier des Iles”
Vietnam	Du du
New Zealand	Papaw
Venezuela	Lechoso (milky)
Cuba	Fruitabomba (fruit bomb)

2. Taxonomy, morphology and botanical description

2.1. Taxonomy

Plant taxonomy is the science that finds, identifies, describes, classifies, and names plants. Taxonomy of *Carica papaya* is given in **Table 1**. Plant taxonomy is closely allied to plant systematic, and there is no sharp boundary between the two. In practice, "Plant systematics" involves relationships between plants and their evolution, especially at the higher levels, whereas "plant taxonomy" deals with the actual handling of plant specimens.

2.2. Morphology

The papaya is a polygamous species. The plants may be classified into three primary sex types such as (i) Male (staminate), (ii) Hermaphroditic (bisexual), and (iii) Female (pistillate). In addition, some plants can produce, at the same time, more than one kind of flower. Also, some produce flowers that are not of these basic forms, but exhibit different degrees of maleness and femaleness. This tendency to change in sexual expression seems to be triggered by climatic factors, such as drought and variable temperatures [17].

The tendency to produce male flowers seems to increase at high temperatures. Since male trees are unfruitful and fruit from bisexual plants is preferred in some markets, it is very important to select seed which will produce fruitful trees of the desired type. One can predict fairly accurately the progeny by knowing the source of pollen and the kind of flower. The fruit came from Pollination studies have shown that (i) Pistillate flowers pollinated by staminate flowers give equal numbers of male and female progeny, (ii) Pistillate flowers pollinated by pollen from bisexual flowers give an equal number of female and bisexual progeny, (iii) Bisexual flowers either self or crossed-pollinated with other bisexuals give a ratio of one female to two bisexual. Bisexual flowers pollinated by staminate ones produce equal numbers of female, male and bisexual progeny. It is evident that the second and third combinations will produce the maximum number of fruit-bearing plants [18].

2.2.1. Leaves

The leaves are spirally arranged in a terminal cluster, simple, on petioles 30-70 cm long. The margins of the lobes are very variable, and range from entire to undulate to deeply lobed. The leaves are rounded in outline, 60-90 cm in diameter, alternately arranged, bundled at the apex between stem and branches, long petioles; widely evident, 25-75 cm diameter, smooth, moderately palm shape with thick middle irradiant veins, the base is deeply string shape with over-imposed lobes; from 7-11 large lobed, each with a wide base or slightly constrained and sharp-pointed, and sharp apex. The bundle of leaves is dark green to yellow-green, bright, visibly marked by the off-white nerves embedded and

reticulated veins; the underneath surface is pale green-yellow and opaque with visibly prominent vascular structures; the petioles are round and yellow-green, with sporadic purple or violet stains, fistulous form, fragile, 25-100 cm length and 0.5-1.5 cm thick. The lifespan of each leaf is 4 to 6 months.

2.2.2. Flowers

Flowers are the reproductive structure found in flowering plants. The biological function of a flower is to facilitate reproduction. Six types of flowers are known in papaya plant.

Typical female flower

It is a rather large flower of conical shape when closed, when open, its five petals spread from the base. The ovary is large with circular and smooth or slightly undulated. Fruits produced by this flower are spherical or ovoid in shape.

Similar to the above when closed

but this type has five short anthers, which correspond in their orientation with the five petals that also spread from the base. The ovary has five deep longitudinal grooves that remain until maturity. Fruit develops a form from globular to egg-shaped.

Hermaphrodite intermediate flower

The organization is undefined; petals may be fused up to two thirds of their length or free from the base. The number of anthers ranges from two to ten; the carpels range from five to ten, with different degrees of fusion. This type of flower produces irregularly-shaped fruit known as carpelodic (cat face), with little commercial value. These flowers appear more frequently when ambient temperatures are 24.5 °C during the day and 15.5 °C at night.

Hermaphrodite elongated flower

Petals of this type of flower are fused from one fourth to three fourths of their total length; ten anthers are observed, five long and five short. The ovary is long and when it contains five or more carpels, the form of the fruit varies from cylindrical to pear-shape. From the different types of hermaphrodite flowers, this is the most commercially important.

