Review Article

COMPARATIVE STUDY OF ANTIFUNGAL AND ANTIMICROBIAL ACTIVITY ON DIFFERENT PART OF *CARICA PAPAYA* LINN

Abstract:
Carica papaya plants used as a nutritious and medicinal purpose. Phytochemical analysis of *Carica papaya* leaf extract show all Phytochemical constituents such as saponin, flavonoid, glycoside, alkaloid, carbohydrate, tannins except steroids. The all extract subjected to systemic phytochemical screening for the presence of phytochemical constituents. Latex of papaya fruits shows significant activity against *candida albicans* reported in the literature, well diffusion method shows stronger activity in methanol extract showing inhibition against in *S. aureus* than *E. coli*. It is used as Antifungal, Antibacterial, Anti-inflammatory, Antioxidant, Antidiabetic, wound healing and Analgesic activity etc.

Keywords: Carica papaya, Papain enzyme, Candida albicans

Introduction

Carica papaya belongs to the family Caricaceae and commonly known as papaya, papayer, tinti, pepol etc. The *Carica papaya* plant is fast growing and it is typically unbranched tree, trunk of about 20 cm in diameter, hollow leaf scars and spongy-fibrous tissue, it having extensive rooting system and 7-8 m tall containing copious latex present in all part of the plant [1].

Papaya is a powerhouse of nutrients and it is available throughout the year. The fruits juicy with antioxidant nutrients like carotene, vitamin C, vitamin B, flavonoids, folate, panthotenic acids and minerals etc. [2] Papain and specific enzymes found in papaya fruits and latex, which has been utilized for meat tenderization. Papaya use for prevention of cholesterol oxidation, treat gastrointestinal tract diseases, nausea and morning sickness, weight loss, dengue fever treatment and in women menstrual regulation in women. Medicinal plants contain carbohydrates, proteins, enzymes, fats and oils, minerals, vitamins, alkaloids, quinones, terpenoids, flavonoids, carotenoids, sterols, simple phenolic glycosides, tannins, saponins, polyphenols [3] etc. The papaya fruit containing a small number of proteins and same amount of minerals consisting mainly of calcium, iron and phosphorus, vitamin A and C and that are present in papain enzyme. Papain enzyme is obtained from green fruits as a latex which is dried and purified. Papain is said to be useful in the treatment of skin blemishes, diphtheria and even cancer. [4]

In world papaya is commonly known for high level

of food and nutritional purpose. Various parts of the papaya plant, such as leaves, fruit, seed, latex, and root, are known to contain bioactive compounds. The various part of plants has medicinal properties like analgesic, amebicide, antibacterial, cardiotonic, cholagogue, digestive, emmenagogue, hypotensive, laxative, stomachic, and vermifuge.[5] The suspension of *Carica papaya* leaves in palm oil was administered for the treatment of dengue. The scientific evidences for the use of *Carica papaya* leaves extract to increase the blood platelet count in dengue [6]. papaya seed oil and the extract of papaya seeds was reported to exhibit an antifungal activity against Candida albicans.[7]

Papain is an endolytic cysteine protease obtained from the latex of papaya, many scientific investigations have been conducted to evaluate the biological activities of various parts of *Carica papaya* including their fruits, shoots, leaves, seeds, roots, or latex [8]. *Carica papaya* part like jam, sweets and pulp have more nutritional value, other parts, leaves and seeds are added to some products in the form of teas and flours. The pulp composition presents three important sources of vitamins with potential antioxidant action, A, C and E [9].

Carica papaya is a short lived, fast growing woody large herb to 10 or 12 feet in height. The papain present in green fruit contains similar to pepsin, a soft yellow resin, fat, albuminoid sugar and pectin. Leaves contain an alkaloid called carpine and glucoside named carposide [10]. The papaya is large tree plant, single stem is grown with spirally arranged leaves arrange to the top of the trunk. The leaves are large, 50–70 centimeters and 20–28 diameter. The papaya tree is unbranched, unless lopped and flowers are similar in shape to the flowers of the Plumeria, but are much smaller and wax-like. They appear on the axils of the leaves, maturing into the large 15–45 centimeters long, diameter of fruit is about 10–30 centimeters. The

fruit is ripe when it feels soft and its skin has attained amber to orange color. It is a melon-like fruit which varies in shape and size, the fruits of papaya hang from short, thick peduncles. [10,11] The plant shows greater medicinal activity and the latex of papaya which play an important role in Antifungal activity and antibacterial activity.

