

Pharmacognostic, Phytochemical and Pharmacology of *Carica papaya* : An Update

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Abstract

Natural products obtained from the plant have important role in the prevention and treatment of diseases. COVID-19 is a new type of virus stain and severe acute transmissible and pathogenic virus. Corona virus is a single stand RNA virus. *Carica papaya* is used in the prevention and treatment of diseases due to their medicinal properties. *Carica papaya* belongs to the family Caricaceae. According to the researchers *Carica papaya* is very effective against COVID-19 due to the reduced production of interleukin IL-6 and TNF-alpha in humans and animals, dengue fever due to the weakened thrombopoiesis is generally the result of decreased megakaryopoiesis at the onset of infection as well as anti-inflammatory, anti-helminthes, anti-bacterial, protect the kidney from toxin induced kidney failure, detoxify the liver, sun scream, soothing slave, dandruff, muscle relaxant, stomach disorder or cramps, ant malarial, anti-fertility and antispasmodic etc. *Carica papaya* contains several chemical constituent like Leaves contain karpain, a chemical compound that kills the microorganism that interferes with digestive function; Papain a chemical constituent is responsible for the manufacturing of different remedies for indigestion and rapidly digests the ascaris. Here, this review tells about the pharmacology, pharmacognosy and various role of *Carica papaya* in different diseases which may be beneficial in the future based on available published data.

Keywords: *Carica Papaya*, Pharmacognosy, photochemical, papain, karpain, pharmacology, COVID-19.

Introduction

Medicinal plants have a capability to heal different disease due to the existence of lots of primary and secondary metabolites. These types of plants act as a backbone of traditional medicines. ⁽¹⁾ Herbal medicines also play an important role in our life because of their different medicinal purposes. Phytomedicine is the second name of the herbal medicines. ⁽²⁾ The Indian holy book Vedas describes treatment with plants, which are plentiful in that country. India originates several plants used even today like Nutmeg, Clove etc. ⁽³⁾ In India materia medica includes about 2000 drugs of natural origin almost all are derived from different traditional systems and folklore practices. Out of these drugs derived from traditional system, 400 are obtained from mineral and animal source whereas the remainder is obtained from plant or vegetable source. ⁽⁴⁾ Viral diseases show a major phytosanitary problem, those transmitted by insect vector. ⁽⁵⁾ The recurrence of the serious infection caused by pathogenic microorganism has risen worldwide and is becoming a major reason of morbidity and mortality in weak immune patients in different countries. Genetic change in the pathogen is an important event in a new disease emergence that makes it viable to become habitual in a new host species, completely infect new individual in the new host and produce health threats. Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), bird flu, swine etc are the deadly viral threats in the recent time. ⁽⁶⁾ The Centre for Disease Control and Prevention (CDC) suggests two levels in the cure of infection within healthcare settings. The

first level includes general precautions and other standard precautions. The risk of the transmission of bloodborne virus and other common organism found within the healthcare settings can be reduced by the first level. The isolation or transmission based precautions are included in the second level.⁽⁷⁾ On the behalf of the literature survey, it is concluded that this compiled data covers the pharmacognosy, pharmaceuticals and pharmacology of *Carica papaya* plant and their medicinal role in different diseases and this may serve as a supporting reference for the future work.

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Carica papaya is also called as 'pawpaw' because it is a herbaceous luscious plant and belongs to Caricaceae family.⁽⁸⁾ It is a fast growing laticiferous tree with a small, soft wooded tree up to 8 cm in height. It has the following characteristics like; straight cylindrical stem having leaf scars throughout and with a tuft of leaves at the top, leaves are extremely lobed, palm like characteristics, long hollow petiole, flowers are unisexual white or yellowish in color but rarely bisexual, males are in long dropping panicles, females are in short clusters.⁽⁹⁾ The size of the fruit of the papaya is too large and secretes a milky sticky juice which contains remarkable property of accelerating the decomposition of muscular fiber.⁽¹⁰⁾ The tree is about 20-30 feet long without branches, leaves are alternate, palmate and 7-partite, segments are oblong, acute, sinuate, the middle one is 3-fid, fruit is succulent, oblong and furrowed in nature, calyx is small, 5-toothed and the corolla is tubular in the male while 5 inches in female, divided nearly to the base into 5 segments.