Hermaphrodite sterile flower

It is a flower that resembles the former, but does not develop an ovary and hence it is sterile, warm temperatures or water stress. Due to the fact that it produces pollen only, it may be considered a functional male flower

Typical male flower

This type of flower has a long and thin corolla contain anthers in two series of five; one series longer than the other. They have a rudimentary pistil no stigma and are non-functional. In nature, these plants are dioecious: male and female flowers are found on separate plants. Male flowers are morphologically distinct from female flowers. Male inflorescences are borne in many-flowered panicles of cymes on horizontal or pendent stalks to 1 m long. The flowers are yellowish, 2-4 cm long. The petals are fused into a long tube, have 10 fertile stamens, and a rudimentary, non-functional ovary. Female inflorescences are much shorter –only 3-4 cm long– and have fewer flowers. Female flowers are larger, usually white or cream in color, with five free petals. There are no stamens, but a large ovary with 5 fan-shaped stigmas.

In cultivation, there are many intermediate forms, including bisexual flowers. At least 15 different flower forms have been named (e.g. Pentandria–5 stamens and a functional ovary) and, because they are correlated with different fruit characteristics, some forms, have been selected by breeders. Environmental factors may also influence sexual expression, and the sexuality of a plant may change seasonally or over the course of its lifetime. Thus the sexuality of any one plant in cultivation depends on a complex mix of genetic, developmental, and environmental factors.

Female flowers have a calyx formed by a crown or five-pointed star easy to differentiate. On top of the calyx, the ovary is located by five yellowish sepals (when young, they show a purple coloration. There are five round-shaped yellow stigmas. Fruits from this flower are usually large and balloon-like. Hermaphroditic flowers have both sexes and the tree bearing these has three different types of flowers. One is called *pentandria*, resembling a female flower, but when petals are taken apart 5 anthers are seen and the ovary is lobed. Fruit are balloon-shaped and lobed. A second type of flower is called *elongata* and bears 10 anthers, arranged in two sets, the flower is elongated and cylindrical as the ovary and

produce elongated fruits. The last type is *intermedia* or *irregular*, which is not a well-constituted flower and produces malformed fruit.

Male flowers grow along peduncles measuring over half a meter length and at the end there are bundles formed by 15-20 small flowers. These flowers are constituted by a long tube formed by fused petals, inside which there are 10 anthers, arranged in two sets of five. The flower has a small rudimentary pistil and has no stigmas. No fruit are usually produced, or if formed these are elongated and of low quality.

2.2.3. Fruits

An ovoid-oblong berry pyriform or almost cylindrical, large, fleshy, juicy, grooved along the upper longer side, green yellow to yellow or yellow-orange color when ripen, single cell of orange or reddish internal color with many parietal seeds and a length of 10-25 cm or longer and 7-15 cm or more of diameter. Generally, the fruit is melon-like, oval to nearly round, somewhat pyriform, or elongated club-shaped, 15-50 cm long and 10-20 cm thick; weighing up to 9 kg. Semi-wild (naturalized) plants bear miniature fruits 2.5-15 cm long. The skin is waxy and thin but fairly tough. When the fruit is green and hard it is rich in white latex. As it ripens, it becomes light or deep-yellow externally and the thick wall of succulent flesh becomes aromatic, yellow, orange or various shades of salmon or red. It is then juicy, sweetish and somewhat like a cantaloupe in flavor; in some types quite musky. Attached lightly to the wall by soft, white, fibrous tissue, are usually numerous small, black, ovoid, corrugated, peppery seeds about 3/16 in (5 mm) long, each coated with a transparent, gelatinous [17,18,19] (**Table 2**).

Table 2 Nutritional value of fruit

Constituent	Ripe Papaya	Green Papaya
Water	89.1 gm	92.6 gm
Proteins	8.26 gm	10.8 gm
Total lipid	0.93 gm	1.35 gm
Ash	4.59 gm	6.76 gm
Carbohydrates	86.2 gm	81.1 gm
Total DF	11.9 gm	27.0 gm
Mineral Macronutrients		
Sodium	128.4 mg	283.8 mg
Potassium	1238 mg	2743 mg
Magnesium	229.4 mg	635.1 mg
Calcium	146.8 mg	635.1 mg
Micronutrients		
Iron	12.84 mg	8.11 mg
Copper	0.18 mg	0.14 mg
Zinc	0.92 mg	0
Vitamins		
Vitamin	568.8 mg	391.9 mg
Thiamine	0.28 mg	0.54 mg
Riboflavin	0.28 mg	26 mg
Niacin	2.80 mg	4.05 mg
Carotene	7807 µg	0

2.2.4. Seeds

The seeds account for about 16 % of the fresh fruit weight and each seed is made up of sarcotesta and endosperm. papaya seed extracts had been shown to have several medicinal as well as nutritional properties Several species of Caricaceae have been used as medication against a variety of diseases It had been argued by scientists that all parts of a pawpaw plant, including the seeds, roots, rinds, and fruits have positive effects on general health preventing diseases. See **Fig. 1** for various parts of plant.

