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## A review on effect of papaya extract on dengue

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### Abstract

Dengue is a viral disease that today affects a vast number of people in over 125 countries and is responsible for a sizable number of deaths. In the absence of an effective antiviral drug to treat the disease, various treatments are being investigated. Studies have indicated that the juice of the leaves of the *Carica papaya* plant from the family Caricaceae could help to increase the platelet levels in these patients. Papaya (*Carica papaya* L.) is a popular and important fruit tree in tropical and subtropical parts of the world. The fruit is consumed worldwide as fresh fruit and vegetable or used as processed product. The fruit is healthy and delicious and the whole plant parts including fruit, root, bark, peel, seeds and pulp are also known to have medicinal properties. The many benefits of papaya are owed due to high content of vitamin A, B and C, proteolytic enzymes like papain and chymopapain which have antiviral, antifungal and antibacterial properties.

**Keywords:** *Carica papaya* leaves, dengue, *Aedes aegypti* and proteolytic enzymes

### Introduction

#### Dengue

Dengue viruses, mosquito-borne members of the Flaviviridae family, are the causative agents of dengue fever <sup>[1]</sup>. Dengue fever is spread through the bite of an infected *Aedes aegypti* mosquito. The mosquito gets the virus by biting an infected person <sup>[2]</sup>. The first symptom of the disease appears in about 5-7 days after the infected mosquito bites a healthy person. The symptoms of dengue fever include high fever, rash, and a severe headache (dengue triad). Additional symptoms include severe joint and muscular pain (break bone fever), nausea, vomiting, and eye pain. Although dengue fever itself is rarely fatal, it can be an extraordinarily painful. The lack of effective therapeutic interventions for dengue has created interest in alternative therapies, i.e., natural and herbal remedies for the disease. *Carica papaya* (CP) leaf extract has recently gained interest in the treatment of dengue, particularly in social media networks, and has shown increasing off-label use in the disease. While the simple extract of papaya leaves is commonly used, there are some commercial preparations containing papaya leaf extract available in certain countries.

#### Active chemical constituents in carica papaya and their uses

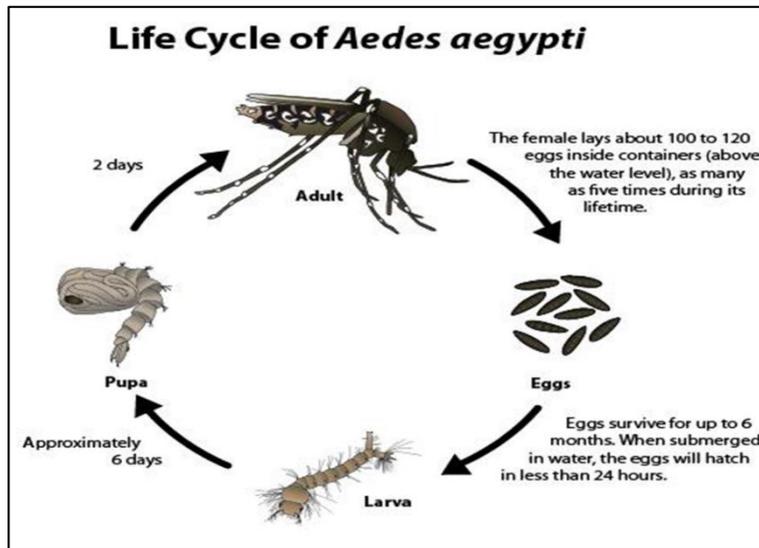
CP is a ubiquitous flowering plant in the tropics; with an edible fruit. The leaves of the plant contain several biologically active compounds, such as papain, caricain, chymopapain, and glycine end peptidase. These compounds have been shown to improve acidic pH, and cause degradation of pepsin <sup>[3]</sup>. CP also contains lipase, which is bound to the water-insoluble component of papain <sup>[4]</sup>. CP leaf extract has been purported to have anti-viral and hematological effects which might have pathophysiological implications for its use as treatment for dengue, such as anti-oxidant and free radical scavenging properties, <sup>[5]</sup> and improved red cell membrane stabilization <sup>[6]</sup>. The flavonoids of CP leaf extract have been shown to inhibit a protease involved in viral assembly <sup>[7]</sup>.

#### Method of preparation of papaya extract

1. Get fresh healthy mature papaya leaves from a fruit-bearing tree.
2. Wash the leaves thoroughly with running tap water and chop the leaves in to small pieces excluding the main stem (not necessary to remove the small stems in the leaves).
3. Weigh 50g of papaya leaves and put it into a mortar and pestle.

4. Add 50ml of boiled cool water and 25g of sugar.
5. Pound the above mixture well for 15 minutes till a uniform pulp is made.
6. Mix this pulp well and keep for about 30 minutes.
7. Squeeze this pulp by hand and get the papaya leaf extract (do not use a cotton sieve to extract the juice).
8. You can store this preparation for 24 hours in the lower compartment of the refrigerator (+40C)
9. Shake the bottle well before the preparation is given.