Plant botany

Common name: papaya, pawpaw

Vernacular names- English: Papaw tree, Papaya; Hindi: Pappya, Pappita; Sanskrit: Brahmairandah, Erandakarkati; Tamil: Pappali; Mal: Pappaya, Karmmusu, Pappali, Karmmatti; Kan: Pappaya, Peragi, Piranji⁽¹¹⁾

Scientific classification

Kingdom: Plantae

Sub-kingdom: Tracheobionta

Class: Magnoliopsida

Sub-class: Dilleniidae

Division: Magnoliophyta

Sub-division: Spermatophyta

Phylum: Stetophyta

Order: Brassicales

Family: Caricaceae

Genus: *Carica*

Botanical name: *Carica papaya* Linn⁽¹²⁾

Cultivation and collection

It is cultivated in tropical and sub tropical areas of America and other tropical zones of the world, which is accessible all over the year. It requires warm and humid climate. Plant growth and the fruit are affected by the low temperature. At 0° C both foliage and fruit get damaged.⁽¹³⁾ Papaya is economically propagated by seed and tissue culture plants. The seedling can be increased in nursery beds 3m long, 1m broad and 10 cm high in addition in pots or polyethylene bags. The seeds after used with 0.1% Monosan (phenyl mercuric acetate), ceresin etc are scattered 1 cm in rows 10 cm aside and covered with fine leaf mould. The nursery beds are enveloped with polyethylene sheets or dry paddy straw to preserve the seedlings.⁽¹⁴⁾ Medium, fertile and well drained and lime free soil are best for papaya cultivation. Planting is done during spring season (February- March), monsoon season (June-July), autumn season (October- November).⁽¹⁵⁾



Fig. 1: Papaya plant⁽¹⁶⁾

Traditional uses

The whole plant of the *Carica papaya* plant has medicinal value. Leaves can be used to cure dengue fever, cancer cell growth inhibition.⁽¹⁷⁾ Seeds are used as a tender purgative for worms. Flower may be taken in an infusion to induce decoction and menstruation of the ripe fruit is helpful for curing diarrhea and dysentery especially in children. The ripe fruit act as mild laxative. Latex is applied externally to accelerate the healing of wound, ulcers, warts and cancerous tumors.⁽¹⁸⁾ Peel can be used as sun scream and soothing slave, effective for dandruff, muscle relaxant etc. Roots can be used to cure stomach disorders or cramps.⁽¹⁹⁾

Pharmacognostic Parameters of *Carica papaya*

Morphological parameters

Pawpaws have a creamy, custard-like flesh with a complex combination of tropical fruit flavors. They are most commonly described as tasting like banana combined with mango, pineapple, melon, berries, or other fruit.⁽²⁰⁾ Epicarp reveals single layer of thin walled cells enveloped with thick cuticle externally. Mesocarp have broad zone consisting of circular to oval shaped parenchyma cells with dispersed and unbranched laticiferous cells. Endocarp made up of 2 to 3 layers of thin walled parenchyma cells. Plentiful calcium

oxalate crystals are found in mesocarp region of the fruit. ⁽²¹⁾ Flower of papaya exist in three types (female, hermaphrodite and staminate). ⁽²²⁾ the morphological characteristics (like fruit weight, fruit length, fruit diameter, internal cavity diameter, internal cavity shape, skin color, flesh color and stalk end fruit shape, fruit shelf life) , physicochemical (like ph, total soluble solids, titratable acid and total and total soluble solid/ titratable acid ratio) , vitamins (ascorbic acid and β carotene) and organoleptic test. ⁽²³⁾.

Microscopically characters and powder analysis of leaves

The papaya plant contains three types of flowers (female, hermaphrodite and staminate) and the seeds-external (shape, size, hilum, micropyle, funicle, raphe and testa) and internal characteristics (endosperm and embryo).

Powder characteristics: Deepa Verma et. al examined the powder characteristics by standard method . she stained the powder with saffranine and studied under microscope for recognition of anatomical characteristics. The powdered characteristics have shown in the Fig 1.

Sectioning: Deepa Verma et. al examined the section of leaf and petiole microscopically. She cut the transverse and longitudinal section and stained with saffranine and hematoxylin and observed under microscope for identification of several tissues.