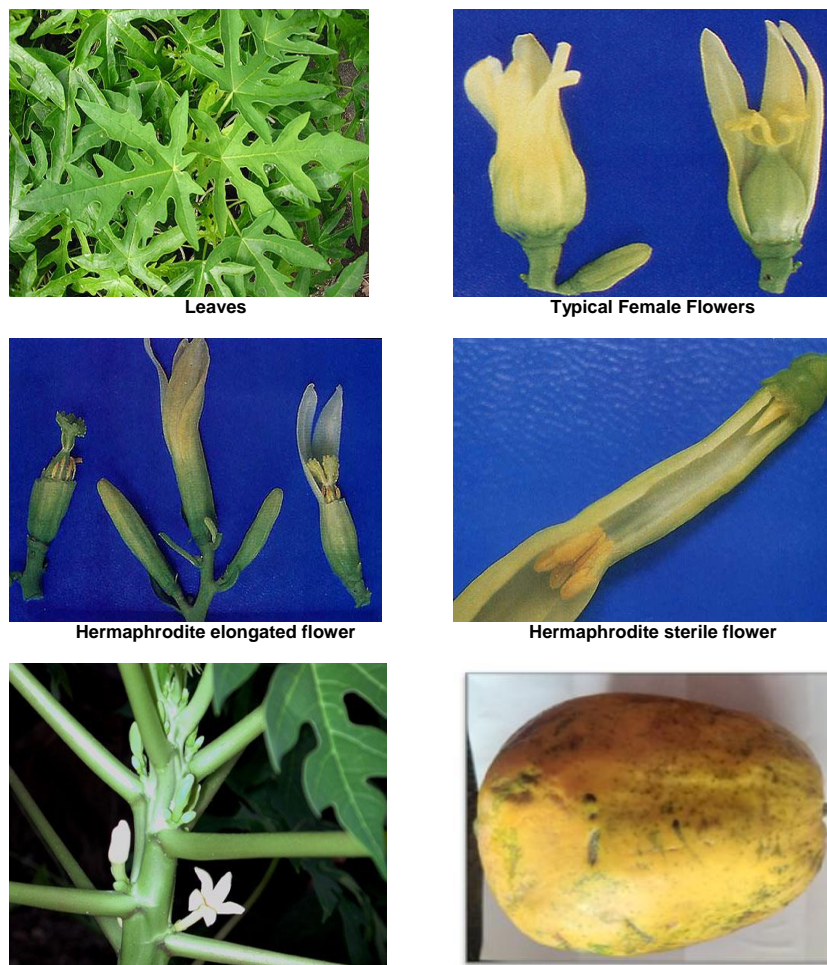


Figure 1 Various parts of *Carica papaya* plant

2.3. Botanical description

Carica branched due to injury, containing white latex in all parts. Stem cylindrical, 10-30 cm in diameter, hollow with papaya is an evergreen, tree-like herb, 2-10 m tall, usually unbranched, although sometimes prominent leaf scars and spongy-fibrous tissue. Has an extensive rooting system. Leaves spirally arranged, clustered near apex of trunk; petiole up to 1 m long, hollow, greenish or purplish-green; lamina orbicular, 25-75 cm in diameter, palmate, deeply 7-lobed, glabrous, prominently veined; lobes deeply and broadly toothed. Flowers tiny, yellow, funnel-shaped, solitary or clustered in the leaf axils, of 3 types; female flowers 3-5 cm long, large functional pistil, no stamens, ovoid-shaped ovary; male flowers on long hanging panicles, with 10 stamens in 2 rows, gynoeceum absent except for a pistillode; hermaphrodite flowers larger than males, 5-carpellate ovary; occurrence depends on the season or age of the tree.

