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Carica Papaya Leaf Extraction in the Management of Human Diseases

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Abstract: *Papaya (Carica papaya Linn.) belongs to the family Caricaceae and is well known for its therapeutic and nutritional properties all over the world. The different parts of the papaya plant have been used since ancient times for its therapeutic applications. Herein, we aimed to review the anticancer, anti-inflammatory, antidiabetic and antiviral activities of papaya leaf.*
The papaya plant, including fruit, leaf, seed, bark, latex, and their ingredients play a major role in the management of disease progression. Carica papaya leaf contains active components such as alkaloids, glycosides, tannins, saponins, and flavonoids, which are responsible for its medicinal activity. Additionally, the leaf juice of papaya increases the platelet counts in people suffering from dengue fever.

Keywords: Carica papaya. Anticancer. Anti-inflammatory. Immunomodulatory. Phytochemical

I. INTRODUCTION

The papaya plant is perennial usually unbranched, smooth stem and long-stalked leaves are having 5–6 lobes and can grow up to 20 m in height . Different parts of papaya plant viz. fruit, bark, roots, seeds, peel, pulp, and leaf have many known therapeutic uses around the world .

In India, about 45,000 plant species have been reported to possess medicinal properties . Natural product or compounds isolated from the plant have shown a major advantage over synthetic drugs such as cost-effective, easy availability and show negligible side effects . Numerous studies have published the use of medicinal plants for the management of a wide range of Diseases. Carica papaya Linn. From the Caricaseae family, is indigenous to Central America and South of Mexico, and commonly grown in India has been used for its medicinal properties around the world.

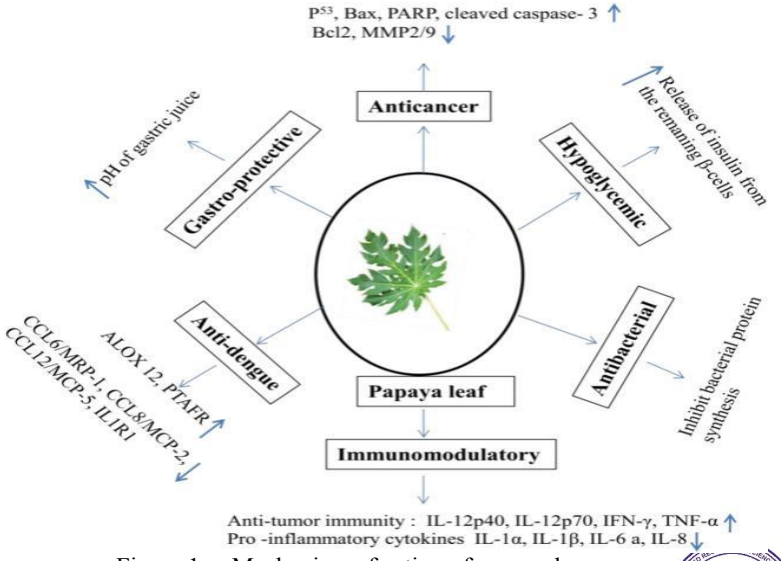

Figure 1. Mechanism of action of papaya leaves.

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A wide range of medicinal plant parts is used for extract as raw drugs and they possess varied medicinal properties. The different parts used include root, stem, flower, fruit, twigs exudate sand modified plant organs. While some of these raw drugs are collected in smaller quantities by the local communities and folk healers for local used, many other raw drugs are collected in larger

Quantities and traded in the market as the raw material for many herbal industries. Medicinal plants are of great importance to the health of individual.

Papaya contains a broad spectrum of phytochemicals including enzymes (in the latex),carotenoids (in fruits and seeds), alkaloids (in leaves), phenolics (in fruits, leaves, and shoots), and glucosinolates (in seeds and fruits). Papaya leaf has a numberless of benefits. Previous studies have shown that papaya possesses activities against protozoan, bacterial, fungal growth, inflammation, hypertension, wound, tumor, free radicals. In India papaya leaves are being used specifically for fever, beriberi, asthma, colic. Also, the young leaves of papaya are eaten like spinach in part of Asia.

Figure 2. Papaya Fruit

Plant Profile:

The papaya is a herbaceous perineal 2–10 m in height. It usually has a single, semi-woody, hollow, erect stem, which terminates with a cluster of large, palmately-lobed leaves with 25–100 cm long petioles and latex vessels in all tissues.