Phytochemical screening, physiological analysis, and quantitative microscopy

Several phytochemicals with different extract are shown in table 1. Several primary and secondary metabolites identified in different extracts of *Carica papaya* are shown in table 1. Physicochemical analysis and quantitative microscopy of leaves are shown in table 2 and 4.^[26-27]

Table 1: Phytochemicals detected in different extract of *Carica papaya*

Plant part used	Type of extract	Phytochemicals found
Leaf	Methanol	Kaemferol-3(2G-rhamnosylrutinoside)
Leaf	Ethanol, methanol and water	Flavonoids
Seed	Hexane , chloroform, diethyl ether and methanol	p-hydroxybenzoic acid, salicylic acid, hyperoside gentisyl alcohol, kaemferol hexosides
Leaf	Methanol	Carpaine, kaempferol 3-(2G-glucosylrutinoside), kaempferol 3-(2"-rhamnosylgalactoside), 7-rhamnoside, kaempferol 3-rhamnosyl-(1->2)-galactoside-7-rhamnoside, luteolin 7-galactosyl-(1->6)-galactoside, orientin 7-O-rhamnoside, 11-hydroperoxy-12,13-epoxy-9-octadecenoic acid, palmitic amide, and 2-hexaprenyl-6-methoxyphenol

Leaves, bark, roots and pulp	n-hexane, dichloromethane, ethyl acetate, ethanol, methanol, n-butanol and water	Phenolics and flavonoids
Seeds	Petroleum ether, ethanol and aqueous	Phenolics and flavonoids
Seeds	Methanol	Carotenoids and α -tocopherol
Flower	Ethanol	Triterpenoid/steroids
Seeds	Methanol	Total phenolic content
Seeds	Methanol	Kaempferol-3-glucoside, p-coumaric acid ferulic acid, caffeic acid, phydroxybenzoic acid, quercetin-3-galactoside Seeds Hexane, ethyl acetate, methanol and aqueous DPPH, FRAP, TBARS Octadecanoic acid, oleic acid, n-hexadecanoic acid, 14-methyl-, methyl ester, 11-octadecenoic acid, methyl ester, and pentadecanoic acid
Peel	Aqueous	Proteins and phenolic groups

Pharmacological Investigation and Molecular Research

Anti-helminthes activity

A proteolytic enzymes present in the *Carica papaya* can digest the nematode cuticle. It has been used as traditional medicine against gastrointestinal nematodes. *Carica papaya* contains papain rapidly digest the ascaris. ⁽²⁴⁾Papaya leaves have the tendency to activate the hormone prolactin because it contains quercetin (one of the galactogogues) and also increase the breastmilk ⁽²⁵⁾

Anti-malarial activity

Carpaine was the active alkaloid extracts in dichloromethane leaf extract and exhibit acceptable activity against both strain of *Plasmodium falciparum*. This alkaloid is extremely selective against the parasite and non-toxic to well uninfected R.B.C additionally; methanol, chloroform, petroleum ether extract of fruit rind, and roots of papaya were examined against *Plasmodium berghei* in mice for their anti-plasmodial activity. Ashutosh Sharma et.al revealed that petroleum ether and chloroform extract of *C. papaya* fruit rind has sustainable antiplasmodial activity in a dose-dependent manner but petroleum ether extract had the largest antimalarial activity. ⁽²⁶⁾

Anti-tumor activity

Carica papaya Linn have been consistently used as ethnomedicine for different diseases, including cancer. Norika Otsuki et. al examined the effect of aqueous extracted CP leaf fraction on the growth of several

tumor cell lines as well as human lymphocytes. The proliferative responses of tumor cell lines and human peripheral blood mononuclear cells (PBMC) and cytotoxic activities of PBMC were obtained by [(3)H]-thymidine incorporation. The production of IL-2 and IL-4 was decreased by the addition of CP extract in the case of PBMC.⁽²⁸⁾ According to investigators, cancer can be cured by using papaya leaf tea extract because it appears to improve the production of Th1-type cytokines, which help to control the immune system. The papaya fibre has the ability to attach with toxin which results in colon cancer and keep them away from the healthy colon cells.⁽²⁹⁾

