

Pharmacological activities and bioactive compounds of papaya (*Carica papaya L.*): A mini topical review

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ABSTRACT

The present review focuses on the pharmacological activities and bioactive compounds of *Carica papaya L.* The plant is well known to us since ancient times. The plant is traditionally used to treat several conditions such as stomach disorders, diarrhea skin diseases, male contraceptives, and home remedies for colds. Phytochemically, the plants have alkaloids, tannins, flavonoids, saponins, glycosides, starch, quinones, etc. Various medicine properties attributed to the plant and parts which include antimicrobial, antioxidant, anti-diabetic, anti-cancer, anti-inflammatory, anti-hypertensive, anti-amoebic, anti-malarial, wound healing, anti-fertility, hepatoprotective, histaminergic, diuretic, immuno-modulatory, and anti-ulcer. In this review article, we have collectively summarized various pharmacological applications of *C. papaya L.*

Keywords: Pharmacological activities, Bioactive compound, *Carica papaya L.*

INTRODUCTION

Carica papaya L. belongs to the family of “Caricaceae” is commonly known as papaya in English, Papita in Hindi, and Erandakarkati in Sanskrit. The native place of this plant is tropical America and it was introduced to India during 16th centuries. Traditionally, their leaves have been used for treatment of a wide range of ailment, such as in treatment of malaria, dengue, immuno-modulatory, and antiviral activity. Young leaves have rich of flavonoids, alkaloids, phenolic compounds, the cytogenetics compound found in leaves. Both leaf and fruit of *C. papaya L.* possess carotenoids namely beta carotenoids, glycosides as compared to mature leaves and hence possess medicinal properties such as anti-inflammatory, hypoglycemic, anti-fertility, hepatoprotective, anti-tumor, and anti-hypertensive wound healing also recently established.^[1] The following are the list of medicinal uses of parts of *C. papaya* such as,

Ripe fruit – carminative, diuretic, chronic, diarrhea, dysentery, wound of urinary tract, stomachic, ringworm, sedative and toni, bleeding piles, and expectorant.
Unripe – diuretic, antibacterial, laxative

Seed- carminative, antifertility in males, counter irritant, as a paste in the treatment of ringworm and psoriasis
Root - antifungal, diuretic, and checking irregular bleeding from uterus, piles
Leaves – asthma, beriberi, fever, abortion, dressing wound, antibacterial, jaundice, gonorrhoea, urinary complaints, and vermifuge.
Flower – febrifuge, jaundice, and pectorial properties
Stem bark- STD, antifungal, jaundice, antihemolytic activity, and sore teeth.^[2]

PLANT CLASSIFICATION

Domain - Flowering plant
Kingdom - Plantae
Subkingdom - Tracheobionta
Class - Magnoliopsida

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Subclass - Dilleniidae
 Subdivision - Spermatophyta
 Phylum - Steptophyta
 Order - Brassicales
 Family - Caicaceae
 Genus - *Carica*
 Botanical name - *C. papaya* L.^[3]

BOTANICAL DESCRIPTION

C. papaya branched, as a result of injury, with all parts containing white latex. The stem is cylindrical, 10–30 cm in diameter and hollow with papaya. It is an evergreen, tree like herb, 2–10 m tall, usually unbranched, but with prominent leaf scars and spongy – fibrous tissue. It has a well-developed rooting system. Leaves are spirally arranged and clustered near the apex of the trunk; Petioles up to 1 m long, hollow, greenish or purplish green; Lamina orbicular palmate, deeply 7 – lobed, glabrous, prominently veined; Lobes deeply; and broadly toothed. Flowers are tiny, yellow, funnel shaped, solitary or in cluster. Female flower is 3–5 cm long, with a large functional pistil, no stamens and an Ovid shaped ovary. The male flower has a long hanging panicle with 10 stamens in 2 rows, no gynoeceum except for a pistillode. Hermaphrodite flower is larger than males, 5 – carpellate ovary; occurrence depends on the season or age of the tree. Fruits are large, cylindrical, and varied, with fleshy orange pulp, hollow berries, and this yellowish skin when ripe. Fruits derived from female flower have oblong, spherical, and pear-shaped shapes; Long, obovoid, or pyriform hermaphrodite flower seeds are many, tiny, black, and spherical, with a gelatinous aril covering them. Small latex vessels can be found all over the tree, but they are especially plentiful in fruit that has achieved full size but has not yet begun to mature. The generic name is derived from because of the likeness of the leaves, the Latin word, “*Carica*” means “edible fig.” *C. papaya* bears fruit in 5 months and has a lifespan of 4–5 years. Male and female flower are usually found on separate trees, though some flowers are bisexual. *C. papaya* thrives in a variety of



Figure 1: Photograph of *Carica papaya*

environments, from the equatorial tropics to temperature latitude. It must, however, be grown in humid, sunny, wind – protected location, ideally below 1500 m. Strong winds are harmful, particularly to soils that cannot compensate for large amount of transpiration loss. *C. papaya* does not frost hardy; when a tree is exposed to frost or cold wind, it usually suffers from leaf damage and eventually dies. Waterlogged roots are extremely sensitive, and even brief episodes of flooding can kill the plant.^[4]

PHARMACOLOGICAL ACTIVITIES

Varies medicinal activities are identified in *C. papaya* such as

1. Anti-microbial activity
2. Antioxidant activity
3. Anti-inflammatory activity
4. Anti-diabetic activity
5. Anti-hypertensive activity
6. Wound healing activity
7. Hepatoprotective activity
8. Anti-fertility activity
9. Anti-cancer activity
10. Histaminergic activity
11. Diuretic activity
12. Anti-amoebic activity
13. Anti-ulcer activity
14. Anti-malarial activity
15. Anti-sickling activity
16. Immuno-modulatory activity
17. Anthelmintic activity
18. Effect on smooth muscle
19. Anti-diarrheal activity
20. Anti-dengue activity

ANTIMICROBIAL ACTIVITY

Romasi *et al.*, have reported the antimicrobial activity of leaf extract of papaya against pathogenic bacteria (*Bacillus stearothermophilus*, *Listeria monocytogenes*, *Pseudomonas* sp., and *Escherichia coli*).^[5] They first took the papaya leaves to make powder form and extracted by using macerated method and three types of organic solvents (ethanol, ethyl acetate, and hexone). After extraction, anti-bacterial activity examined is done by agar diffusion method. The influence was checked in extraction by PH, heat process and NaCl. This resulted in ethyl acetate extract; it inhibits the growth of *B. stearothermophilus*, *L. monocytogenes*, *Pseudomonas* sp., and *E. coli*. The activity was influenced by using pH and it's more effective at low pH. The extraction activity was influenced by NaCl against *B. stearothermophilus* and *E. coli*. But it did not influence by in NaCl in bioassay against *L. monocytogenes* and *Pseudomonas* sp. The extraction activity influenced against all test organisms by heating process. The extraction inhibits the *B. stearothermophilus* spores as well.^[5]

Gupta *et al.* have examined the anti-microbial activity in aqueous extract of papaya leaf against Gram-positive bacteria (*Bacillus subtilis*) and Gram-negative bacteria (*P. fluorescens*, *E. coli* and *S. typhi*).^[6] The bacteria sample was grown on media and then colonies are identified by using Bergey's manual. The bacteria strain (Gram-positive and Gram-negative bacteria) was taken in 96 well plates and it exposed to the human blood samples without any infection (100 µl). Finally, treated with various concentrations of plant extracts (50 µl) for identification of antimicrobial activity the results as the decline phase in bacteria population and proliferation rate at high doses. Finally, it revealed the high doses on antimicrobial activities.^[6]

Doughari *et al.* have investigated the antibacterial activity in root extract of *C. papaya* L.^[7] The papaya root was collected and to make the powder form. The root extract is done using organic solvents (methanol, acetone, and water). The antibacterial was carried out by cup plate agar diffusion method against test organisms (*Streptococcus aureus*, *Streptococcus pyrogenase*, *Streptococcus pneumoniae*, *Bacillus cereus*, *E. coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Salmonella typhi*, and *Shigella flexneri*). The extraction revealed the high activity against gram positive bacteria when compared to gram negative bacteria along with high activity as 14mm zone of inhibition against *S. typhi*. Enhance the activity of extract when increase the temperature at same time alkaline PH decrease the activity. 50–200 mg/ml is the extraction range between the minimum inhibition concentration (MIC) and minimum bactericidal concentration (MBC).^[7]

ANTIOXIDANT ACTIVITY

Antioxidant activity in papaya leaf extract has been reported by Aboobacker *et al.*^[8] The papaya leaves were collected and to make the powder form. The extraction is done by using methanol solvent. DPPH free radicals assay is used to carry out the antioxidant activity to evaluate the activity. The percentage of DPPH scavenging effect was calculated by using the below formula

DPPH scavenging effect (%) or percentage inhibition = $A_0 - A_1/A_0 \times 100$

A_0 – Absorbance of control reaction

A_1 – Absorbance in presence of test or standard sample.