Crude drug: Papaya

Common Name: Papaya, Betik, Pawpaw, Betek, Melon Tree

Type : large, palmately-lobed leaves

Biological source: Papain is the dried and purified latex of the green fruits and leaves of Carica papaya.

Family: Caricacceae

Native Range: Central and South America

Height:2-10 m

Geographical source:

Papaya (Carica papaya) is a tropical fruit having commercial importance because of its high nutritive and medicinal value. Papaya cultivation had its origin in South Mexico and Costa Rica. Total annual world production is estimated at 6 million tone's of fruits.

Chemical constituents:

Papain, cystatin, chymopapain, tocopherol, phenolic acids, cyanogenic glucosides, glucosinolates, and vitamin C

Uses:

Cure Cancer
Prevent Heart Burn
For Acne
Increase Platelet Count
Prostate Enlargment
Reduce Skin Problems

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II. MATERIAL AND METHODS

Extraction method:-Maceration

Rinse the leaves with distilled water, then dry them in an oven at 60°C. Grind the dried leaves into a coarse material with a diameter of about 1 mm. Soak the ground leaves in a solvent, such as 96% ethanol, for 48 hours. You can use an intermittent shaking method. Use a rotary evaporator to concentrate the extract at 40°C and 50 rpm.Put the concentrated extract in a beaker, cover it with aluminum foil, and store it in the refrigerator at 4°C.

Separation Method:

Prepare the TLC plate by cleaning and activating the silica gel.Apply 5-10 µL of papaya leaf extract to the TLC plate. Develop the plate with the mobile phase.Dry the plate and detect the separated compounds using:
Iodine vapor: yellow/brown spots
Ninhydrin: purple/pink spot
Vanillin-sulfuric acid: red/orange spots.
Visualize the plate under UV light (254 nm).

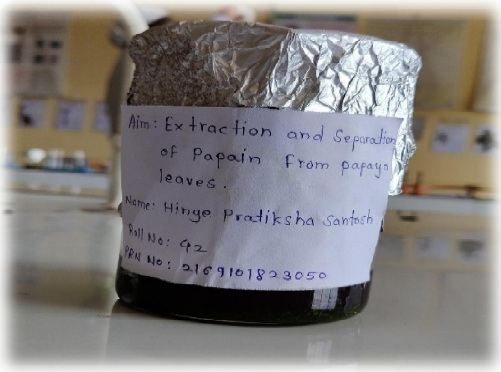

Fig., Maceration procedure

Fig., Filtration assembly

EVALUATION TEST:

A. Alkaloid Test:

Wagner's Test :

Add a few drops of Wagner's reagent (iodine in potassium iodide) to the extract.
Observation: A reddish-brown precipitate indicates the presence of alkaloids.

B. Saponin Test:

Froth Test:

Shake a small amount of the extract with water.
Observation: Formation of stable froth indicates the presence of saponins.

C. Flavonoids Test:

Shinoda Test:

Add a few drops of hydrochloric acid and a small piece of magnesium to the extract.
A pink to red color indicates the presence of flavonoids.

D. Tannin Test :

Ferric Chloride Test:

Add a few drops of ferric chloride solution to the extract.
A blue-black coloration indicate.

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Fig. Evaluation Test:

Thin Layer Chromatography (TLC):
MATERIAL:
APPARATUS: slide, beaker, stirrer.
EQUIPMENT: hot air oven, UV chamber
CHEMICAL: silica gel, chloroform, methanol, distilled water.
Stationary phase: silica gel.
Mobile phase: Ethyl acetate: methanol: water (7:2:1)
Procedure:
1. Prepare the TLC plate by cleaning and activating the silica gel.
2. Apply 5-10 µL of papaya leaf extract to the TLC plate.
3. Develop the plate with the mobile phase.
4. Dry the plate and detect the separated compounds using:
- Iodine vapor: yellow/brown spots Ninhydrin: purple/pink spots
- Vanillin-sulfuric acid: red/orange spots
5. Visualize the plate under UV light (254 nm).