**Life cycle *Aedes Aegypti* mosquito**

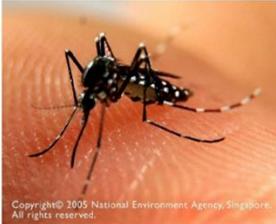


**Note:** The number of mosquitoes depends on environmental conditions such as rain, humidity, and temperature. The total time for development is dependent upon water temperature and food supply, and typically range from 7 to 10 days. Larvae do not develop at temperatures below 12 degrees and above 39 degrees Celsius

**Characteristics of the Aedes Mosquito**

### Characteristics of the *Aedes* Mosquito

- One distinct physical feature - black and white stripes on its body and legs.
- Bites during the day.
- Lays its eggs in clean, stagnant water.



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*Close-up of an Aedes mosquito*



**Introduction to plant of Carica Papaya**



**Fig:** Papaya Tree

**Part of plant and its constituents**

Parts	Chemical Constituent
Fruit	Protein, fat, fiber, carbohydrates, minerals(calcium, phosphorous, iron), Vitamin (vitamin C, thiamine, riboflavin, niacin, and carotene), amino acids, citric and malic acids (green fruits), volatile compounds (linalool, benzyl iso-thiocyanate, cis and trans 2, 6-dimethyl-3,6 epoxy-7 octen-2-ol), Alkaloid (carpaine, benzyl- $\beta$ -D glucoside, 2 phenylethyl - $\beta$ -D-glucoside, 4-hydroxy- phenyl-2 ethyl- $\beta$ -D-glucoside and four isomeric malonated benzyl- $\beta$ -D-glucosides).
Juice	N-butyric, n-hexanoic and n-octanoic acids, lipids; myristic, palmitic, stearic, linoleic, linolenic and cis -vaccenic and oleic acids.
Bark	B-Sitosterol, glucose, fructose, sucrose, galactose and xylitol
Seed	Fatty acids, crude protein, crude fibres, papaya oil, alkaloid Carpaine, some volatile compounds benzyl iso-thiocyanate, benzyl glucosinolate, glucotropacolin, benzyl thiourea, hentriacontane, $\beta$ -sitosterol, caricin and myrosin
Root	Carposide and an enzyme myrosin
Leaf	Alkaloids carpain, pseudocarpain and dehydrocarpaine I and II, choline, carposide, vitamin C and E
Lat x	Proteolytic enzymes, papain and chemopapain, glutamine cyclotransferase, chymopapains A, B and C, peptidase A and B

**Guidelines in using carica papaya leaf extract for Dengue fever patients**

1. In anyone suffering from fever, headache or body pain, it is advisable to do Dengue NS1 antigen test as early as possible.
2. If the Dengue NS1 antigen test is positive, it is very likely that you are suffering from Dengue fever.
3. When you are diagnosed with Dengue fever you should immediately get treatment from an allopathic doctor. Papaya leaf extract should be used in addition to the usual Dengue management.
4. Papaya leaf extract could be given at any stage of the disease. But for best results it should be given from the first day of fever.
5. Papaya leaf extracts could be taken as syrup; 30ml three times a day before meals for an adult and 5-10ml three times a day for a child until you have fully recovered from the illness. It is advised not to stop the treatment halfway.
6. A few sips of cold water could be taken immediately after the Papaya leaf extract, to overcome the bitter taste.
7. Do not take Papaya leaf extract if you are allergic to Papaya.

**Possible mechanism of action of papaya extract in dengue**

The papaya plant possibly brings about its effect in dengue by treating the thrombocytopenia associated with the condition. A study has reported membrane stabilizing properties of *C. papaya* L. leaf extracts in *in vitro* studies. The study found that *C. papaya* L. leaf extracts inhibited heat induced and hypo tonicity induced hemolysis of erythrocytes obtained from both healthy individuals and individuals with dengue infection; the effect was observed at the lower concentrations of the extracts. Thus, the extracts are likely to possess membrane stabilizing properties and protect blood cells against stress induced destruction. This property may be useful in patients with dengue infection where the leaf extracts could possibly prevent platelet lyses. The authors postulate that this effect could be due to the presence of flavonoids and other phenolic compounds in the papaya leaves [8].

**Studies in animals**

A study in mice found an increase in thrombocyte counts in mice administered 15 mg of powdered papaya leaves/kg body weight between 1 and 12 h following dosing [9] Another study found that the *C. papaya* leaf aqueous extract at concentrations of 400 mg/kg and 800 mg/kg significantly increased the platelet counts in cyclophosphamide induced thrombocytopenic rat Model. It also reduced the clotting time in the treated rats [10].

**Studies in humans**

Treatment of dengue using *C. papaya* leaf extract in humans has been reported in very few studies conducted in Asia. A pilot study was conducted in Sri Lanka on 12 patients suspected of suffering from dengue. The patients had a platelet count of <130,000/cu mm, but only six patients were serologically confirmed to be suffering from dengue. The patients received 2 doses of papaya leaf extract at intervals of 8 h. They also received standard symptomatic care for dengue. The study found an increase in platelet count and total

white blood cell count in patients administered papaya leaf extract within 24 h of treatment with the extract [11].

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