

Pharmacological Activities of *Carica papaya* Linn

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Abstract: *Carica papaya* is a tropical fruit, present in orange red to yellow orange color. The whole plant including fruit, leaves, roots, peel, bark, seed and pulp served as medicine. It is rich in minerals, carotenoids, vitamins, alkaloids, enzymes, lycopene, and flavonoids that provide the papaya with special importance. It is used as a remedy for the treatment of many skin infections, anti fungal, anti viral infections. Its milky juice extracted and dried is used as medicine for digestive disorders and as toothpaste. *Carica papaya* helps in the treatment of different types of cancer, kidney infections, nervous disorders, etc. Now a days papaya is known as a nutraceutical fruit because of its multifaceted properties. The most enhanced properties of papaya are anti-fungal, anti-fertility, uretonic, anti-hypertensive, hypolipidemic, dengue fever, diuretic, anti-helminthic, wound healing, antibacterial and antitumor activities. This review summarizes the magical pharmacological benefits of *Carica papaya*.

Keyword: *Carica Papaya*, Papain, Wound healing, Chymopapain, Neutraceutical.

1. INTRODUCTION

Carica papaya Linn commonly known as Pawpaw or papau, Kapaya, Papyas, Papye, Fan mu gua belongs to the family Caricaceae. It is believed that it is a powerhouse of nutrients. It grows in all seasons. It is the first genetically modified fruit [1]. Usually its leaves are used for the treatment of different diseases by our ancestors, including malaria, dengue, jaundice and viral disorders. Young leaves have more importance in pharmacological studies, as its constituents are more effective than the mature leaf. The behavior of leaves also depends on different parameters like ash value, moisture, swelling index etc. [2]. The papaya plant has special cells called laticifers [3]. Laticifers are dispersed in all tissues of the plant. All parts of *Carica papaya* have pharmacological importance due to its laticifers and its active components. As studies showed these parts are active for anti-inflammatory, anti-fertility, hepatoprotective wound healing, antihypertensive and antitumor activities. Additionally it has enzyme-papain. This enzyme is used in the treatment of allergies and sports injuries. All its magical nutrients are very helpful for the cardiovascular system and protection from heart attacks and colon cancer. Its magical fruit has beta-carotene and it fights against free radicals. It is rich in fiber and maintains the high-density cholesterol level. Its fruit is also helpful in all abdominal disorders and the peel of papaya is used as wound healing medicine and gives cooling effect. Papaya helps to increase the immunity against cough. Besides that *Carica papaya* has an alkaline

combination with K_2CO_3 that is effective for tumor and for skin treatments like warts, sinuses, and cutaneous tubercles.

1.1. APPEARANCE

1.1.1. Plant

This plant has a soft and unbranched weak stem having latex. This white latex has many leaves joint with long stalk. Its growth is rapid and about 20m in height [4]. It has an herbaceous single stem. Leaves are wide about 2.5 feet and 1-3 feet long. Leaves have plenty of lobes with a central margin. The stem has scars with a diameter of approximately eight inches. Its color is green to brown and it is hollow inside [5].



Figure 1: *Carica papaya* tree.

1.1.2. Fruit

The fruit is oval having a central seed cavity that resembles a melon. Fruits are present on the main stem sometime single but usually in clusters. The weight of the fruit is from half to 9kg and green to

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yellow or orange in color. At maturity the flesh is yellow to pinkish orange. Ripening of the fruit depends on temperature and condition of growth. It takes 5 to 9 months for the fruit to ripen while a plant bears the fruit after 6-12 months [5].



Figure 2: *Carica papaya* fruit.

1.1.3. Flowers

Flowers of *Carica papaya* are dioecious because male and female flowers are separate. Sometimes it is called trioecious because it also has bisexual flowers. Its female flower is waxy and white. It is born on a short pendule beside the central stem and has a stigma but fewer stamens. Bisexual flowers also have the same position as the female flower but in a tubular shape and its size is in between the male and female flower while female flower has the shape of a pear. Ovary is superior. Bisexual plants are more ideal as compared to a single flower because of its self-pollinating property. The male flower is born on long stalks and has a smaller size as compared to the female flower [5]. The main difference in the flowers is determined by their difference in shape and size of stamens, stigma



Figure 3: Male and female flower of *Carica papaya*.

and ovary. The bisexual flower has the best structure of stamen and ovary and is as thin as the male flower.