The percentage of the inhibition was plotted against the concentration and from the graph. IC50 was calculated. IC50 is the concentration of substrate that causes 50% loss of DPPH activity (color). The result as an increase the activity along with increase in concentration. The IC50 value was 213.68 µgm/ml. Ascorbic acid used as a control for this study.

Banik *et al.* have reported the antioxidant activity of papaya leaf extract.^[9] The papaya leaf extract is performed using methanol, water, and chloroform solvent. DPPH and

H₂O₂ radical scavenging method is used for determining the antioxidant activity. Percentage of hydrogen peroxide scavenging is calculated by the following formula:

Scavenging % = $(AC - AS)/AC \times 100$

AC – The absorbance of control

AS – The absorbance in the presence of samples extract and standard.

In DPPH, % of scavenging activity calculated by below formula

Scavenging % = $(\text{Absorbance of control} - \text{Absorbance of test}) / \text{Absorbance of control} \times 100$

The result of this activity can be showed the percentage. In DPPH method, the scavenging activity of *C. papaya* reached to 96% in methanol, 96% in water, 98% in chloroform and standard garlic acid found 83%. The percentage of H₂O₂ reached to 82% in methanol, 95% in water, 66% in chloroform and garlic acid found 95%.^[9]

ANTI-INFLAMMATORY ACTIVITY

Amazu *et al.* have reported the anti-inflammatory examined in rat by methanolic extract of seed *C. papaya*.^[10] The *C. papaya* seed was collected and made as powder form, and then extracted. 0.1 ml of fresh ovalbumin was injected to the right hind paw of adult white Wistar rat to give an intraperitoneal (IP) dose of 50–200 mg/kg of the extract 1 h later to three groups, each with five rat inducing inflammation. The four groups of five rats were used as negative control and received 2 ml/kg and (IP) 150 mg/kg of aspirin. Before and after injection of the extract the increase in paw diameter was measured with a Vernier caliper. The percentage of edema suppression for each dose group was calculated and the result was statistically analyzed using student *t*-test and analysis of variance (ANOVA). Finally, all the result was compared with negative control at time *t* and the below formula for calculating the percentage for inhibition of inflammation,

Average inflammation of negative control at time *t* / Average inflammation of treated group at time 1 × 100

%inhibition of inflammation = $100 - \% \text{ inflammation}$

The result as this experiment revealed the dose and time dependent inhibition effect of edema ($P < 0.05$).^[10]

Owoyele *et al.* have investigated the anti-inflammatory activity in ethanol extract of *C. papaya* leaves.^[11] They have investigated in rat by using carrageenan induced paw edema, arthritis model induced by the cotton pellet granuloma and formaldehyde. The extract was given to the experiment animal in dose of 25–200 mg/kg (orally) or saline (control group), while the reference group got 5 mg/kg of indomethacin. The ulcerogenic active of extract was also done. The result

revealed that the extract significantly ($P < 0.05$) decreases the paw edema in the carrageenan test. Similarly, the extract significantly reduced the amount of granuloma generated, reducing it from 0.58 ± 7 to 22 ± 0.03 g. The extract significantly decreases the persistent edema in formaldehyde arthritis model from 4 to 10-day investigation. Slight mucosal irritation when given the high dose of extracts.^[11]

ANTI-DIABETIC ACTIVITY

Solikhan *et al.* have recently reported the anti-diabetic activity in mice.^[12] The papaya leaves were extracted using ethanol and check the blood glucose levels in diabetic mice it's induced by alloxan. The mouse was acclimated for 7 days before being stimulate with 180 mg/kg alloxan intraperitoneally on day of 8. A dose of 250,500, or 1000 mg/kg body weight of papaya leaves extract was given for 14 days. Only distilled water and alloxan act as negative control. Glibenclamide at a dose of 2 mg/kg body weight act as positive control. The blood sample was collected on 1, 7, and 14 to assess blood glucose levels before and after treatment. The result of this experiment, 3 does of papaya extract and 2 mg/kg of body weight glibenclamide were administered in diabetic mice. Hence, it decreases the blood glucose levels. 1000 mg/kg of papaya extract administrated is more effective for reducing the blood glucose levels in diabetic mice when compared to 2 mg/kg of body weight glibenclamide administration. However, it did not reduce body weight of diabetic mice.^[12]

Nimenibo-Uadiaand Nwachukwu have examined the anti-hyperglycemic in alloxan induced albinorats using aqueous root extract of male *Caricapapaya*.^[13] For 7 days a 500 mg/kg body weight extract was gavaged orally twice daily. After 1 week of providing the extract, the elevated level of blood glucose, cholesterol, bilirubin, alanine aminotransferase (ALT), and alkaline phosphatase (AP) that result from the induction of diabetes was considerably ($P < 0.05$) reduced. When compared to diabetic control rats, the considerable decrease in total plasma protein of rats injected with alloxan was considerably ($P < 0.05$) exacerbated following administration of extract. The result shows that an aqueous extract of male *C. papaya* root improved the condition. Finally, the result revealed the aqueous extract of male *C. papaya* root reduced hyperglycemia and hypercholesterolemia, confirming its folkloric use as a diabetic treatment. Furthermore, the extract helped diabetic rat with hepatic tissue damage.^[13]

WOUND HEALING ACTIVITY

Nayak *et al.* have reported the wound healing activity in diabetic rat.^[14] The papaya fruit was extracted by aqueous method. Excision and dead space wound models were used to test the wound healing activity in papaya fruit extract (10 mg/kg. day for 10 days) in streptozotocin induced diabetic rat. When compared to control, which had a wound area of

59%, extract treated animal had a wound area reduction of 77%, in compared to control wound area treated with the extract epithelize faster. Finally, the *C. papaya* extract play a wound healing activity.^[14]

ANTI-HYPERTENSIVE ACTIVITY

Enoetal. have studied the antihypertensive activity using ethanol extract of ripe fruit papaya.^[15] The basal mean arterial blood pressure (MAP) was (93.8 ± 4.5), (175.2 ± 5), (181.3 ± 6.2) mm Hg in the normotensive, renal and DOC A – salt hypertensive animal. Both hydralazine (200 μ l/100 kg, i.v) and ethanol extract it papaya fruit (20 mg/kg, i.v) gives the significance depression of MAP in hypertensive animal group when compared to the control. However, extract gives the 25% more depression of MAP in the hypertensive animal group than hydralazine.^[15]

Ravikant *et al.* have utilized the ethanol extract of *C. papaya* root powder to evaluate the anti-hypertensive activity in renal artery occluded hypertensive rats.^[16] For 6 weeks, male Wistar rat (180–200 g) was given an ethanolic extract of *C. papaya* root bark. Animals were given a 4-h clamping of the renal artery with a renal building clamp to produce hypertension. The renin- angiotensin system is activated when the kidney is ischemia. This can cause blood pressure to rise. The ethanolic extractor *C. papaya* root bark at dose level of 25, 50m and 100 mg/kg, i.v., considerably ($P < 0.001$) reduced the animal elevated blood pressure. Furthermore, at a dose of 1 mg/kg, i.v., captopril, an angiotensin converting enzyme inhibitor (ACE-I), resulted in a substantial ($P < 0.001$) reduction in raised blood pressure at various time intervals. Among all the extract doses, 100 mg/kg was equivalent to and equipotent with captopril. The Antihypertensive activity of *C. papaya* root bark ethanol extract may be due to its action on the rennin-angiotensin system.^[16]