Effect of *Carica papaya* on metabolic syndrome

Obesity is observed due to the accumulation of body fat, which may be identified by various factors like several ethnological, social, behavioral, environmental, cultural, physiological, metabolic and genetic factors.⁽³⁰⁾ Uncontrolled fat accumulation can be an important condition in the development of metabolic dysfunction, like arterial hypertension, dyslipidemia and insulin resistance, diabetes mellitus type 2, cardiovascular illness.⁽³¹⁾ Tumor necrosis factor (TNF- α), interleukin 6 (IL6), monocyte chemoattractant protein, leptin, adiponectin and resistin are the adipokines secreted by adipose tissues.⁽³²⁾ The accumulation of adipose tissue is directly proportional to adipokines. This results to a variation in their secretion, with raised pro-inflammatory and reduced anti-inflammatory adipokines, stimulating the systemic and local inflammatory process, giving to the development of insulin resistance.⁽³³⁾ Metabolic syndrome is related with the generation of reactive oxygen species (ROS), can persuade insulin resistance.⁽³⁴⁾ Lidani F. Santan et. al estimated that the presence of vitamins, bioactive compounds and lipids in the *Carica papaya* can be good for the treatment of metabolic dysfunction.⁽³⁵⁾

Anti-fertility effect

It was examined that the *Carica papaya* shows the anti-fertility effect by feeding pregnant rat with dissimilar components of the fruit. No attempt was assembled to force feed the nimal and the outcome specified that the immature fruit the estrous cycle and cycle and persuade abortion. The over ripped *Carica papaya* does not have this kind of effect⁽³⁶⁾

Effect of *Carica papaya* on dengue fever:

According to the investigators, Dengue hemorrhagic fever is identified by a thrombocyte count, it could be responsible for dengue-induced thrombocytopenia-impaired **thrombopoiesis and peripheral platelet demolition**. Many researchers have proposed that weakened thrombopoiesis is generally the result of decreased megakaryopoiesis at the onset of infection. The direct exposure of the virus on the megakaryocytes or the effect on the stromal cells (connective tissue cells of any organ) which could be the reason for the release of cytokines and control of megakaryopoiesis.⁽³⁷⁾ The raised peripheral platelet demolition could be the other important cause of thrombocytopenia. This is caused by an autoimmune reaction, where antibodies generated by the host against the dengue virus created activation and destruction of platelets.⁽³⁸⁾

Effect of *Carica papaya* on hepatic and renal toxicity:

The *Carica papaya* leaf extract shows antimicrobial activity on the inhibition of some human pathogens like *Escherichia coli*, *Pseudomonas aeruginosa*, *Kleibseilla pneumonia*, *Staphylococcus aureus* and *Proteus mirabilis*.⁽³⁹⁾

Effect of *Carica papaya* on COVID-19

The Corona virus can be spread in the form of respiratory droplet nuclei, other body fluids and secretions like feces, saliva, urine, semen and tears. It is commonly spread by the respiratory droplet formed while coughing, sneezing and talking of an infected person⁽⁴⁰⁾. According to the researchers *Carica papaya* reduces interleukin IL-6 and TNF-alpha in humans and animals. Interleukin IL-6 and TNF-alpha are mainly responsible for producing inflammation of lungs leading to pneumonia. TNF-alpha is an inflammatory cytokine generated by macrophages/monocytes during acute inflammation leading to necrosis or apoptosis. TNF-alpha shows various effects by binding, as a trimer to either a 55 kDa cell membrane receptor called as **TNF-1** or 7 kDa cell membrane receptor called as **TNF-2**⁽⁴¹⁾. Cytokine storm is most prime mechanism that leads to death of COVID-19 infected person. According to the scientist, an enormous production of a host of arbitrator such as interleukins, interferon, tumor necrosis factor (TNF), and macrophage occurs. These mediators are combined together like cytokines or chemokines and this causes the serious effect on the lungs of the infected person followed by the death of the infected cell by apoptosis and necrosis. Due to this, the multiple organ failure occurs.⁽⁴²⁾ Papain is found in the papaya latex. Papain is a cysteine proteinase which has the capacity to break a wide variety of necrotic tissue at Ph 3.0-12.0. This factor may help in wound healing and may decrease the oxidative tissue damage; similarly, they show burn healing property as the increment in the hydroxyproline content.⁽⁴³⁾ Chen et al. observed that papain from *Carica papaya* latex was very efficient in curing histamine-induced ulcer in the rat by obstructing the acid secretion.⁽⁴⁴⁾

Effect of *Carica papaya* on Sickle Cell Disease (SCD)

Mutation in hemoglobin inside the RBC is the major cause of Sickle Cell Disease (SCD) where a glutamic acid at 6th position is replaced by valine. Anjali pal et al. reported that the potent antisickling property of *Carica papaya* leaf extract of unripe fruit in a dose-dependent way.⁽⁴⁵⁾

Anti-inflammatory activity:

Papain, chymopapain are the protein enzymes, the nutrients, vitamin C & E and betacarotene decreases the serious conditions like asthma and osteoarthritis.