1.1.4. Leaves

Its leaves are large with a diameter of 50 to 70 cm. The leaves are wide about 2.5 feet and 1-3 feet long and have plenty of lobes with a central margin.

1.2. Some Informal Names

Some common names of *Carica papaya* in all over the world are given in Table 1:

Table 1: Some Common Name of *Carica papaya*

| | |
|----------|-------------------|
| English | papaya |
| Hindi | Papita |
| Sanskrit | Erandakarkati |
| Arabic | Babaya |
| French | Papaye or Papayer |
| Spanish | Papayo |

1.3. Taxonomical Place of *Carica papaya* Linn

The taxonomical place of *Carica papaya* Linn is as follows [6]:

1.4. Distribution

During the 16th century Spanish explorers spread *Carica papaya* in Central America to the Caribbean. It originated from Mexico and Central America. Now it is present in the tropic areas of South America, Africa and Asia. It is also grown in the U.S. state of Hawaii, Philippines, Australia, Malaysia and Indonesia [7]. Its best growth requires the temperature range 21- 33°C



Table 2: Taxonomical Distribution of *Carica papaya*

| | |
|----------------|---------------------------|
| Domain | Flowering plant |
| Kingdom | Plantae |
| Sub Kingdom | Tracheobionta |
| Class | Magnoliopsida |
| Subclass | Dilleniidae |
| Superdivision | Spermatophyta |
| Phyllum | Steptophyta |
| Order | Brassicales |
| Family | Caricaceae |
| Genus | <i>Carica</i> |
| Botanical Name | <i>Carica papaya</i> Linn |

with annual rainfall of 1200mm. The pH of the soil is 6.0- 6.5 with loaded organic compounds. A sunny season and windbreaks improve the fruit quality. Shade also plays an important role in growth. It is sensitive towards salinity, water logging, and frost.

1.5. Soil Types and Location

It can grow in many types of soil but mostly in drained soil. Undrained soil can cause root disorders. In low rainfall areas its production is limited. Soil with heavy clay should be kept away. A pH between 6 to 7 is best for ideal growth. Sometimes it requires a phosphorous fertilizer. Papaya can handle medium winds depending on its roots. Evenly distributed rainfall from 40- 60in is good. If more than 60in rainfall is present then porous, sloped hills can help to protect water logging [8].

1.6. Environmental Impact

Carica papaya requires heavy fertilizer. It requires 1 kg nitrogenous fertilizer, 0.2 kg phosphorous-based and 2.5 kg potassium-based fertilizer per ton production of fruit. For that purpose manure and mulch can be used for nutrients [9].

1.7. Chemical Composition

Immature leaves have flavonoids, phenolic compounds, alkaloids, and cynogenetic compounds in large amounts. *Carica papaya* Linn is wealthy with vitamins A, C, E especially in fruit and leaves which are the best antioxidants. Leaves and fruit are also loaded with minerals, Mg, K and fiber. Its fruit has papaintha enzyme that helps in digestion [10]. Some of its common isolated compounds are given in Table 3:

1.8. Benefits of Papaya

1.8.1. Leaves

Leaves are the most useful part of the plants as it shows plenty of its activities. It can serve as medicine for skin treatments like acne, relieving nausea and menstruation pain. It also increases the appetite.

1.8.2. Fruits

Fruit of the papaya is a factory of vitamins and minerals. Fruit showed antifungal activity. Its mature fruit is good for bowel movement. Its green fruit produced milky juice having an enzyme called "papain". This enzyme used as a remedy by native people for the digestive system.

1.8.3. Seeds

The seed of papaya has a sharp and spicy taste. Sometimes it is used as a replacement for black pepper. Seeds help in nephro-protective activity that is dose dependent. Its seed has more potential than the flesh. It is active against *E.coli*, *Salmonella* and *Staphylococcus* infections. Seeds work as a kidney protector, remove intestinal parasites and detoxify the liver. It also protects skin from irritation, lowers fever and typhoid. So it is not worthless to say that it is simply a way to add extra enzymes to the diet.