Plant Profile of Carica papaya:

Fig. 1: Photograph of *Carica papaya*

Synonym: **-** Papaya, papayer, tinti, pepol

Biological Source: It is Cultivated fruiting tree known as *Carica papaya* belongs to family Caricaceae and one of the most popular and economically important plants for nutrient and higher health benefit in the world as a food source and as an herbal medicine [9].

chart 1

Different species of *Carica papaya* Linn: -

Carica candamarcensis	*Carica glandulosa*
Carica Mexicana	*Carica goudotiana*
Carica caudate	*Carica heterophylla*
Carica cauliflora	*Carica candicans*
Carica chilensis	*Carica longiflora*
Carica horovitziana	*Carica crassipetala*
Carica cundinamarcensis	*Carica weberbaueri*

[10,11,13,21,24]

Taxonomical Classification:

Kingdom : Plantae

Subkingdom: Tracheobionta

Division : Magnoliophyta

Class : Magnoliophyta

Family : Caricaceae

Genus : Carica L.

Species : *Carica papaya* L [9]

Varnacular Names

Hindi : Papita

English : Papaya

Brazil : Mamao [12]

Morphological Characteristics:

***Carica papaya* plant:** It is dicotyledonous, polygamous and diploid species, rapid growth rate of papaya plant and large perennial herb. The papaya plant has a branchless and soft wooded trunk 6-20 feet (1.8-6.1m) [11].

Leave: Leaves are the 50-70 cm in diameter in which long petioles and 5-7 lobes. The leave is deeply incised and lobed, mature leave are palmitate with deep lobes and leaves are large. [11]

Flower- Male flowers in lack many-flowered, densely pubescent cymes at the tips of the pendulous, female flowers large, solitary or in few flowered racemes. [13]

Fruit-It is a large central cavity, varying widely in size, elongate shape.

Seed-Seeds are black, tuberculous and enclosed in a transparent aril.

Latex- Unripe fruit contain milky juice is called as latex and in which the protein ferment papain is present. [11,13]

Chemical constituents:

The different parts of papaya such as fruit, fruit juice, seed, root, leaves, bark, latex contain various chemical constituents, which are shown as follows:

Fruit-Protein, fat, fibre, carbohydrates, minerals: calcium, iron, vitamin C, thiamine, riboflavin, niacin, and carotene, amino acid, citric acid and volatile compounds: benzylisothiocynate, alkaloids, carpain. [14]

Juice-N-butyric, n-hexanoic and n-octanoic acids, lipids; myristic acid, palmitic acid, stearic acid, linolenic acid, linoleic acid, oleic acid. [15]

Seed-Fatty acids, crude protein, crude fibre, papaya oil, carpain, caricin and an enzyme myrosin. [15]

Root-Carposide and an enzyme myrosin.

Leaves-Alkaloids contain carpain, pseudocarpain, dehydrocarpaine I and II, choline, vitamin C and E, carposide. [16]

Bark-Glucose, fructose, sucrose, xylitol, β-sitosterol.

Latex- Papain, chymopapain, peptidase A and B, lysozymes. [16]

chart 2

Nutritional value of the macronutrients and fibres of *Carica papaya* L. (papaya) per 100 g of pulp of ripe fruit, seeds and leaves:

Composition	Pulp	Seeds	Leaves
Protein	0.6g	2.6g	5.8g
Lipids	0.1g	3.1g	1.8g
Carbohydrates	7.2g	43.6	74.2g
Fibres	0.8g	2.1g	13.1g
Energy	32.1kcal	212.7kcal	348.6kcal

[12] [15]

Application:

Ripe fruit extracts:
Used for a medicinal purpose ranging from treatment of ringworm, malaria and hypertension.

Leaves extract:
Increase the blood platelet count in dengue. It is also used as antibacterial, anti-fertility, anthelminthic and antiamoebic activities.

Papaya seed extract:
Antifungal activity against *Candida albicans*. It is also used as analgesic, amebicide, pectoral, cardiotonic, cholagogue, digestive, stomachic and antitumor febrifuge, hypotensive, laxative, wound-healing, etc.