ANTI -FERTILITY ACTIVITY

Kusemiju *et al.* have investigated the antifertility activity using a crude extract of *C. papaya* bark on *Seminiferous tubules* of rats.^[17] On the *S. tubules* of rats, a crude extract of *C. papaya* bark (5–10 m/[kg.d], p.o for 4 days) caused complete loss of fertility which was attributed to a decline in sperm count. Motility of sperm and changes in their morphology was observed. As result bark demonstrated that he was safe and capable acting like guy. In animals, it acts as a contraceptive.^[17]

HISTAMINERGIC ACTIVITY

Adebiyi *et al.* have reported the histaminergic activity in crude extract of papaya latex on the pig ideal strips.^[18] The crude extract of *C. papaya latex* (0.5–51.2 g/ml) caused the

ideal strips suspended in the thyroid solution to contract in a concentration-dependent manner, which was mediated by H1 receptor that receptor is reliant on extracellular Ca^{2+} influx.^[18]

HEPATOPROTECTIVE ACTIVITY

Sadeque and Begum have studied the hepatoprotective activity in rats using ethanol and aqueous extract of *C. papaya* dried fruit.^[19] The extraction of dried papaya fruit, it play an important role in hepatoprotective activity against carbon tetrachloride induce the hepatotoxicity. The hepatoprotective activity is assessed using biochemical parameters such as serum bilirubin, serum alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase. The liver histopathological changes were compared to a control.^[19]

ANTHELMINTIC ACTIVITY

Roy *et al.* have investigated the anthelmintic activity using different extraction method (hydroalcoholic and chloroform).^[20] Various concentration of extraction (5%, 2.5%, and 1%) was examined *in vitro* and the finding were analyzed in term of paralysis (P) and death (D) when compared to the normal dryalbendazole, it displayed the shortest time for paralysis at a concentration of 5%, while the time for paralysis and death increased by 2.5% and 1%, respectively.^[20]

Satrija *et al.* have reported the high anthelmintic activity against *Heligmosomoides polygyrus* in infected mice using papaya latex extract.^[21] This suggests that it could be used as anthelmintic against mammalian intestinal worms.

Kermanshai *et al.*,^[22] Panse *et al.*,^[23] Kumari *et al.*,^[24] and Bose *et al.*^[25] have reported the anthelmintic activity using dried papaya seed extract. Dried papaya seed extract provided as an elixir with honey has been shown to have a major effect on human intestinal parasites without any side effects. The main anthelmintic is benzylisothiocyanate which is found in seed.^[22-25]

ANTI-CANCER ACTIVITY

Mahendran *et al.* have studied the anti-cancer activity in MCF- 7 breast cancer cell lines by leaf extract of papaya.^[26] First papaya leaves are collected and extracted using ethyl acetate solvents. Then various tests were carried out such as MTT assay, wound healing assay, DNA fragmentation assay, Caspase 7/9 induction assay and Annexin V assay for assist the anticancer and anti-metastatic activity of *C. papaya* extract in MCF – 7 cell lines. Finally, these all test reveals the *C. papaya* act as against breast cancer along with increased the dose, it results in increase the efficiency of *C. papaya* on the cancer cell lines.^[26]

DIURETIC ACTIVITY

Adam *et al.* have studied the diuretic activity of root extract of *C. papaya*.^[27] The papaya root was extracted using water solvents, it administrated orally at dose (5 and 10 mg/kg) to Sprague Dawley rats. Commercial diuretics, furosemide, and hydrochlorothiazide were given at a dose of 10 mg/kg to two different groups. The volume of pH, density and electrolytes of urine were measured every 4 h for 4 h. The serum levels of glucose, albumin, blood urea nitrogen (BUN), and creatinine were measured. *C. papaya* extract had mild to strong diuretic activity. *C. papaya* extract increase urine volume at 4 h when administered of 5 and 10 mg/kg. The removal of Na^+ and Cl^- remained the analysis. The extraction, on the other hand, substantially increased K^+ urinary excretion after 4 h. Extract resulted in the induction of when compared to control; there was a substantial increase in serum BUN and creatinine level ($P < 0.05$). However, these levels were still within the normal range. The papaya extract had no effect on blood glucose or albumin level. The extract of papaya root had diuretic activity; it is having the statistically similar potency to furosemide and hydrochlorothiazide.^[27]

Sripanikulchai *et al.* have investigated the diuretic activity in rat by aqueous extract of papaya root.^[28] When rat was given aqueous root extract of *C. papaya* orally at a dose of 10 mg/kg, urine output increased significantly and showed the urinary electrolyte excretion profiles that were like hydrochlorothiazide.^[28]

ANTI-AMOEBIC ACTIVITY

Tona *et al.* have reported the anti-amoebic activity against *Entamoeba histolytica*.^[29] The mature papaya extracted using aqueous method. 100 μl /ml of papaya extract gives the significance role in anti-amoebic activity against *E. histolytica*.^[29]

In another study, Sarkar *et al.* have reported the anti-amoebic activity of a methanol extract of mature *C. papaya* seed.^[30] They investigated the *in vitro* on an exenic culture of *E. histolytica* using metronidazoles as control. Seed extract had a MIC of >62.5 $\mu\text{g}/\text{ml}$, whereas metronidazoles had a MIC of <0.8 $\mu\text{g}/\text{ml}$. According to the findings, the mature seed of *Caricapapaya* has an anti-amoebic effect, but it is not as strong as metronidazole.^[30]

ANTI-ULCER ACTIVITY

Tolunigba and Adekunle have studied the gastroprotective activity of the ethanol extract of *C. papaya* seed on ethanol induced the gastric ulcer in male rat. 50 mg/kg and 100 mg/kg, p.o aqueous seed papaya extract against ethanol induced acute gastric damage and oxidative stress in rat blood. The gastric acidity was significantly decreased in rat when treated with 100 mg/kg of the extract.^[31]

Kaur, and Sen have reported the anti-ulcer activity of hydroalcoholic extract of *C. papaya* unripe fruit in rat.^[32] The unripe of *C. papaya* extracted using hydroalcoholic solvent was used in this study. In a pyloric ligation induced gastric ulcer model, treatment with 500 mg/kg of hydroalcoholic extract of *C. papaya* unripe fruit was successfully in reducing ulcer index. This extract showed a dose-dependent decrease in the ulcer index which was supported by physiological and histological studies.^[32]

ANTI-MALARIAL ACTIVITY

Kovindan *et al.* have investigated the antimalarial activity against *Plasmodium falsiparum*.^[33] The *C. Papaya* was extracted using ethanol solvent and then to make the 1% stock solution. The different concentrations were prepared; it ranges from 2, 4, 6, 8, and 10%, respectively, from this stock solution. The ethanol extract has the high larval mortality against the 1–4th stage instar larvae and pupae value of LC50 = 3.65%, 4.28%, 5.41%, 6.70%, and 7.80% and LC90 value as 9.61%, 11.75%, 13.53%, 16.36%, and 16.92 %, respectively. The extract revealed the moderate to good activity against CQ sensitive strain with (IC50) value of 40.75%, 36.54%, 25.30%, and 18.0% and in CQ resistant 50.23%, 32.50%, 21.45%, and 23.12% against *P. falciparum*.^[33]

Bhat and Surolia have studied the anti-malarial activity using rind of raw papaya extract.^[34] The raw fruit extraction was obtained using petroleum ether. The extraction at various concentration ranges from 0.05 to 1000 g/ml. The extract significantly plays the role in antimalarial activity.^[34]