Fruits large, cylindrical, with fleshy orange pulp, hollow berry, thin yellowish skin when ripe, varied. Fruits formed from female flowers are oblong, spherical, and pear-shaped; from hermaphrodite flowers, long, obovoid or pyriform. Seeds numerous, small, black, round, covered with gelatinous aril. Small latex vessels extend throughout the tree and are particularly abundant in fruit that has reached full size but has not yet begun to ripen. The generic name is from the Latin 'carica', meaning 'edible fig', on account of the similarity of the leaves.

Carica papaya comes into fruiting within 5 months and lives for 4-5 years. Usually male and female flowers are on different trees, but some flowers are bisexual. Pollinating agents include various insects such as larger bees

(Xylocarp, Trigona), honeybees, long-tongued sphinx moths (Sphingidae), humming-bird moths (Macroglossa) and wind. With open (uncontrolled) pollination, a cultivar may lose its identity in a few generations.

C. papaya grows satisfactorily in a wide range of areas from the equatorial tropics to temperate latitudes. However, it must be grown in warm, sunny sites sheltered from wind; preferably below 1500 m. Strong winds are detrimental, particularly on soils that cannot make up for large transpiration loss. *C. papaya* is not frost hardy; exposure to frost or cold wind usually results in leaf damage and subsequent death of the tree. Roots are very sensitive to water logging, and even short periods of flooding can kill the plant [20, 21] (see **Table 3**).

Table 3 Botanical Classification of plant

Domain	Flowering plant
Kingdom	Plantae
Sub Kingdom	Tracheobionta
Class	Magnoliopsida
Subclass	Dilleniidae
Super division	Spermatophyta
Phyllum	Steptophyta
Order	Brassicales
Family	Caricaceae
Genus	Carica
Botanical name	<i>Carica papaya</i> Linn.

3. Phytoconstituents of plant

Medicinal activities of the plants are attributed to active chemical compounds (ACC) present in the plant. These compounds may be volatile or non-volatile [22-35]. There are various analytical techniques by which active chemical compounds are determined. These methods can also be used for analysis of ACC in pharmaceutical formulations including ayurvedic products [36-41].

Papaya leaves contain tannin, saponin, alkaloids, flavonoids, and glycosides; while shoots contain various minerals like Ca, Fe, Mg, K, Zn, Mn etc. Enzymes are present in the unripe fruit such as papain and chymopapain. Fruit also contains carotenoids β carotene and cryptoxanthin. The chemical composition of the root showed the presence of benzyl isothiocyanate, glucosinolatescarposide. Papaya oil is found in seeds and also contains flavonoids, kaempferol, myricetin, and fruit contains Linalool, 4-terpinol, monoterpenoids. Papaya leaves contain tannin, saponin, alkaloid, flavonoid, and glycoside; while shoots contain various minerals like Ca, Fe, Mg, K, Zn, Mn etc. Enzymes are present in the unripe fruit such as papain and chymopapain.

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Enzymes were found in latex as well as in other parts of plants for example, papain, chymopapain, caricain, and protease omegan Latex of *C. papaya* was also reported to have enzymes like cysteine endopeptidases, chitinase, and glutaminyl cyclase Seven flavonoids were obtained from the papaya leaves, named as quercetin, kaempferol, kaempferol 3-rutinoside, quercetin3-(2G-rham nosylrutinoside), quercetin 3-rutinoside, kaempferol 3-(2G-rhamnosylrutinoside), myricetin 3-rhamnoside. Fruit contains phytochemicals flavonoids-kaempferol, myricetin, quercetin and carotenoids lycopene, zeaxanthin, cryptoxanthin, β -carotene and violaxanthin.

Leaves the presence of the various phenolic compound in the leaves for example kaempferol, protocatechuic acid, quercetin, 5,7-dimethoxy coumarin, caffeic acid, p-coumaric acid, and chlorogenic acid in plant leaves. Another study by reported that n-hexane extract and methanolic extract of leaves showed the presence of different components such as

anthraquinone, glycoside, tannin, saponin, flavonoid, steroid and resin. The major isolated compounds from leaves are protocatechuic acid, chlorogenic acid, caffeic acid, quercetin, kaempferol, quercetin 3-O- α -1C4-rhamnopyranoside, quercetin-3-O-glucopyranoside, quercetin-3-O-rutinoside, p-coumaric acid [42, 43, 44]. The chemical structures of phytoconstituents of plant are shown in Fig. 2 and phytoconstituents are shown in Table 4.