Unripe fruits extract:
In the treatment of ulcer in traditional medicine. Nutrient purpose, cardiovascular system and provide protection against colon cancer.

Leaf extracts:
Leaf extract inhibit the formation of sickle cell.

Latex:
Antifungal activity, Anti-inflammatory, analgesic, amebicide, cholagogue, digestive, febrifuge, laxative, Dermatitis and psoriasis, Abortion.

Papaya juice:
Antioxidant nutrients like carotene, vitamin C, vitamin B.

Flowers:
Infusion, decoction Jaundice, cough, hoarseness, bronchitis, laryngitis, and tracheitis.

Roots/barks:
Decoction, poultice, infusion Digestive, tonic, abortifacient, sore teeth. [2,5,6,7,15,16]

Reported Pharmacological Activity:
Carica papaya possesses anthelminthic, anti-viral, protozoan, antibacterial, antifungal, anti-viral, anti-inflammatory, antihypertensive, hypoglycaemic and hypolipidemic, wound healing, free radical scavenging, anti-sickling, neuroprotective, diuretic, abortifacient and antifertility properties.

Antibacterial activity

Antibacterial activity found in papaya seed extracts against *B. cereus, E. coli, S. faecalis, S. aureus, P. vulgaris*. Similarly, such as *B. subtilis, S. typhi, S. aureus, P. vulgaris, P. aeruginosa* and also found maximum inhibition zone (15.0 mm). Anti-fungal activity against *Candida albicans* by papaya latex shows 60% of inhibitory effect against fungal pathogen. [24]

Wound Healing Activity:

Analogous factor may be present in latex coagulation in papaya and the mammalian coagulation. Formation of cloth in mammals during healing process. Some plant metabolites during plant healing may likewise. Papain shows burn healing properties. [25]

Anti-inflammatory Activity:

The ethanolic extract of *Carica papaya* L. leaves have also investigated for its anti-inflammatory activity in rats using paw oedema. The extract gives significant reduction in persistent oedema from the 4th day to the 10th day of the investigation was observed in formaldehyde arthritis model. [26]

Antidiabetic Activity:

Antidiabetic activity of *Carica papaya* L. leaf extract was carried out in an experimental rat model. After the administration *Carica papaya* L. leaf chloroform extract of diabetic rats shows significant reduction in serum glucose, transaminases and triglyceride level. [27]

Antimicrobial activity:

Antimicrobial activity of different extracts of leaves of *Carica papaya* L. There is various different solvent used for extract prepare like ethanol, methanol, ethyl acetate, acetone, chloroform, petroleum ether, hexane and aqueous extract showed activity against bacteria and fungus. Acetone extract was more active against *Candida albicans* fungus. [2]

Analgetic Activity:

The three extracts of leaves of *Carica papaya* L. have been evaluated for their analgesic activity in mice model having acetic acid induced pain. These three extracts (n-hexane, ethyl acetate, and ethanol extracts) exhibited significant analgesic activity, when compared to aspirin as the standard drug. [28]

Anti-hypertensive activity: -

Decoction of papaya leave can be used as an anti-hypertensive agent. It shows hypotensive activity of papaya plant when administered orally. [29]

chart 3

Isolation of Latex:

Collection of Latex

↓

Attaching Aluminium tray on the Carica papaya trunk

↓

Incision at 3mm deep on mature *Carica papaya* fruit

↓

Dripping of exuded latex into Aluminium trays

↓

Isolation of Latex

↓

Spreading of latex on the trays

↓

Oven/Sun drying

↓

Grinding

↓

Papain Storage

(Storage in plastic bottle and freezing of Dried Latex) [17]

Material and Methods

Collection of plant materials

The collection of latex from *C. papaya* fruits by incisions of fruit using a stainless-steel knife. The exuded fresh latex was running down the fruit and that are collected in beaker.[1] In that latex mix 500 µl methanol and shaken for 5 minutes to dissolve the latex into methanol uniformly.

Latex Extraction and Collection

The latex of mature unripe fruit was tapped early in the morning with the help of stainless-steel knife. A beaker or plastic dish was used to collect the latex. That collected latex was mixed with potassium meta-bisulphite (K2S2O5) by ratio of 0.5% W/W [6].