EFFECT ON SMOOTH MUSCLE

Adebivi *et al.* have reported the reduction of muscle contraction in rabbits using ethanol extract of papaya seed.^[35] The inhibition of jejunam contraction by ethanol extract of papaya seed at concentration range from 0.1 to 6.4 mg/ml was found to be concentration dependent and irreversible. The extraction was capable to reduce the contractile strength of the jejunam rabbit.^[35]

ANTI-SICKLING ACTIVITY

Imaga *et al.* have investigated the *C. papaya* extract by using methanol. The 10 mg/ml of *C. papaya* extract dose decrease the hemolysis and promote the erythrocytes membrane integrity under the osmotic stress.^[36]

IMMUNO-MODULATORY ACTIVITY

MohdAbdRazak *et al.* have performed the immunomodulatory activities of freeze dried *C. papaya* leaf juice on

AG129 mice infected with a clinical DENV – 2 isolates.^[37] The infected AG129 mice were orally treated with 500 and 1000 mg/kg of FCPLJ for 3 days. The platelet, leukocyte, lymphocytes, and neutrophils were identified by microscope based on morphology. The multiplex immunoassay used for measuring the level of plasma pro-inflammatory. RT – qPCR is used to detect the level of intercellular cytokines and viral RNA. The result as FCPLJ treatment reduces the total WBC and neutrophils count in the mice. It also reduces the level of GM – CSF, GRO – alpha, IL- 1 beta, IL – 6, MCP – 1, and MIP 1 beta in the plasma of infected mice. The intercellular IL- 6 and viral RNA level in the liver of infected mice were decrease by FCPLJ treatment.^[37]

Amin *et al.* have utilized the *C. papaya* pulp and seed extract by methanolic extract in mice infected with *L. monocytogenes*.^[38] The animal divided into two groups as negative control (G1) and positive control (G2). Pulp extracts treat with G3 and seed extract treat with G3. After infected animal (G2, G3, and G4), treat was started for 3 weeks. Estimated the immunological parameters showed the marked reduce in the IgM level and increase in IgG level in the treatment group (G3 and G4) compared to G2. The pro-inflammatory cytokines were reduced in treated group (G3 and G4) compared to G2. Nitric oxide level also reduced and the % of phagocytosis could be increased compared to G2.^[38]

ANTI-DIARRHEAL ACTIVITY

Prabhu *et al.* have investigated the anti-diarrheal activity against gut pathogen using of papaya raw and ripe fruit extraction.^[39] The *C. papaya* fruit was extracted using the different solvents method (ether, benzene, chloroform, acetone, ethanol, and aqueous). MIC of the extraction is determined using 96 well plates. The extract has inhibiting activity against gut pathogen. The result as the raw and ripe fruit extract, the acetone extracts ripe fruit (0.3 mg/ml) and chloroform raw fruit extract (25.0 mg/ml). Thus, it revealed that the good activity of papaya extract against gut pathogen. The MIC and MBC values range from 100 to 0.39 mg/ml. The activity of *C. papaya* seen in *P. shigelloides*, it ranges from 50 to 0.3 g/ml.^[39]

ANTI-DENGUE ACTIVITY

Sharma *et al.* have studied the anti-dengue activity against the dengue virus (DENV) and its effect on the platelet augmentation using aqueous extract of *C. papaya* leaves.^[40] The dengue activity of *C. papaya* leaves extract in the DENV infected THP1 cells was determined by using immunoblotting and flow cytometry technique. Hemolytic and anti-hemolytic assay used for detecting the erythrocytes damage due to effect of leaf extract. IFN secretion was measured in virus infected THP1 cells. In addition, the effect of papaya extract on platelet augmentation on rat

with cyclophosphamide induced thrombocytopenia were studied on the 4, 5, 7, 11, and 14 days of the analysis, the platelet count of blood from retro – orbital Plexus of rats was calculated. The rat was sacrificed on 14th day for histopathological analysis of the liver, kidney, and spleen. TPO and IL – 6 secretions were measured in the plasma of thrombocytopenia rat. The finding indicates the papaya extract reduce the expression of the envelope and NSI protein in DENV infected THP1 cell significantly. The antiviral activity of papaya extract was confirmed by a significant reduction in intracellular viral load after treatment. There was also significant reduction in erythrocytes damage and hydrogen peroxide induced lipid peroxidation as a result of this. The thrombocytopenia rat treated with papaya extract, there was significantly increase in platelet number as well as increase in IL – 6 and TPO.^[40]

BIOACTIVE COMPOUNDS

In *C. papaya*, different bioactive compounds are present such as alkaloids, flavonoids, glycosides, and steroids etc. It is playing an important role in medicinal as treat the disease. These bioactive compounds are identified using photochemical screening methods and GCMS analysis.

PHYTOCHEMICALS ANALYSIS IN LEAVES

Subham *et al.* have analyzed the photochemical constituent in papaya leaves is done by photochemical screening method.^[41] The test showed the present of bioactive compounds such

1. Alkaloids
2. Flavonoids
3. Reducing sugar
4. Saponin
5. Steroids
6. Tannins

Glycosides compounds did not present in papaya leaves.^[41]

PHYTOCHEMICAL ANALYSIS IN ROOT

Singh *et al.* have performed the phytochemicals analysis for determining the bioactive components in aqueous extract of papaya root.^[42] The result as the present of bioactive components

1. Alkaloids
2. Sugar
3. Flavonoids
4. Protein

Terpenoids, phenol and tannins, saponins, and Quinone's components absence in root extract of papaya.^[42]

PHYTOCHEMICAL ANALYSIS IN SEED

Neethu *et al.* have investigated the photochemical analysis in different extract of papaya seed (ethanol, chloroform, and acetone).^[43] The result revealed as in ethanol extract, the present of bioactive components such as

1. Alkaloids
2. Flavonoids
3. Carbohydrates
4. Protein
5. Starch
6. Steroids
7. Saponins
8. Terpenoids
9. Glycosides

Amino acids, tannins, and gum components absence in this extract. In chloroform, the presence of bioactive compound such as

1. Alkaloids
2. Carbohydrates
3. Protein
4. Starch
5. Amino acids
6. Saponins

Flavonoids, steroids, tannins, glycosides, and gum components are absent in this extract. In acetone extract, the presence of bioactive compound such as

1. Alkaloids
2. Carbohydrates
3. Protein
4. Amino acids

Flavonoids, starch, steroid, tannins, saponins, terpenoids, glycosides and gum components are absent in this extract.^[43]

PHYTOCHEMICALS ANALYSIS IN FLOWER

Dwivedi *et al.* have investigated the phytochemicals analysis in different extract of papaya flower (methanol, chloroform, n-hexane, and aqueous).^[44] The test showed as in methanol extract, presence of bioactive compound such as

1. Alkaloids
2. Flavonoids
3. Saponins
4. Tannins

Phlobatanine, glycosides are absent in this extract. In chloroform extract, presence of components such as saponins and tannins were observed. Remaining components are absence in this extract. In n – hexane extract, flavonoids, steroid, saponins, and terpenoids are present and remain components are absent in this extract. In aqueous extract, the presence of bioactive compound was observed such as

Table 1: Phytochemicals analysis of papaya flower

Phytochemicals	Methanol	Chloroform	N – hexane	Aqueous
Alkaloids	+	-	-	-
Flavonoids	+	-	+	+
Saponins	+	+	+	+
Steroids	+	-	+	-
Tannins	+	+	+	+
Phlobatannins	-	-	-	-
Glycosides	-	-	-	-

+ indicate present, - indicate absent

Table 2: Phytochemicals screening of papaya fruit

Phytochemicals	Ethanol	Chloroform	Benzene
Steroids	+	-	-
Flavonoids	+	-	-
Alkaloids	+	+	-
Carbohydrates	+	-	-
Cardiac glycosides	+	-	-
Tannins	-	+	-
Anthraquinone	+	+	-