Table 4 Phytoconstituents of plant (8)

Part	Phytoconstituents
Fruits	Protein, fat, carbohydrates, minerals, vitamins, volatile compound, alkaloids, Glycosides.
Juice	N-butyric, n-hexanoic and n-octanoic acid, lipid, myristic, palmitic, stearic linoleic, linolenic acid and oleic acid
Seed	Fatty acid, crude protein, crude fibres, papaiya oil, carpaine, benzyl isothiocyanate, benzylthiourea, β -sitosterol, carcin and enzyme myrosin.
Root	Caproside and enzyme myrosine
Leaves	Alkaloids carpain, pseudocarpain and dehydrocarpain 1,2, choline, caproside, vitamin C and E.
Bark	β -sitosterol, glucose, fructose, galactose and xylitol.
Latex	Proteolytic enzyme papain, chemopapain, glutamine cyclotransferase, Chymopapain A,B,C, peptidase A and B, lysosome.

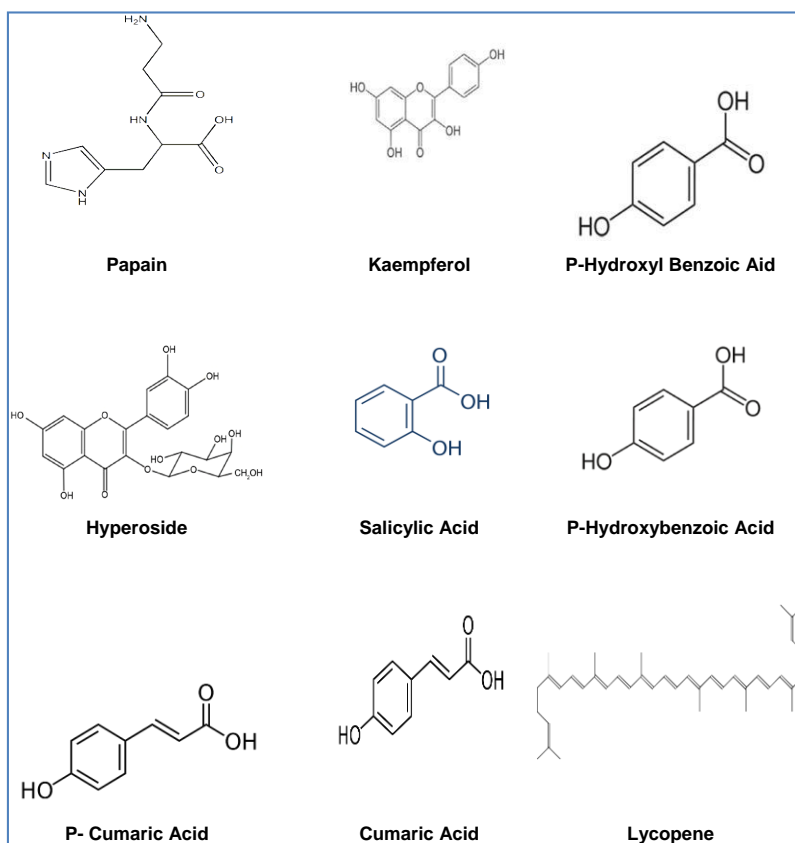


Figure 2 Phytoconstituents of the plant

The result revealed that 56% average inhibition for synthesized Ag-NPs and 38% for CPPE at different concentrations and the activity is concentrations dependent on Ag-NPs. One recent research investigation reported that the antioxidant activity of methanolic extract of seeds was determined by DPPH free radical scavenging activity. In another study, papaya seed extracts were used to examine the antioxidant activity and results revealed that the highest DPPH free radical scavenging ability was found in hexane extract and the least activity in the aqueous extract study.