1.8.4. Peel

Papaya peel is served as a remedial component in many areas. It is used as a cosmetic, as sunscreen, as a skin lighting agent and as a soothing moisturizer. It fights against dandruff if the mixture of vinegar, peel and lemon juice applied on the scalp for 20min and then washed. The peel works as a muscle relaxant. It is believed by ancients that if oil of papaya and vinegar are add to bath water it provide freshness, nourishing the skin and also helpful in the relief of pain.

1.8.5. Roots

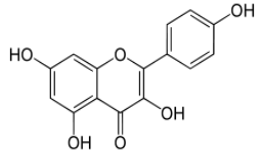
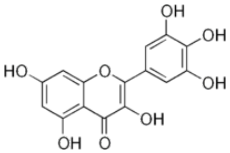
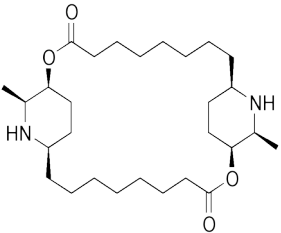
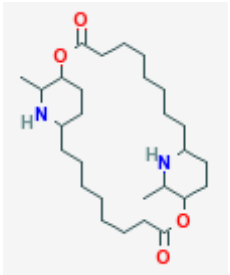
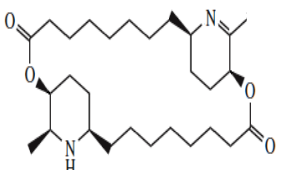
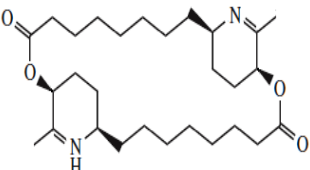
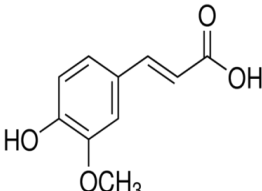
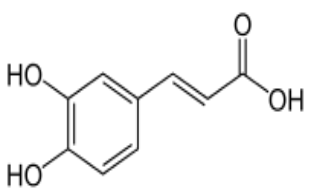
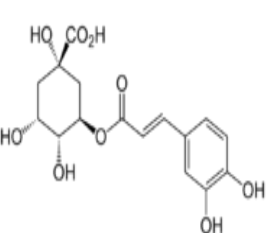
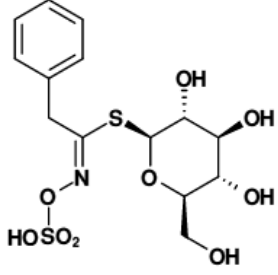
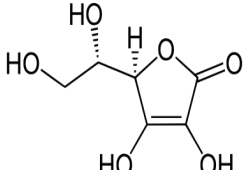
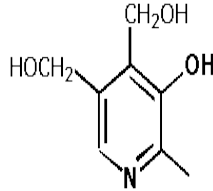
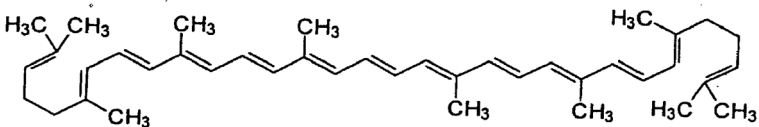
Root extract is used to relieve urinary scrapes and dyspepsia.

2. PHARMACOLOGICAL PROPERTIES

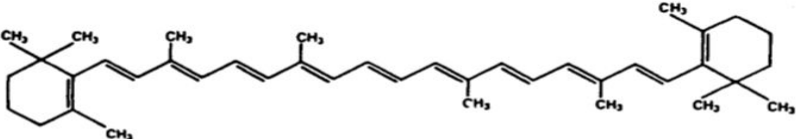
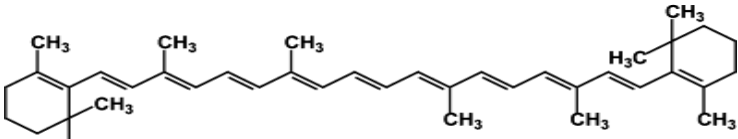
2.1. Anti-Inflammatory Activity

Anti-inflammatory properties have already been studied in literature. In medicinal treatment the papain enzyme showed effectiveness towards inflammation and even helpful in chronic inflammations [11]. Papaya seed was also reported in the literature for its good