+ indicate present, - indicate absent

Table 3: Compound in butanol extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
20.55	Ascorbic 2,6 dihexadecaoate	C ₃₈ H ₆₈ O ₈	652	16.67
23.293	9-octadecenoic acid ethyl ester	C ₂₀ H ₃₈ O ₂	310	28.86
23.632	Octadecanoic acid	C ₁₈ H ₃₆ O ₂	284	14.22

flavonoids, steroids, and terpenoids. Remain components are absent in this extract [Table 1].^[44]

PHYTOCHEMICALS ANALYSIS IN FRUIT

Eke *et al.* have analyzed the phytochemicals analysis in different extract of papaya fruit.^[45] In ethanol extract, the presence of bioactive components such as

1. Steroids
2. Flavonoids
3. Carbohydrates
4. Alkaloids
5. Cardiac glycosides
6. Anthraquinone

Tannins only absent in this extract. In chloroform extract, alkaloids, tannins, and anthraquinone are present and remain

components are absent in this extract. In benzene extract did not contain any bioactive components [Table 2].^[45]

GCMS ANALYSIS OF PAPAYA LEAVES

Chidozie and Adoga have investigated the bioactive compound using GCMS in crude extract of *C. papaya* of different solvents.^[46] *Butin butanol* extraction have high compounds and its had high activity. Hence, the analysis of fraction obtained from the n-butanol extract of *C. papaya* after it was subjected to column chromatography and thin layer chromatography. The compound or compounds group are identified through GCMS analysis. The substances in the plant extract are used in herbal medicine. Eight peaks were found in the GCMS analysis of *C. papaya* leaf extract, indicating the present of eight compounds. Three compounds are identified based on the molecular structure, molecular mass, molecular weight, and calculated fragment. The compounds such as ascorbic 2,6dihexadecaoate,9-octadecenoic acid ethyl ester and octadecanoic ascorbic acid 2,6 dihexadecaoate have antibacterial, anti-inflammatory, antioxidant, and antimociceptic activities [Table 3].^[46]

Using gas chromatography– mass spectroscopy (GCMS) analysis in the selected ion monitoring (SIM) mode, *C. papaya* leaves were extracted with methanol in a Soxhlet apparatus and with liquid chromatography (LLC) with the goal of identifying and quantifying metabolites for this plant.^[47] Derivatization is a term that refers to the process of to examine the polar compound in GCMS, a method of the extract was required. In qualitative examination, 5,7- dimethozycoumarin and polar compound such as protocatechuic, chlorogenic acid, kaempferol, and quercetin were found and identified. In comparison to flavonoids and coumarin compound, quantitative analysis revealed the existence of phenolic acids as the major constituent, with chlorogenic acid identified in minimal level. Caffeic acid was found in concentration of 0.25 mg/g (dry leaf), 0.33 mg/g for p-coumarin acid and 0.11 mg/g for protocatechic acid. Kaempferol and quercetin had concentration of 0.03 and 0.04 mg/g, respectively, whereas 5,7- dimethozycoumarin had a concentration of 0.14 mg/g [Table 4].^[47]

Table 4: Compound in methanol extraction by GCMS analysis

Retention time	Compound	Molecular weight	TMS group	TMS derived molecular weight
11.02	Protocatechuic	154	3	370
11.78	P-coumarin acid	164	2	308
11.89	5,7 Dimethoxy coumarin	206	0	-
12.97	Caffeic acid	180	3	396
19.53	Kaempferol	286	4	574
20.77	Quercetin	302	5	662
20.07	Chlorogenic acid	354	6	786

Table 5: Compound in papaya extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
6.539	Glycerin	C ₃ H ₈ O ₃	920.9	4.15
9.792	Benzyl nitrile	C ₈ H ₇ N	117.1479	1.04
10.30	2-phenyl-1,3-oxazol-2-line	C ₉ H ₉ NO	147.17	2.45
11.69	2-methoxy-4-vinylphenol	C ₉ H ₁₀ O ₂	150.174	1.04
14.614	Chloroacetic acid 2,2-dimethyl	C ₇ H ₁₃ CO ₂	164.62	1.22
15.567	9-octadecyne	C ₁₈ H ₃₄	250.46	4.14
15.535	3,4-Altrosan	C ₆ H ₁₀ O ₅	162.140	2.64
15.442	L/(D) arabinitol	C ₅ H ₁₂ O ₅	152.14	3.48
15.601	Citronellyl butyrate	C ₁₄ H ₂₆ O ₂	226.355	0.83
15.776	3,7,11,15 tetra methyl-2- hexadecanoic acid	C ₂₀ H ₄₀ O	296.53	1.21
16.801	N-aminomorpholine	C ₄ H ₁₀ N ₂ O	102.135	1.30
16.807	Methyl-2(methoxy (methyl) amino)-2N methylpropanoate	C ₇ H ₁₅ N ₃ O	161.198	1.30
17.446	n-Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	256.42	14.73
17.722	4((CIE)-3hydroxy-1-propanyl)-2-methoxyphenol	C ₁₀ H ₁₂ O ₃	180.200	1.70
18.651	Pytol	C ₂₀ H ₄₀ O	296.53	3.64
19.77	9,12,15 octadecatrienoic acid	C ₁₈ H ₃₀ O ₂	278.42	2.11
24.519	Crotonoyl bromide	C ₄ H ₅ BrO	148.98	1.56
24.501	4-cyclopropylcarbonyloxytetradecane	C ₁₈ H ₃₄ O ₂	282.461	1.56
27.133	2-chloro-11H-pyrido (3,2-4,5) pyrolo (3,2-C) quinioline	C ₁₄ H ₈ ClN ₃	253.68	0.71
23.182	(3-Bromo-1-methylpropoxy methyl) benzen	C ₁₁ H ₁₅ BrO	243.140	3.47
27.670	Vitamin-E	C ₂₉ H ₅₀ O ₂	430.70	2.70
29.05	5methyl-2-(N-ethyl-P-chlorophenylamine)-2-thiazoline	C ₁₂ H ₁₅ ClN ₂ S	254.77	3.20
29.396	1,2-Dihydropyrido (3,2,1-KI) phenothiazin-3-one	C ₁₅ H ₁₁ NOS	253.31	3.27
30.023	Beta-sitosterol	C ₂₉ H ₅₀ O	414.711	11.04
32.535	2,4,7 trinitrofluorenone	C ₁₃ H ₅ N ₃ O	315.1947	2.18

GCMS used to determine the phytochemicals in methanol of *C. papaya*.^[48] Fresh *C. papaya* leaves were harvested carefully washed and shade dried for 8–10 days using methanol, 200 g of crush leaves were extracted progressively in a Soxhlet device. The chemical compounds of the extract as studied using Perkin –Elmer gasch – ms and the mass spectra of the substance detected in the extract were compared to NIST library. Totally 25 compounds were detected [Table 5].^[48]

GCMS ANALYSIS OF PAPAYA SEED

Iyappan *et al.* have investigated phytochemicals present in the ethanolic crude extract of *C. papaya* var.co.7 seeds.^[49] Mass spectrum was interpreted with the help of NIST, library and 27 different compounds were identified. It consists mostly of fatty acid, ester, and phenolic hydrocarbon [Table 6].^[49]