The antioxidant activity of papaya leaves with different varieties, maturity, and solvent. The solvents used for extraction were water, methanol, and ethanol 70%. Results showed that mature leaves extracted with water exhibited the highest antioxidant activity higher than others. The enzyme PaMsrB1 (Plant methionine sulfoxidereductaseB1) from papaya was examined with *Escherichia coli* which contain MBP (Maltose binding protein) at its N terminal protease activity help in the digestion of MBP-tag and leads to the isolation of recombinant PaMsrB1. The purified recombinant protein PaMsrB1 showed the reductase activity against methionine sulfoxide (MetSO), DabsylMetSO in the presence of dithiothreitol. Various proteins that interact with PaMsrB1 were obtained and identified by affinity chromatography and LC-MS/MS. These results provide a platform to understand the defense mechanism of PaMsrB1 against oxidative stress [45,46].

The seed extract of *C. papaya* (petroleum-ether, benzene, ethyl acetate, chloroform: methanol (1:1 v/v) and crude extract can be useful for their larvicidal, pupicidal, adulticidal, repellent effects and smoke toxicity against *Culex quinquefasciatus*, malaria and *Anopheles stephensi*, respectively. The mortality rate of *A. stephensi* and *C. quinquefasciatus* at 0.5% concentration is more effective. It was found that the repellent effect against both female mosquitoes with protection percentages 78 and 92 respectively. Protection time against biting was 4 h for *C. quinquefasciatus* and 5 h for *A. stephensi*. One research study showed toxic smoke test, 186 mosquitoes of *An. stephensi* and 190 mosquitoes of *C. quinquefasciatus*, out of 200 mosquitoes, died after 5 h of smoke. IR study provides information about the nature of the active component, polyhydroxyaliphatic amide.

One research study showed that peel and seed aqueous extract of papaya has a larvicidal activity for *Aedes aegypti*. It was also found that seed extract has higher larvicidal activity in comparison to peel extract. Perhaps, due to the presence of phytochemicals in extract such as flavonoids, tannins, and alkaloids. Another study showed that leaf, bark, root, and seeds possess insect repellent activity against *Aedes aegypti*. It was also found that crude ethanol extract was much effective in controlling the vector as compared to aqueous extract. Also, it was found that *C. papaya* leaf extract has the potential to develop as a source of natural insecticide against chikungunya, filaria and malaria vector mosquito.

Leaf extract of papaya in ethanol has the potential to act as natural insecticides to control the population of German cockroaches which are known to resistant against synthetic insecticides. Another research study revealed the toxic effect of leaf extract against Mustard aphid which is an important insect pest of various mustard species. Papain (enzyme) found in papaya has also been reported for its insecticidal activity [47,48,49].

4.1. Antibacterial activity

Research investigation was carried out to check the antimicrobial activity of fresh and dried leaves extracts (acetone, aqueous, and ethanol) of papaya by disc diffusion method. Results exhibited that aqueous extracts were less effective as compared to organic extracts. It was also found that a fresh sample was more efficient against Gram-negative bacteria and the dry sample showed great efficiency against both Gram-positive and Gram-negative bacteria. Research investigation reported that ethyl acetate, chloroform, hexane, methanol, acetone, hot water, ethanol and petroleum ether leaf extracts of papaya extract exhibited antibacterial activity. antimicrobial activity of that methanolic and aqueous root extract papaya against seven were bacteria and four were fungi.

Papaya leaf extract showed antimicrobial activity against *Pseudomonas aeruginosa*. The leaf extract showed superior effects against all Gram-positive bacteria as compared to Gram-negative bacteria also reported the antibacterial activity of papaya leaf aqueous and methanolic extracts against *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans*. The antibacterial activity of the methanolic extract was significant compared to aqueous extract. Another report showed that methanolic seed extract was examined for the antibacterial activity by using Agar well diffusion method [50, 51, 52] (see **Table 5**).

Table 5 Antimicrobial activities of *Carica papaya*

Parts	Type of extract	Activity against
Seeds	Methanol	<i>E. coli</i> , <i>K. pneumonia</i> , <i>P. vulgaris</i>
Seeds & Leaves	n-hexane, ethanol, ethyl acetate, diethyl ether	<i>E. coli</i> , <i>S. aureus</i> , <i>Bacillus subtilis</i> and <i>C. albicans</i>
Leaves	Methanol and aqueous	<i>E. coli</i> , <i>S. aureus</i> and <i>C. albicans</i>
Peels	Aqueous	<i>E. coli</i> , <i>S. aureus</i> , <i>B. subtilis</i> , <i>B. pumilus</i> , <i>K. pneumonia</i> , <i>Aspergillus niger</i> , <i>Candida Tropicalis</i> <i>S. aureus</i>
Latex	Aqueous	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>K. aerogenes</i> and <i>Pseudomonas desmolyticum</i> , <i>E. coli</i> , <i>P. fluorescens</i> , <i>B. subtilis</i> , <i>Salmonella typhi</i>