RF value:
Standard RF value of Papain: 0.6

Formula: Rf value: Distance travelled by solute from origin/ Distance travelled by solvent from origin
= 3/5 = 0.6

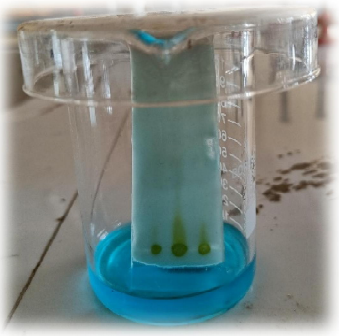

Fig. Thin layer chromatography

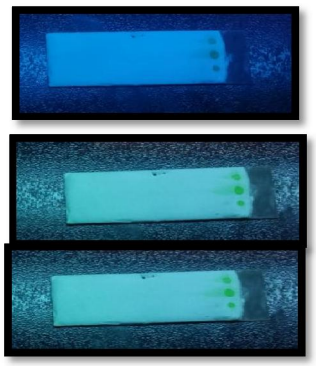

Fig. UV Visible Spectroscopy

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Various effect of Papaya Leaf Extraction (PLE):

Anti-cancer effect of PLE:

Cancer is one of the most deadly diseases which arises due to the uncontrolled division of genetically unstable cells and significant causes of deaths that occur worldwide. Among different types of cancers including colon, cervix, liver, stomach, lung, pancreas and breast cancer reported in the human, lung cancer is the most prevalent cancer among males, followed by breast cancer in females . Currently, depending upon the type, stage and location of cancer, there are many treatments available for cancer like surgery, chemotherapy, radiotherapy, immunotherapy, vaccinations and combination therapy, where chemotherapy is a widely used treatment for highly metastatic cancer .

Carica papaya is widely cultivated in tropical and subtropical countries and is used as food as well as traditional medicine to treat a range of diseases. Increasing anecdotal reports of its effects in cancer treatment and prevention, with many successful cases, have warranted that these pharmacological properties be scientifically validated. A bibliographic search was conducted using the key words “papaya”, “anticancer”, and “antitumor” along with cross-referencing. No clinical or animal cancer studies were identified and only seven in vitro cell-culture-based studies were reported; these indicate that C. papaya extracts may alter the growth of several types of cancer cell lines. However, many studies focused on specific compounds in papaya and reported bioactivity including anticancer effects. This review summarizes the results of extract-based or specific compound-based investigations and emphasizes the aspects that warrant future research to explore the bioactives in C. papaya for their anticancer activities.

Immunomodulatory effect of PLE:

The experimental evaluation of different parts of papaya plant show that it has high medicinal values and beneficial in many pathological conditions including wound healing, cardiovascular diseases, dengue fever, cancer etc. Recently, a strong immunomodulatory, antitumor and anti-inflammatory properties of PLE have been reported on several cancer cell lines . However, with very few reports on peripheral blood mononuclear cells (PBMC)

Since Carica papaya leaf extract can mediate a Th1 type shift in human immune system, our results suggest that the CP leaf extract may potentially provide the means for the treatment and prevention of selected human diseases such as cancer, various allergic disorders, and may also serve as immunoadjuvant for vaccine …

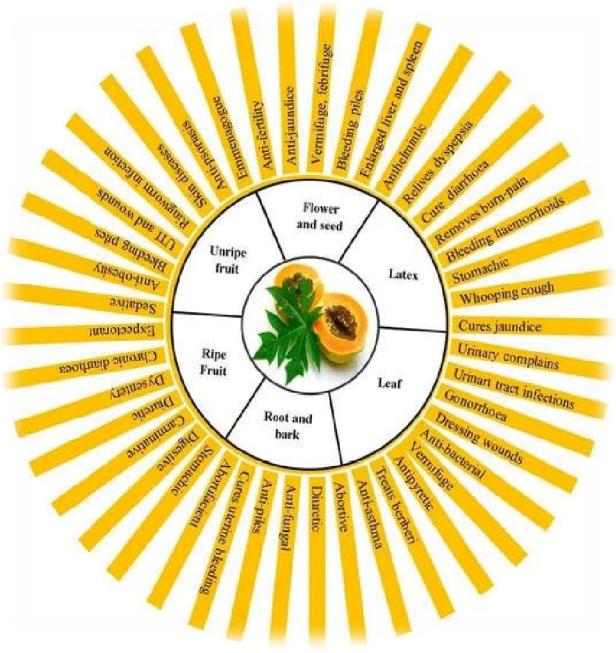

Fig., effect of Papaya leaf extraction.

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Anti-dengue effect of PLE:

Dengue is an alarming disease that affects people globally and estimated to have 50–100 million cases every year . Dengue is caused by dengue virus (DENV) 1–4, belongs to the Flaviviridae family and transmitted through the bite of infected mosquito, Aedesaegypti . The symptoms of the disease appear within 4–7 days after incubation of dengue virus that include high fever, rash, headache, vomiting and muscular pain . Thrombocytopenia, the decline in platelet count, is one of the main hallmarks of dengue and used for the diagnosis of dengue patients. World Health Organization (WHO) reported that thrombocytopenia is a rapid decrease in platelet count and confirmed by a platelet count of below 150,000 per microliter of blood .