Table 6: Compound in ethanol extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
13.19	1-(2-methoxy-5-nitrophenyl) ethanone	C ₁₁ H ₁₃ NO ₄	223	0.02
19.8	Phenol, 2- methyl-5-(1,2,2-trimethylcyclopentyl),(S)	C ₁₅ H ₂₂ O	218	0.02
29.5	Tributylacetyl citrate	C ₂₀ H ₃₄ O ₈	402	0.02
30.83	2-propenoic acid, 3-(4-2-methoxyphenyl)-ethylhexylester	C ₁₈ H ₂₆ O ₃	290	0.02
12.82	(11R)-(-)-11-carbomethoxy-11-(1-)-methoxyacetyl)-9,10-dihydroxy-9,10- ethanoanthracene	C ₃₀ H ₃₆ O ₄	460	0.03
13.76	2-.methoxy-5H-dibenz (b, f) azepine	C ₁₅ H ₁₃ N	207	0.03
20.92	3-methyl-5-trifluoromethyl-3,4-diazatetracycol (7.3.1.(7,11).o (2,6)) tetradeca-2 (6),4-diene	C ₁₄ H ₁₇ F ₃ N ₂	270	0.03
27.45	(2S, 3R-2-tert- Butylthio-1-phenylbutan-2-ol	C ₁₄ H ₂₂ OS	238	0.03
29.01	1-octadecanamide	C ₁₈ H ₃₅ NO	251	0.03
21.66	Hexadecanoic acid, methyl ester	C ₁₇ H ₃₄ O ₂	270	0.04
24.82	Hepatadecanoic acid, ethyl ester	C ₁₉ H ₃₈ O ₂	298	0.04
33.43	Hexadecanoic acid, phenylmethylester	C ₂₃ H ₃₈ O ₂	346	0.05
29.75	cis-11-Eicosenoic acid, methyl ester	C ₂₁ H ₄₀ O ₂	324	0.14
36.59	Supraene	C ₃₀ H ₅₀	416	0.28
23.02	Hexadecanoic acid, ethylester	C ₁₈ H ₃₆ O ₂	284	4.72
14.68	Dodecanoic acid, ethylester	C ₁₄ H ₂₈ O ₂	228	1.13
30.3	i-propyl9-octadecenoate	C ₂₁ H ₄₀ O ₂	324	0.04
25.37	9-octodecenoic acid (Z)-, methyl ester	C ₁₉ H ₃₆ O ₂	296	0.34
18.91	Tetradecanoic acid, ethylester	C ₁₆ H ₃₂ O ₂	256	0.85
35.67	Ethyl tetracosanoate	C ₂₆ H ₅₂ O ₂	396	0.04
27.24	Ethyl linoleolate	C ₂₀ H ₃₆ O ₂	308	0.05
32.21	6-methyl-3-methylimino-4-oxo-34-Dihydro-2h-1-Benzothiopyran-N--oxide	C ₁₁ H ₁₁ NO ₂ S	221	0.11
32.21	L-(+)-Rhamnopyranose, tetrakis (trimethylsilyl) ether	C ₁₈ H ₄₄ O ₅ Si ₄	452	0.11
33.88	Tetramethyl Diabenzotetraaza-18-crown-6	C ₂₄ H ₃₆ N ₄ O ₂	412	0.11
31.15	1 (10) dibenzacyclodeca-2, 9-diynaphane	C ₃₃ H ₂₂ OS	466	0.14
37.55	2-Heptyl-6,7-dihydro-3-methyl-4H-pyrol (2,1-b)(1,3) oxazine-4, 8 (8aH)-dione-8-oxome	C ₁₅ H ₂₄ N ₂ O ₃	280	0.21
23.87	1-(1H-indil-2-yl)-1,3,3-trimethyl-1,2,3,4-tetrahydroxyclopint (6) indole	C ₂₂ H ₂₂ N ₂	314	11.37

Table 7: Compound in methanol extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
15.974	n-Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	256	71.55
16.966	13-Hexyloxacyclotride-10-en-one	C ₁₈ H ₃₂ O ₂	280	1.19
17.718	Oleic acid	C ₁₈ H ₃₄ O ₂	282	30.21
17.868	Oleic acid	C ₁₈ H ₃₆ O ₂	284	5.28
18.905	Hexadecanoic acid, 3-dihydropropylester	C ₁₈ H ₃₈ O ₉	330	2.37
19.512	Undecylenic acid	C ₁₈ H ₂₀ O ₂	184	40.33
20.412	9-octadecenal	C ₁₈ H ₃₄ O	266	7.09
23.345	9,17-octadecadienal,(Z)-	C ₁₈ H ₃₂ O	264	5.98

Table 8: Compound in aqueous extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
15.987	n-Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	256	7.83
16.109	Hexadecanoic acid methyl ester	C ₁₈ H ₃₆ O ₂	284	3.65
16.970	13-Hexaloxacyclotride-10-en-one	C ₁₈ H ₃₂ O ₂	280	2.72
17.733	Oleic acid	C ₁₈ H ₃₄ O ₂	282	31.58
17.877	Octadecanoic acid	C ₁₈ H ₃₆ O ₂	284	5.68
17.983	Octadecanoic acid, ethyl ester	C ₂₀ H ₄₀ O ₂	312	2.73
18.910	Hexadecanoic acid, 1-[[[(2-aminoethoxy) hydroxyphenyl] oxy] methyl]-1,2-ethanediyl ester	C ₂₇ H ₇₄ NO ₈ P	69211	2.26
19.439	Undecylenic acid	C ₁₁ H ₂₀ O ₂	184	12.60
20.408	10-undecenal	C ₁₁ H ₂₀ O	168	7.44
20.591	1-octanol, 2-butyl	C ₁₂ H ₂₆ O	186	1.72
20.777	Hexadecanoic acid 2,3-dihydroxypropylester	C ₁₉ H ₃₈ O ₄	330	4.08
22.091	10-undecenoylchloride	C ₁₁ H ₁₉ C ₁₀	202	4.55
22.369	9,12-octadecadienoyl chloride	C ₁₈ H ₃₁ C ₁₀	298	13.18

Table 9: Compound in aqueous extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
6.121	Dianhydromannitol	C ₆ H ₁₀ O ₄	146	7.36
15.695	Methyl-11-hexadecanoate	C ₇ H ₃₂ O ₂	268	4.91
15.968	Hexadecanoic acid, methyl ester	C ₁₇ H ₃₄ O ₂	270	35.63
18.679	10-octadecanoic acid, methyl ester	C ₁₉ H ₃₆ O ₂	296	30.13
19.069	Octadecanoic acid, methyl ester	C ₁₉ H ₃₈ O ₂	298	3.49
24.669	1,1,3,3,5,5,7,7,9,9,11,11-Dodecamethylhexasiloxane	C ₁₂ H ₃₈ O ₅ Si ₆	439	6.97
31.657	Ergosta-5, 22-dien-ol acetate (3 beta-22E)	C ₃ H ₄₈ O ₂	440	11.50

Table 10: Compound in aqueous extraction by GCMS analysis

Retention time	Compound name	Molecular formula	Molecular weight	Peak%
25.183	Hexadecanoic acid, 2,3-dihydroxypropyl	C ₁₉ H ₃₈ O ₄	330	4.72
19.703	Octadecanoic acid	C ₁₈ H ₃₆ O ₂	284	23.84
18.709	12,15 octadecanoic acid, methyl ester	C ₁₉ H ₃₄ O ₂	294	5.38
16.568	n-Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	256	0.78
16.269	Hexadecanoic acid, Z-11	C ₁₆ H ₃₀ O ₂	254	19.17
27.983	9,12,15-octadecatrienoic acid, 2-[(trimethyl)-1-[[trimethylsilyl] oxy] methyl] ethyl (9E,12E,15E)-9,12,15-octadecatriene	C ₂₇ H ₅₂ O ₄ Si ₂	496	3.85
4.614	4 (1H)-pyrimidin one, 2,6-diamino	C ₄ H ₆ H ₄ O	126	2.27
4.764	1,2,3-propanetriol, monoacetate	C ₅ H ₁₀ O ₄	134	2.19
5.517	4H pyranone-2, 3-dihydro-3,5-dihydroxy-dihydroxy-6-methyl	C ₆ H ₈ O ₄	144	4.25
6.451	6-Acetyl-veta-D-mannose	C ₈ H ₁₄ O ₇	222	3.31
8.588	2,4-Hexadienedioic acid	C ₆ H ₆ O ₄	142	4.06
13.05	1-Gala-1-ido-octose	C ₈ H ₁₆ O ₆	240	3.19
13.58	Tetradecanoic acid	C ₁₄ H ₂₈ O ₂	223	3.88
15.52	Benzoic acid, 14-hydroxy-3,5-dimethoxy	C ₉ H ₁₀ O ₅	198	1.13
16.52	Hexadecanoic acid, methyl ester	C ₁₇ H ₃₄ O ₂	270	18.25