4.2. Anti-diarrheal responses

Chloroform extract (25 mg/mL) of raw *C. papaya* and acetone extract (25–0.39 mg/mL) of ripe *C. papaya* had essential antidiarrheal activity against the gut pathogens. The antidiarrheal activity of ripe *C. papaya* extract was extensively seen against *Plesiomonas shigelloides* with ranges from 50 mg/mL 0.39 mg/mL. DAS-77 (herbal mixture prepared dried root of *C. papaya* with young bark of *Mangifera indica*) effective in the treatment of diarrhoea. DAS-77 was tested on mice and the result showed that DAS-77 possesses antidiarrhoeal activity. In another study antidiarrheal activity of leaf aqueous extract of *C. papaya* was tested in rats' model and found that extract has good antidiarrheal activity and the extract was observed to be safe at 200 mg/kg in the case of rats model [53,54,55].

4.3. Wound-healing activity

Various skin disorders as well as wounds can be cured by papaya. The ethanolic papaya seed extract was tested in Sprague-Dawley rats, for its wound-healing activity. Results showed that the seed extract assists wound healing in rats. *C. papaya* loaded PVA/Gelatin nano fibrous was prepared from leaves of *C. papaya* by electrospinning process. The fabricated nano fibers were hydrophilic and showed wound healing activity. It also exhibited strong antibacterial activity against both *S. aureus* (Gram-positive) and *E. coli* (Gram-negative). In a research investigation, the effect of aqueous extract of the root of *C. papaya* on wound healing in albino rats was checked and root extract showed wound healing activity. It was concluded that the extract-treated wound shows remarkable wound healing activity like standard FSC (Framycetinsulpha cream) [56, 57].

In comparison with control (80.38%), tested animals reveal 89.40% reduction in wound part after treated by latex of *C. papaya*. In one research study, *C. papaya* stem was analyzed for its wound healing property in albino rats. Ten albino rats were used as experimental animals in two groups. The first group of five animals was treated with an antiseptic named Betadine, whereas other groups of five animals were treated with ointment obtained from *C. papaya*. Initial and mean size of the wound every two days interval showed no major effect. The final wound size in millimeters after fifteen days showed a major effect. This result suggested the wound healing activity of *C. papaya* in albino rats [58,59].

4.4. Anticancer activity

In vitro investigation of *C. papaya* suggested that it has anti-cancer properties. The plant contains an enzyme, namely papain which is a constituent of papaya and very helpful in cancer treatment. Fibrin breaks down by papain which coats the tumor cells into amino acid. The pigment lycopene is found inside the papain which is highly reactive towards free radical and oxygen. Papaya also contains isothiocyanate which protects the breast, prostate, pancreas, lung, leukemia, and colon cancer.

In a research study, it was revealed that the leaf extract of *C. papaya* can prevent the progression of cancerous cells. Various markers such as CA15-3 and LDH are the important biochemical parameter for the detection of cancerous cells; and it was found that the leaf extract in a dose of 200 mg/kg body weight has a significant effect to decrease both markers in the treatment of cancer.

Petroleum ether, ethyl acetate, chloroform, and methanol (80%) extracts of aerial parts *C. papaya* were analyzed for their anticancer effect against three types of cancer cells such as UACC62 (melanoma) TK10 (renal) and MCF7 (breast) cancer cells. It was concluded that the petroleum extract of papaya aerial parts had a significant effect on MCF7 (breast) cancer cells. One research report concluded that black seed from yellow ripe papaya has a direct effect to reduce the growth of prostate cancer cells. Methanolic extract of black seed (ripe papaya) and white seed (unripe papaya) was tested against the prostate cancer cell line. It has been reported that the black seed extract is effective against prostate cancer cells whereas the white seed shows a stimulating effect on pre-existing prostate cancer cells. Another research study reported that papaya leaf juice has also an anti-proliferative effect on prostate cancer cells [60].