Table 3: Some Major Constituents of *Carica papaya*

| Chemical constituent | Structure | Chemical constituent | Structure |
|----------------------|--|----------------------|---|
| Kaempferol |  | Myricetin |  |
| Carpaine |  | Pseudocarpaine |  |
| Dehydrocarpaine I |  | Dehydrocarpaine II |  |
| Ferulic acid |  | Caffeic acid |  |
| Chlorogenic acid |  | Benzylglucosinolate |  |
| Vitamin C |  | Pyridoxine |  |
| Lycopene |  | | |

(Table 3). Continued.

| | |
|--------------|--|
| Provitamin A |  |
| Carotenoids |  |

effects against inflammation [12], while the leaves were not so effective as the seeds and fruit. Anti-inflammatory activity of leaf extract was performed by the carrageenan method. The maximum effect of leaves extract was noted as 2.7% after carrageenan injection to 100 mg/kg in 3hr while 6.7% effective with the same conditions at 200 mg/kg extract was noted. Indomethacin was used as a reference drug and the reduction is time dependent. The effect was more prominent, 11.4%, with the same conditions. It is concluded that the aqueous extract of leaves is less effective than the reference drug [13].

2.2. Wound Healing Activity

Coagulation process of latex of papaya and mammalian has many similarities. These similarities provide the basis of some common factories present in both species. If reputed similarities are present then it is possible that healing metabolites are the same in mammalian and plant working for clot formation [14]. It is reported that this property is present due to a number of proteolytic enzymes like Papain [15]. Another study showed the effectiveness of papain in curing a histamine-induced ulcer. They concluded that papain helps to block the secretion of acid [16]. The major component of papain is a nonspecific cysteine proteinase and it can break it into a variety of necrotic tissue. These tissues are affected in a pH range from 3.0 to 12.0 [17]. Papain enzyme also worked as an anti-inflammatory agent, antibacterial agent, as antioxidizing agent and may form chelates with iron [3, 18].

2.3. Anti-Fertility Activity

An anti-fertility effect was noted on adult and pregnant rats. The activity of different components of fruit was investigated. The result showed that unripe fruit of papaya disrupted the estrous cycle and caused

abortion. It was also noted that as the fruit over ripened the effect on the estrous cycle decreased [19]. It also has an effect in anti-implantation [20].

2.4. Anti-Helminthic Activity

Papaya is used as a remedy for the treatment of helminthes infections. Papaya has proteolytic enzymes that have low toxicity and was used as medicine for the treatment of gastrointestinal nematodes in the past [21]. In the middle nineteenth century papain enzyme of papaya latex shows its effectiveness against worm digestion as it helps in the rapid digestion of ascaris cuticle.

2.5. Anticancer Activity

A lot of proteolytic enzymes were used in pharmaceutical formulation for the treatment of malignant diseases. In the past the mode of action of these proteolytic enzyme was unknown but still these plants served as medicine. Many studies showed that the whole plant of papaya has a lot of active ingredients against different types of cancer cell lines such as Papain, Isothiocyanate, Vitamins, Carotenoids etc. These constituents provide strength to the immune system. Studies showed that Papain helps to break the cancer cell wall. Lycopene is active against free radicals. Papaya has isothiocyanate and it is very effective against lung cancer, breast cancer and leukemia. All these enzymes have components to protect against formation as well as development of cancer cells [22]. Jayakumar and his coworker worked on breast cancer. They used ethanolic extract of papaya pericarp with doses between 50–640 g/ml. The result showed a decrease in cell feasibility [23]. Another study was carried out by Otsuki and his coworkers on T cell lines, lymphoma cell lines, cervical carcinoma cell lines and Hepatocellular carcinoma cell lines. They used aqueous extracts of leaves of papaya.

The dose range was 0.625–20 mg/ml. The outcome showed good results against haematopoietic and solid tumor cells. It is also increased the production of cytokines Th1ion and enhanced 23 immunomodulatory genes [24].