Latex Drying and Storage

Collected latex was take in aluminum trays and dried in a tray drier at 40°C, 746.6 mbar pressures for 2hr. After drying, the latex was transferred to a plastic bottle and stored at about −20°C until used for analysis.[7]

Collection of microorganisms

Bacterial cultures of Gram-negative bacteria *Escherichia coli, Agrobacterium sp. Rhizobium sp. and Gram-positive bacteria Bacillus subtilis* were collected from the microbiology laboratory, these all-test strains were maintained on nutrient agar and were sub cultured once in every 2-week in LB broth medium. [3,7]

Preparation of culture medium

For the preparation of 1 L broth media, all the ingredients (10 g/L of peptone, 5 g/L NaCl except agar), 5 g/L of yeast extract, were suspended in 1 L of double distilled water and were mixed properly. For preparing agar plates, 15 g/L of agar added to desired medium for solidification.[5] The pH of the medium was adjusted at 7.0 using 1 N NaOH and autoclaved at about 121°C for 20 minutes.[6]

Disk diffusion assays

The disk-diffusion method for the determination of antimicrobial activity of leaf extracts. Take 20 ml sterile agar medium that agar medium inoculated with 100 µl microbial cell suspension and poured into sterile petri dishes. [2,3] The Whatman No.1 cut with punch machine used and make disks at 6 diameters. The paper disks were making different concentrations (1, 2, 5, 7, 10, 15 and 20 mg/disk) of papaya latex with micropipette and kept for 5-10 minutes in laminar air flow for drying. The sterile spreader for the inoculation of test organisms on the surface of agar solid medium in plates and then agar plates inoculated.[4]

Anti-fungal activity:

Ethanolic extract of papain which produce maximum growth inhibition observed to be higher than the positive control. The result shows that the papain has the significant antifungal property against Candida albicans fungus. The enzyme papain was extracted from the crude latex and it obtained from unripe fruit of papaya and the presence of protein in the sample confirmation observed using ammonium per sulphate precipitation technique. The basic confirmatory test shows the presence of papain. [19]

Fungi	Papain (conc.) µl				
	10	20	30	40	50
Candida albicans	-	-	13mm	15mm	18mm

chart 4 Basic confirmatory test shows the presence of papain [19]

Physiochemical parameters

The essential oil extracted from the C. Papaya seeds was yellow in colour. The overall yield was 0.2% (w/w). The specific density of essential oil about 1.124 g·mL-1 at 25 °C. and the refractive index was 1.6026 at 20 °C [30]

Zone of Inhibition:

The antifungal activity of the papaya seed essential oil was examined using the filter paper disc diffusion Method. EO inhibited the growth of fungal strains tested in our study. The EO exhibited the greatest antifungal effect against C. parapsilosis.[30]

Fungal strain	Zone of inhibition	
	EO (100µg)	FLZ (25µg)
C. albicans	29.6±1.5	43.3±0.3
C. glabrata	29.6±0.8	24.1±0.9
C. krusei	32.9±1.1	21.7±0.4
C. parapsilosis	33.2±0.8	40.9±0.3
C. tropical	27.2±0.8	42.1±0.9

Chart 5. Greatest antifungal effect against C. parapsilosis [30,31]

Mycelial inhibition (radial diffusion) of evaluated *Carica papaya* L. by product ethanolic extracts (Table 1)

Fungi spp.	**Mycelial inhibition (%)**			
	LE	SUE	SRE	Ridomil
Fusarium spp.	18.17±1.8	8.99±1.5	1.60±08	60.82±0.3
Colletotrichum gloeosporioides	21.84±1.3	0	0	51.20±1.3
Rhizopus stolonifer	0	0	0	32.56±0.9

LE Leaf extract, SUE seed (unripe) extract, SRE seed (ripe) extract [5]

Determination of antimicrobial activity:

For the evaluation of antibacterial activity of the aqueous and organic extracts of *Carica papaya* plant sample using cup plate agar diffusion method. The bacterial cultures were adjusted to 0.5 McFarland turbidity standard and A liquors of 100 µl of extract dilutions, reconstituted in 50% DMSO and distilled water at concentrations of 200, 150, 100 and 50 mg/ml, were applied in each of the wells in the culture plates previously seeded with the test organisms.[9]

The cultures were incubated at 37ºC for 24 h. A well was made in each of the agar culture plates and filled with 20 µl of 10 mg/ml of ciprofloxacin antibiotic as a standard and streptomycin as positive controls.[8] Antimicrobial activity was determined by measuring the zone of inhibition and the each well.