4.5. Anti-malarial activity

There were several reports available that support the anti-malarial activity of *C. papaya*. Papaya along with other plants used by peoples in the treatment of malaria and related symptoms. Another study also revealed about antimalarial effect of methanolic extract of *C. papaya* in mice on Plasmodium bergheiNK65 strain. Also, leaf extract was tested against Plasmodium falciparum 3D7 and Dd2 strains. Carpaine was the most active alkaloid extract in dichloromethane leaf extract and displayed good activity against both strain of Plasmodium falciparum IC₅₀ of $2.01 \pm 0.18 \mu\text{g/mL}$ ($4.21 \mu\text{M}$) and $2.19 \pm 0.60 \mu\text{g/mL}$ ($4.57 \mu\text{M}$). This alkaloid is highly selective against the parasite and non-toxic to healthy uninfected R.B.C.

Further, methanol, chloroform, petroleum ether extract of fruit rind, and roots of papaya were tested against Plasmodium berghei in mice for their antiplasmodial activity. The result showed that petroleum ether and chloroform extract of *C. papaya* fruit rind has considerable antiplasmodial activity in a dose-dependent manner but petroleum ether extract had the highest antimalarial activity [60].

4.6. Anti-dengue activity

Larvicidal efficiency of chloroform, methanol and aqueous extracts of *C. papaya* latex against larvae of *C. quinquefasciatus* and *A. aegypti* which were effective in a dose-dependent manner. Order of toxicity effect is as chloroform extract > methanol extract > aqueous extract. One report on the clinical trial of *C. papaya* suggested that improve in platelet count of dengue patients and faster improvement. *C. papaya* leaf juice prepared by the traditional method; and two tablespoons of juice were given to 5 dengue patients three times/day after 6 h. It was found that leaf juice causes a significant intensification in the platelet counts within 24 h of treatment (An increase in platelet count was observed when a patient was given *C. papaya* leaf extract tablet three times daily for five days and it was suggested that this effect may be due to the expression of the gene responsible for platelet construction named as platelet-activating factor receptor gene. Another investigation has also shown that the leaves of *C. papaya* have a promising effect on to increase in the platelet counts of a dengue patient [60].

4.7. Anti-inflammatory and immunomodulatory responses

Papaya contains an extensive range of secondary metabolites such as alkaloids, tannins, flavonoids, saponins, which have been shown to a marked effect to reduce chronic inflammatory reaction. Proteolytic enzymes that are present in papaya such as papain and chymopapain also showed an anti-inflammatory effect as well as an effect on immunomodulation. Papain in combination with other proteolytic enzyme such as trypsin and chymotrypsin reduce TGF- β 1 level in osteo-myelo-fibrosis, rheumatoid arthritis and herpes zoster. Alkaloids of papaya such as choline and nicotine showed anti-inflammatory potential. In vivo research was performed to investigate the immunomodulatory activities of fruit.

It is also reported that transgenic and native papaya fruit (both ripe and unripe) have significant immunomodulatory properties. These immunomodulatory effects were observed in the ovalbumin sensitized mouse model. A remarkable decrease in OVA-specific IgE titre was noticed with native green papaya fruit, whereas an increase in OVA-specific IgG2a titre was observed with green and ripened papaya fruit. The ripened transgenic papaya fruit has a significant increase in IgM level which leads to enhanced humoral immunity. Another study also showed that the seed extract of this plant has both anti-inflammatory activity and immunomodulatory effects. For instance, the bioactive reactions and immunomodulatory effect of crude seeds extract of this plant were investigated in vitro using comp Papaya contains an extensive range of secondary metabolites such as alkaloids, tannins, flavonoids, saponins, which have been shown to a marked effect to reduce chronic inflammatory reaction. Proteolytic enzymes that are present in papaya such as papain and chymopapain also showed an anti-inflammatory effect as well as an effect on immunomodulation [61].

5. Conclusion

From the research study, it is concluded that phytoconstituents obtained from *c. papaya* are best alternative to combat the diseases. This is one of most versatile plants which has been used for medicinal as well as in household purposes. All parts of plants had been used in the prevention and treatment of various diseases. Different extracts have been found possessing various pharmacological activities. Further comprehensive work is required, because the literature shows limited research in several areas to understand and disclose the mode of its pharmacological activities.

Compliance with ethical standards

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Disclosure of conflict of interest

The author declares no conflict of interest

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