Rheumatoid arthritis:

Papaya protects the human against inflammatory polyarthritis, a type of Rheumatoid arthritis involving two or more joints.

Promote lung health:

Papaya is a rich source of vitamin A and may help your lung healthy and safe in life.⁽⁴⁶⁾

Helps to prevent attack or stroke

Cysteine or methionine is the folic acid found in papaya converts homocysteine into amino acids. Homocysteine can injure blood vessel walls, may be the reason of heart attack and stroke.

Analytical analysis:

Transmission electron microscope:

The morphology of the Carica papaya leaf-AgNPs. can be visualized by TEM. The size of the silver nanoparticles can be examined by using the picture magnifying software and the particle size less than 10 nm can be magnified by this software and finally give clear morphological data.

Scanning Electron Microscopy:

Image magnification software can be used to analyze the size of the particle and the texture of the nanoparticle and also helps in identifying the presence and formation of silver nanoparticles.

UV- Visible spectrophotometer:

An ELICO SL-159 UV- Visible spectrophotometer was used for the analysis of biosynthesized silver nanoparticles. ⁽⁴⁷⁾

Powder characteristics of female and male plant

Female characteristics of plant



Sclereids



Epidermal
Cells



Sieve Tube



Crystals
& Tracheid



Fibre

Male characteristics of plant



Sieve tube
with sieve
plates



tracheids



Fibre



Crystals

Table 2: Phytochemical analysis of papaya extract with different reagents

Material	Reagent	Color change	Phytochemical
<i>Carica papaya</i> extract	Meyer	Cream yellow ppt	Alkaloid
	Wagner	Brown ppt	
	FeCl ₃	Greenish	Tannins
	KOH	Dirty white ppt	
	NaOH+AlCl ₃ +H ₂ SO ₄	Yellow ppt	Flavonoid
	Olive oil	Stable emulsion	Saponin
	Distilled water	Persistent foam	
	Fehling solution	Brick ppt	
	Distilled water, H ₂ SO ₄ and Fehling solution	Brick red ppt	Glycosides

Table 3: Quantitative microscopy of leaf of *Carica papaya*

Parameter	Result
Stomatal index (male plant)%	32.57+ _ 3.21
Stomatal index (female plant)%	34.46+ _ 3.41

Table 4: Physiochemical analysis of leaves of *Carica papaya*

Parameters	results
Ash value	08.63%
Acid insoluble value	00.79%
Water soluble ash value	05.30 %w/w
Foaming index	Less than 1 cm
Swelling index	Less than 100
Loss on drying	09.41%
Resin content	03.08%

Future aspects of *Carica papaya*

It is demonstrated that papaya contains nutrients like vitamins A,B and C and enzymes like papain, minerals and amino acids which provides the better immunity against several diseases⁽⁴⁸⁾

Papaya has an important role in cosmetics industry like tonic in shampoo and anti-aging creams

Papaya can also moisturize and boost elasticity for skin and hairs

For future aspects, papaya has been used to cure abortifacient, amebicide, asthma, cancer, corns and bile⁽⁴⁹⁾

Conclusion

According to the above study the *Carica papaya* is a nutraceutical plant that shows both the nutritional and medicinal values. The *carica papaya* also contains a wide range of pharmacological activity like anticancer, anti-inflammatory, antispasmodic, and anticoagulant and especially in COVID-19 and dengue fever. *Carica papaya* is a nutraceutical plant because it contains a wide range of enzymes, vitamins, amino acids, flavonoids, alkaloids and other chemical constituents. Papain, chymopapain are effective in treating serious diseases like asthma and osteoarthritis. Carica papaya leaf extract also effective against *Escherichia coli*, *Pseudomonas aeruginosa*, *Kleibseilla pneumonia*, *Staphylococcus aureus* and *Proteus mirabilis*. The size and texture is accessed by SEM and TEM and the biosynthesized silver nanoparticles by UV spectroscopy. The present review is based on the pharmacognosy, phytochemicals and pharmacological activity of *Carica papaya*

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Conflict of interest

There are no conflicts of interest.

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