Determination of Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC): The Minimum Inhibitory Concentration of the extracts was determined using test organisms. To take 0.5 ml of varying concentrations of the extracts (5, 25, 50, 75, 100, 125, 150, 175 and 200 mg/ml) in test tubes, Nutrient broth (2 ml) was added and then a loopful of the test organism, previously diluted to 0.5 McFarland turbidity standard, was incorporated. The procedure for test organisms and ciprofloxacin as a standard. Nutrient broth was

seeded in test tube with the test organisms. The culture tubes were then incubated at 37ºC for 24 h. After incubation the tubes were then examined for microbial growth by observing for turbidity.[9]

A loopful of broth was collected from those tubes that did not observed any growth of microorganism and inoculated onto sterile Nutrient agar medium. Nutrient agar plates only were also streaked with the respective test organisms to serve as controls. All the plates were then incubated at 37oC for 24 hr. [9]

Antibacterial activity of acetone extract of *Carica papaya* leaf (Table 2)

S.NO	Wound pathogen	Diameter of zone of inhibition (mm)			
		25mg/ml	50mg/ml	75mg/ml	100mg/ml
1	Staphylococcus aureus	0	0	10	14
2	Escherichia coli	0	12	13	17
3	Klebsiella pneumonia	0	10	12	15
4	Proteus vulgaris	0	11	14	16
5	Pseudomonas aeruginosa	0	13	24	26

[8,9]

Antibacterial activity of methanol extract of *Carica papaya* leaf (Table 3)

S.NO	Wound pathogen	Diameter of zone of inhibition (mm)			
		25mg/ml	50mg/ml	75mg/ml	100mg/ml
1	Staphylococcus aureus	0	0	10	12
2	Escherichia coli	0	10	12	13
3	Klebsiella pneumonia	0	10	11	14
4	Proteus vulgaris	0	12	13	15
5	Pseudomonas aeruginosa	0	14	17	24

[7,11]

Antibacterial activity of aqueous extract of *Carica papaya* leaf (Table 4)

S.NO	Wound pathogen	Diameter of zone of inhibition (mm)			
		25mg/ml	50mg/ml	75mg/ml	100mg/ml
1	Staphylococcus aureus	0	0	0	10
2	Escherichia coli	0	0	11	11
3	Klebsiella pneumonia	0	0	10	11
4	Proteus vulgaris	0	0	12	13
5	Pseudomonas aeruginosa	0	0	14	15

[8,9,6]

Result and Discussion:

Carica papaya genus of papaya plant belonging to family Caricaceae, papaya fruit is very popular to farmers. The cultivation of papaya plant is easy to cultivate and provides more income per hectare. The *Carica papaya* plant materials higher amount of phytoconstituent were carried out and the results were recorded. The papaya plant part such as leaf, fruit and seed extracts indicate the presence of, protein, vitamin C, carbohydrates, alkaloids, flavonoids, tannin, steroids, vitamin C, phenolic compounds and saponins. The presence of as the antibacterial activity of the plants may be attributed to the presence of bioactive compounds such as

phenols, saponin, steroids, alkaloids and flavonoids.

Antibacterial activity if acetone, methanol and aqueous extract of carica papaya leaf are summarized in Table 2, 3 and 4. The higher wound healing activity show the methanolic extract of papaya leaf against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia, Proteus vulgaris, Pseudomonas aeruginosa* at concentration 25mg/ml, 50mg/ml, 75mg/ml, 100mg/ml.
Antifungal activity of ethanolic extract of papaya leaf summarized in Table 1, The higher antifungal activity against *Colletotrichum gloeosporioides and* the papain shows antifungal activity against *candida albicans* at concentration 50 µl which give inhibitory growth of fungi about 18mm diameter. Essential oil extracted from seed of papaya which give greater antifungal activity against *candida parapsilosis.*

Conclusion:
This study has shown the ability of *Carica papaya* leaf extract show higher antifungal activity against *Colletotrichum gloeosporioides* than *Fusarium spp*, *Rhizopus stolonifer* and antibacterial activity show higher in methanolic and acetone leaf extract than aqueous extract of papaya leaf at Conc. 50mg/ml, 75mg/ml, 100mg/ml.

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