Carica papaya leaf extract (CPLE) can help with dengue fever by increasing platelet count and reducing hospitalization time:

Platelet count :CPLE can increase platelet count in patients with dengue fever and dengue hemorrhagic fever. In one study, patients who were given 10 ml of CPLE every 8 hours for five days had a faster increase in platelet count than the control group.

Hospitalization time : In one study, patients who were given papaya leaf capsules three times a day had a significantly reduced hospitalization time.

Red and white blood cells :

CPLE can also increase red and white blood cells in patients with viral fever. Ayurveda practitioners in India recommend boiled papaya leaves to help with dengue and malarial fevers.

Antibacterial activity of PLE:

Carica papaya leaf extract presented the highest antibacterial activities . PLE strongly inhibited the growth of the tested gram-positive bacteria (Pseudomonas aeruginosa, Bacillus subtilis and Staphylococcus aureus) and had lesser effect on gram-negative (Klebsiella pneumoniae and Escherichia coli) bacteria . The thick murein layer present in the outer membrane of gram-negative bacteria prevents the entry of plant extract inhibitor substance into the cell. In another study, papaya leaves extracted with ethanol, methanol, ethylacetate, acetone, chloroform or hot water extracts showed excellent bactericide action against Bacillus cereus, Klebsiella pneumonia, Micrococcus luteus, Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus .

Antibacterial activity against gram-positive bacteria

Carica papaya leaf extract (PLE) has been shown to strongly inhibit the growth of gram-positive bacteria like Pseudomonas aeruginosa, Bacillus subtilis, and Staphylococcus aureus.

Antibacterial activity against gram-negative bacteria

PLE has also been shown to have antibacterial activity against gram-negative bacteria like Klebsiella pneumoniae and Escherichia coli. However, the effect on gram-negative bacteria is less than on gram-positive bacteria.

Antibacterial activity against other bacteria

PLE has also been shown to have antibacterial activity against Bacillus cereus, Micrococcus luteus, and Shigella flexneri.

Antibacterial activity against Propionibacterium acnes

The ethanol extract of PLE has been shown to inhibit the growth of Propionibacterium acnes, the bacteria that causes zits.

Antibacterial activity of seed extracts

A 2021 study found that the seeds of Carica papaya are the best source of antibacterial agents.

Antibacterial activity of combined extracts

A study found that the combination of Carica papaya leaf extract and Allium sativum clove extract is more effective than the individual extracts at retarding microbial growth.

The antibacterial activity of PLE can be affected by the solvent used to extract it. For example, one study found that the ethanol extract of PLE had the highest inhibition zone against tested bacteria.

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Gastro-protective effect of PLE:

Ulcers are a common gastrointestinal tract disorder that influences a massive population of human worldwide. Many risk factors could be associated with this disorder such as smoking, stress, alcohol, nutritional deficiencies, non-steroidal anti-inflammatory drugs (NSAIDs) and infections (Helicobacter pylori). investigated the effect of ethanolic extract of papaya leaves in the treatment of experimentally caused gastric ulcer in rats. The result obtained shown the significant ($P < 0.05$) decreases in ulcer index and gastric juice volume, and increase in the pH of gastric juice in aspirin-induced gastric ulcer bearing rats.

Two weeks after the oral administration, gastric ulcer was induced in all rats with 95% ethanol (2 mL). The aqueous and methanol leaf extract of C. papaya showed a significant ($p<0.05$) dose-dependent protection against peptic ulcer. The effects produced by the methanol leaf extract of C. papaya were comparable to those of the standard drugs (Omeprazole). Phytochemical analysis of the aqueous and methanol leaves extracts of C. papaya revealed the presence of flavonoids, tannins, alkaloids, terpenoids, cardiac glycosides, reducing sugar and saponins, some of which have been reported to elicit cytoprotective effect. Gas chromatographic analysis showed the presence of cytoprotective agents.

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III. CONCLUSION

The major findings revealed that papaya leaf extract has strong medicinal properties such as antibacterial, antiviral, antitumor, hypoglycaemic and anti-inflammatory activity. Furthermore, clinical trials are needed to explore the meditative potential of papaya .

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