2.6. Antifungal Activity

Papaya has the potential to work against fungal diseases. Ethanolic extract of seed, leaves and unripe fruit was studied by Quintal and his coworker against antifungal activity. Extraction time, solvent and extraction ratio was noted. The result showed that an increase in time and highest ratio is more effective and gives the best yield. Efficiency of extract with respect to time was measured qualitatively. Phytochemical studies show the presence of flavonoids, terpenes and alkaloids in leaf extract. *Rhizopus stolonifer*, *Fusarium* spp. and *Colletotrichum gloeosporioides* were used in this study. Mycelial growth inhibition is about 20%. They conclude that leaf extract of papaya has secondary metabolites and antifungal properties [25].

2.7. Antibacterial Activity

Literature has shown that Seed of papaya can serve as an antibacterial agent. *Bacillus subtilis*, *Escherichia coli*, *Enterobacter cloacae*, *Klebsiella pneumonia*, *Salmonella typhi*, *Proteas vulgaris*, *Pseudomonas aeruginosa* and *Staphylococcus* were commonly used. Gram-positive and gram-negative bacteria were tested under different conditions while gram negative bacteria showed more good results [26, 27].

2.8. Anti-Hypertensive Activity

Leaves of papaya served as an anti-hypertensive agent. An Agboville villager situated in West Africa worked on the anti-hypertensive effect of leaf extract by oral administration [28].

2.9. Immunomodulatory Activity

It was reported that the tea extract of papaya leaves is good in an immunomodulatory effect. However the mechanism of cell action is unknown. An aqueous extract of leaves was tested on Wistar rats. Under observation 400 and 800 mg/kg doses were given orally for 14 days. The results showed that paw edemas increased as compared to the control while levamisole had the highest paw volume than other groups. They concluded that leaf extract of papaya has potential to fight against cancer, allergic disorders, and immunomodulatory effect up to an extent [29].

2.10. Anti-Sickling Activity

Sickle cells are produced due to the mutation in blood cell (RBC'S) where valine is present at 6th position instead of glutamic acid. Current studies showed that the extract of unripe fruit could serve as an anti-sickling agent [30]. Leaves of papaya also effective for anti-sickling depending on dose [31].

2.11. Hypoglycemic and Hypolipidemic Activity

Adeneye and his coworker worked on hypoglycemic and hypolipidemic effect of papaya seed. 0.1 mg/kg per day of glibenclamide and aqueous extract of seed with 100-400 mg/kg per day are effective in hypo-glycemia and hypo-lipidemia [32].

3. SAFETY PROFILE

The entire discussion centers on the benefits of papaya but it has some side effects too if taken in excess amounts. Only the infertility is discussed however papaya has cyanogenetic glucosides. Cyanogenetic glucosides produce cyanide that can cause fatal consequences. Papaya is safe to eat by most people as food and medicine. It may be unsafe when taken in large amounts or applied on the skin excessively. Excess amounts can damage the esophagus (the food tube present in the throat). It may cause allergy or several irritations when applied on the skin for long periods of time [33].

3.1. Pregnancy

Papaya is not safe during pregnancy. There is some evidence that papaya produces some unprocessed papain, which acts as a poison for the fetus.

3.2. Diabetes

Papaya can lower the blood sugar as it has fermented. Diabetic patients who are taking medicine to lower blood sugar should be careful. They may need to revise the amount of dose as papaya itself decreases the blood glucose.

3.3. Allergy

Some people has allergy towards papain and with latex of papaya. So if the irritation presents then avoid eating papaya and products having papaya.

3.4. Surgery

Fermented papaya can lower the blood sugar. Literature showed that Papaya might affect the blood

level during and after surgery. It is recommended that one stop eating papaya two weeks before surgery [34].

3.5. Papaya Dosing

The suitable dose of papaya as medicine depends on numerous factors like age of patient and health. In literature there is no defined range of papaya used as a dose but it is true that natural products are not completely safe but depends on dose. So be sure to follow the direction present on product labels and as directed by a pharmacist or other healthcare professional [35].

4. CONCLUSION

Papaya (*Carica papaya* Linn.) is famous in over the world due to its exceptional and magical medicinal properties. Papaya tree including root, leaves, fruit and their juice served as remedies in medicine. *Carica papaya* has a wide range of pharmacological activities. It has a wide range of vitamins, minerals and enzymes. This review summarizes the biological activities of *Carica papaya* Linn and some of its side effects.

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Received on 07-07-2017

Accepted on 12-12-2017

Published on 22-06-2018

<https://doi.org/10.6000/1927-5129.2018.14.33>

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