Table 11: Compound in methanol extraction by GCMS analysis

S. No	Compound name
1	10-Heptadecen-8-ynoic acid, nethu ester
2	3,6-octadecadignoic acid, methyl ester
3	7-epi-cis-sesquisabinene hydrate
4	Methyl5-Cyclopropyl-1-(4-fluorophenyl)-1H-pyrazole-3 carboxylate, c-copaene
5	Tetradecanoic acid
6	Tridecanoic acid
7	Pentade acid
8	Hexadecanoic acid, methyl ester, n-Hexadecanoic acid
9	Hexadecanoic acid
10	1-(+)-Ascorbic acid2, 6-dihexadecanoate
11	9,12-octadecadienoic acid (Z, Z), methyl ester, methyl 9-cis
12	11-trans-octadecadienoate
13	9,12-octadecadienoate, methyl ester, methyl 9-cis
14	9-octadecenoic acid (Z)-, methyl ester
15	11-octadecenoic acid, methyl ester
16	Trans-13-octadecenoic acid, methyl ester, methyl stearate
17	Hepatadecanoicacid, 16-methyl-, methyl ester
18	Cyclopropanebutanoic acid
19	2-[[2-[[2-[(2-pentacyclopropyl) methyl]cyclopropyl]cyclopropyl]-, methyl ester
20	Y, 9,12-octadecatrienoic acid, methyl ester, methyl 6-cis, 9 cis
21	11-trans-octadectrienoate
22	13,16-octadecadinoic acid, methyl ester
23	[1,1-Bicyclopropyl]-2-octanoic acid, 2-hexyl, methyl ester
24	Chloest-ZZ-one-21-ol
25	3,5-dehydro-6-methoxy, pivalate
26	Ethyl-iso-allochololate
27	Stigmasterol
28	1-Heptatriacotanol
29	a-sitosterol
30	c-sitosterol
31	Cholesta-8, 24-diess-3-ol, 4 methyl-, (3a, 4a)-
32	5-chloestene-3-ol, 2u methyl

The *C. papaya* seed were collected and then air dried. Finally, it was made as fine powder. The extract is prepared by using methanol and aqueous solvents by Soxhlet extractor. From this, 21 compounds were identified. These compounds were investigated the pharmacological activities [Tables 7 and 8].^[50]

GCMS ANALYSIS OF PAPAYA ROOT

Ezekwe and Chikezie have investigated the GCMS analysis of papaya root.^[51] 7 compounds are detected in aqueous extract of papaya root by using GCMS analysis [Table 9].^[51]

GCMS ANALYSIS OF PAPAYA UNRIPE FRUIT

Ezekwe and Chikezie have identified the phytochemicals in aqueous extract of unripe fruit of *C. papaya* by GCMS detection system.^[52] The result revealed the 15 phytochemicals present in aqueous extract of unripe fruit of *C. papaya*. In term of relative abundance, the major phytochemicals present in aqueous extract of *C. papaya* were octadecanoic acid, hexadecanoic acid, Z-11 and hexadecanoic acid, methyl ester, which accounts for 23%, 48%, 19.17%, 18.25%, respectively. The relatively abundance of minor photochemical compound contained in *C. papaya* aqueous extract of unripe fruit ranges from 0.78 to 5.38%. The current study discovered that the aqueous extract of papaya unripe fruit contained a wide range of metabolites, therapeutic active substances, and novel substances. These compounds might be isolated and empirically examined to confirm their biological and therapeutic action as well as investigate their mechanism of action [Table 10].^[52]

GCMS ANALYSIS OF PAPAYA FLOWER

Singh *et al.* have analyzed the bioactive compound in methanolic extract of *C. papaya* male flower.^[53] The GCMS spectra of the identified compounds are identified compounds were compared with NIST database library. The result showed the presence of 32 compounds [Table 11].^[53]

CONCLUSIONS

The whole plant has own medicinal value. The *C. papaya* has the wide range of pharmacological activities. By traditionally claims papaya is a powerful medicine. The different extracts have been found possess various pharmacological activities. The present review is all about pharmacological activities and the bioactive compounds.

REFERENCES

1. Anjum V, Ansari SH, Kamaran J, Arora P, Ahmad A. Development of quality standards of *Carica papaya* Linn. leaves. *Sch Res Lib* 2013;15:370-6.
2. Vijay T, Parashar Y. A review on medicinal properties of *Carica papaya* Linn. *Asian Pac J Trip Dis* 2015;5:1-6.
3. Yogiraj V, Goyal PK, Chauhan CS, Goyal A, Bhupendra V.

- Caricapapaya* Linn: An overview. *Int J Herb Med* 2014;2:1-8.
4. Wadekar AB, Nimbawar MG, Panchale WA, Gudalwar R, Manwar JV, Bakal RV. Morphology, phytochemistry and pharmacological aspect of *Carica papaya*; an review. *GSC Biol Pharm Sci* 2021;14:234-48.
 5. Romasi EF, Karina J, Jan A, Parhuship N. Antibacterial activity of papaya leaf extract against pathogenic bacteria. *Makara Teknol* 2011;15:173-7.
 6. Gupta A, Patil SS, Pendharkar N. Antimicrobial and anti-inflammatory activity of aqueous extract of *Carica papaya*. *J Herbmed Pharmacol* 2017;6:148-52.
 7. Doughari JH, Elmahmood AM, Mansara S. Studies on the antibacterial activity of root extract of *Carica papaya* Linn. *Afr J Microbiol Res* 2017;21:37-41.
 8. Aboobacker HK, Valoth G, Kizhedath S. *In vitro* study on the anti-oxidant activity of methanolic leaf extract of *Carica papaya*. *Int J Basic Clin Pharmacol* 2020;9:652-6.
 9. Banik B, Sahu N, Chetia N, Saikia M, Boruah P. Evaluation of anti-oxidant and antimicrobial activity of *Carica papaya* (Amita) leaf extract. *Pharm Res* 2017;24:16-25.
 10. Amazu LU, Azikiwe CC, Njoku CJ, Osuala FN, Nwosu PJ, Ajugwo AO, *et al.* Anti-inflammatory activity of the methanolic extract of the seeds of *Carica papaya* in experimental animal. *Asian Pac J Trop Med* 2010;3:884-6.
 11. Owoyele BV, Adebukola OM, Funmilayo AA, Soladoye AO. Anti-inflammatory activities of ethanolic extract of *Carica papaya* leaves. *Inflammo Pharmacol* 2008;16:168-73.
 12. Solikhhan TI, Setiawan B, Ismukada DR. Anti-diabetic (*Carica papaya* Linn) isolated with maceration method in alloxan induces diabetic mice. *Sys Rev Pharm* 2021;11:774-8.
 13. Nimenibo-Uadia R, Nwachukwu K. Anti-diabetic effect of aqueous root extract of *Carica papaya* L. in alloxan induced diabetic rats. *J Natl Sci Res* 2020;10:2224-3186.
 14. Nayak BS, Pereira LP, Mahar D. Wound healing activity of *Carica papaya* Linn. Experimentally induced diabetic rats. *Indian J Exp Biol* 2007;45:739-43.
 15. Eno AE, Owo OI, Itam EH, Konya RS. Blood pressure depression by the fruit of juice of *Carica papaya* (L.) in renal and DOC A-induced hypertension in the rat. *Phytother Res* 2000;14:235-9.
 16. Revikant T, Nishant G, Shashipal S, Samriti T, Rajeevkumar T, Vikas V, *et al.* Antihypertensive effect of ethanolic extract of Indian *Carica papaya* Linn. Root bark (Caricaceae) in renal occluded hypertensive rats. *Int J Pharm Clin Res* 2012;4:20-3.
 17. Kusemiju O, Noronha C, Okanlawon A. The effect of crude extract of the bark of *Carica papaya* on the semiferoustubules of the male sprange-pawleyrats. *Niger Postgrad Med J* 2002;9:205-9.
 18. Adebisi IA, Adaika PG, Prasad RN. Histaminergic effect of crude papaya latex on isolated guinea pig ileal strips. *Phytomedicine* 2004;11:65-70.
 19. Sadeque MZ, Begum ZA. Protective effect of dried fruit of *Carica papaya* on hepatotoxicity in rat. *Bangladesh J Pharmacol* 2010;5:48-50.
 20. Roy SD, Goswami R, Das S, Shil D, Baniya P, Halder S. Pharmacognostic evaluation and anthelmintic activity of leaf and stem extract of *Carica papaya*. *J Pharm Res* 2012;15:4763-6.
 21. Satrija F, Jansen P, Murtni S, He S. Anthelmintic activity of papaya latex against *Heligmosomoides polygrus* infection in mice. *J Ethnopharmacol* 1995;48:161-4.
 22. Kermanshai R, Mccary BE, Rosenfeld J, Summers PS, Weretilnyk EA, Sorger GJ. Benzyl isothiocyanate is the chief or sole anthelmintic in Papaya seed extract. *Photochemistry* 2001;57:427-38.
 23. Panse TB, Paranjpe AS. Carpasemine isolated from *Carica papaya* seeds. *Proc Indian Acad Sci* 1943;18:140.
 24. Krishnakumari MK, Majumder SK. Studies on anthelmintic activities of seed of *Carica papaya* Linn. *Ann Biochem Exp Med* 1960;20:551-6.
 25. Bose BC, Saifi AQ, Vijayrargiya R, Bhagat AW. Pharmacological study of *Carica papaya* seed with special reference to its anthelmintic action, preliminary report. *Indian J Med Sci* 1961;15:888-92.
 26. Mahendra VS., Sophiya K, Malavika SS, Suganthi B, Sujitha E. *Carica papaya*: Anthelmintic activity in MCF-7 breast cancer cell lines. *IJPSR* 2021;12:176-82.
 27. Adam Y, Nasaraddin AA, Zuraini A, Arifah AK, Fauze MS, Zakaria ZA, *et al.* Diuretic activity of roots from *Carica papaya* Linn and *Ananas comosus* Linn. *Int J Pharm Sci Res* 2013;23:163-7.
 28. Sripanikulchai B, Wongpanich V, Laupattarakasem P, Suwansakri J, Jirakulsomchok D. Diuretic effect of selected Thai indigenous medicinal plant in rats. *J Ethnopharmacol* 2001;75:185-90.
 29. Tona L, Kambu K, Ngimbi N, Cimanga K, Vlietinck AJ. Anti-amoebic and photochemical screening of some Congolese medicinal plant. *J Ethnopharmacol* 1998;6:57-65.
 30. Sarkar SK, Begam N, Mondal D, Siddique MA, Rashid MA. *In-vitro* study of anti-amoebic effect of methanol extract of mature seed of *Carica papaya* on trophozoites of *Entamoeba histolytica*. *Bangladesh J Pharmacol* 2010;5:45-7.
 31. Tolunigba AO, Adekunle WO. Gastroprotective activity of aqueous *Carica papaya* seed extract on ethanol induced gastric ulcer in male rat. *Afr J Biotechnol* 2012;11:8612-5.
 32. Kaur R, Sen K. Antiulcer activity of hydroalcoholic extract of unripe fruit of *Carica papaya* in experiment rat. *Int J Basic Clin Pharmacol* 2017;6:432-40.
 33. Kovendan K, Murugan M, Paneerselvam C, Aarthi N, Kumar PM, Subramanian J, *et al.* Anti-malarial activity of *Carica papaya* Linn. (Family: Caricaceae) leaf extract against *P. falciparum*. *Asian Pac J Trop Dis* 2012;2:306-11.
 34. Bhat GP, Sarolia N. *In-vitro* anti-malarial activity of extract of three plant used in the traditional medicine of indica. *Am J Trop Med Hyg* 2001;65:628-32.

35. Adebivi A, Adaikan PG. Modulation of jejuna contraction by extract of *Carica papaya* Linn. seeds. *Phytother Res* 2005;19:628-32.
36. Imaga NO, Gbenle GO, Okochi VI, Akanbi SO, Edeoghon SO, Oligbochie V, *et al.* Anti-sickling activity of properties of *Carica papaya* leaf extract. *Afr J Biochem Res* 2009;3:102-6.
37. Razak MR, Norahmad NA, Jelas NH, Afan A, Misnan NM, Ripen AM, *et al.* Immuno-modulatory activities of *Carica papaya* Juice in a non-lethal, symptomatic dengue mouse model. *Pathogen* 2021;10:501.
38. Amin AH, Bughdadi FA, Abo-Zaid MA, Ismail AH, El-Agamy SA, Alqahtani A, *et al.* Immuno-modulatory effect of papaya (*Carica papaya*) pulp and seed extract as a potential natural treatment for bacterial stress. *J Food Biochem* 2019;43:1-8.
39. Prabhu AK, Devadas SM, Richard LO, Udupa P, Chawla K, Ballal M. Anti-diarrheal activity and phytochemical analysis of *Carica papaya* fruit extract. *J Pharm Sci Res* 2017;9:1151-5.
40. Sharma N, Mishra KP, Chandra S, Bhardwaj V, Tanwar H, Ganju L, *et al.* Evaluation of anti-dengue activity of *Carica papaya* aqueous extract and its role in platelet aggregation. *Arch Virol* 2009;164:1095-110.
41. Subham S, Mishra R, Gautam N, Nepal M, Kashyapa N, Dutta K. Phytochemical analysis of papaya leaf extract: Screening test. *EC Dent Sci* 2019;18:485-90.
42. Singh P, Tanwar N, Saha T, Gupta A, Verma S. Phytochemical screening and analysis of *Carica papaya*, *Agave americana* and *Piper nigrum*. *Int J Curr Microbiol Appl Sci* 2018;7:1786-94.
43. Neethu EK, Joseph S, Rajeev KR, Kavya V, Anjali KM, Bharath MS. Preliminary phytochemical and biochemical analysis of *Carica papaya* Linn. seed. *I J Res Pharm Pharm Sci* 2018;3:19-22.
44. Dwivedi MK, Sonter S, Mishra S, Patel DM, Singh PK. Anti-oxidant, antibacterial activity, and phytochemical characterization of *Carica papaya* flower. *Beni Suez Univ J Basic Appl Sci* 2020;9:23.
45. Eke ON, Augustine AU, Ibrahim HF. Qualitative analysis of phytochemical and antibacterial screening of extract of *Carica papaya* fruit and seed. *Int J Modern Chem* 2014;6:48-56.
46. Chidozie VN, Adoga GI. Gas chromatography mass spectrometry of N-butanolic leaf extract of *Carica papaya*. *Int J Adv Res* 2020;8:496-504.
47. Canini A, Alesiani D, Arcangelo GD, Jagliatesta P. GCMS analysis of phenolic compounds from *Carica papaya* Linn. *J Food Compos Anal* 2007;20:584-90.
48. Upgade A, Bhaskar A. Characterization and medical importance of phytoconstituents of *Carica papaya* from down South Indian region using GCMS. *Asian J Pharma Clin Res* 2013;6:101-6.
49. Iyappan G, Daniel D, Poovanaligam T. Ascertaining the phytochemicals in the crude ethanolic extract of *Carica papaya* seed by GCMS. *World J Pharm Pharm Sci* 2014;3:942-9.
50. Agada R, Usman WA, Shehu S. GCMS and FTIR analysis of crude extract of *Carica papaya* seed. *Aust J Basic Appl Sci* 2019;13:51-9.
51. Ezekwe SA, Chikezie PC. GCMS analysis, hypoglycemic activity of aqueous root extract of *Carica papaya* and its effect on blood lipid profile and hepatorenal issue biomarker of diabetic rat. *J Diabetes Metab* 2017;8:10-4.
52. Ezekwe SA, Chikezie PC. GCMS analysis of aqueous extract of unripe fruit *Carica papaya*. *J Nutr Food Sci* 2017;7:1-7.
53. Singh P, Kumawat H, Agarwal T. Bioactive compounds of *Carica papaya* male flower. *Int J Chem Sep Tech* 2020;6:23-34.

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