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ABOUT DENGUE FEVER AND CARICA PAPAYA, A LEAF EXTRACT OF PAPAYA IS USE TO TREAT DENGUE FEVER:-A REVIEW

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ABSTRACT

The main objective of current study is to investigate the potential of *Caricapapaya* leaves extract used as a herbal medicine to control or treat the dengue in human being, but the effectiveness of this extract in the treatment of dengue has the conflicting reports. In this presentation a brief overview of dengue. The investigated herbal medicine is used to control the mammoth problem of dengue is the extract of the leaves of the papaya plant, *Caricapapaya* plant from the family *caricaceae* could be helped to increase the platelet levels in these patients. This review describes some of the published studies and articles on the topic. The search was done by the authors using Google and the library database and included relevant articles of the last 10 years what is dengue fever and about it, detail pharmacognosy study of papaya, one human study, possible mechanism of action of papaya leaf extract in dengue.

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INTRODUCTION

What is Dengue Fever?

Dengue fever is an infectious disease which is spread by mosquitoes and caused by any of the four related dengue viruses. This disease was called to be "break-bone" fever because it sometimes causes severe joint and muscle pain that feels like bones are breaking. Health experts were known about dengue fever for more than 200 years.

Dengue fever is mainly caused during and shortly after the rainy season in tropical and subtropical areas of the Caribbean, Africa, , South America, China, Southeast Asia and India, the Middle East, Australia and the South and Central Pacific. Worldwide, about 50 to 100 million cases of dengue fever occur every year. This includes 100 to 200 cases in the United States, mostly in people who have recently traveled foreign countries. Many cases likely go unreported because of some health care providers do not recognize this infection.



Cause

Dengue fever may be caused by any one of the four types of dengue viruses: DEN-1, DEN-2, DEN-3, and DEN-4. Person can be infected by at least two if not all four types at different times during their lifetime, but only once by the same type.

Transmission

Dengue virus can be transmitted into person from the bite of an infected Aedes mosquito. This infection can be transmitted by the mosquitoes when mosquitoes become infected when they bite infected humans, and can later transmit the infection to other people. Mainly two species of mosquito, *Aedes aegypti* and *Aedes albopictus*, are being responsible for the all cases of dengue transmitted in Mexico. Mosquito is an intermediate vector for the transmission of dengue infection from person to person.

Symptoms

Symptoms of typical dengue usually start with fever within 4 to 7 days after you have been bitten by an infected mosquito. These symptoms include mainly high fever, up to 105°F, severe headache, retro-orbital (behind the eye) pain, severe joint and muscle pain, nausea and vomiting, and rashes. The rash may appear mostly within 3 to 4 days after the fever begins, and then lasts for 1 to 2 days. Later, there may be a second rash after few days.

Symptoms of hemorrhagic dengue fever include all of the symptoms of classic dengue plus bleeding from the nose, gums, or under the skin, causing purplish bruises, which results from damage to blood vessels. This form of dengue disease may cause death.

Papaya

Papaya is a common fruit usually found in the tropical regions. It can be seen in Mexico, Southern Asia, Central America and some regions of Africa. The papaya is now cultivated in most of the tropical countries. The fruit is also called as pawpaw or papaw in United Kingdom and Africa. It was considered as toxic fruit during the ancient days. But now it is widely cultivated.

[1],

Biological Sources

Botanical Name: *Carica papaya*

Family Name: Caricaceae

Common Name: Papaya, Paw Paw, Kates, Papawa

Part Used: Leaves, Fruits, bark, leaves [2],



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Nutritional Value

The papaya, papaw, or pawpaw is the fruit of the plant *Carica papaya*, the only species in the genus *Carica* of the plant family Caricaceae. It is native to the tropics of the Americas. The papaya is a large, tree-like plant, with a single stem growing from 5 to 10 m (16 to 33 ft) tall, with spirally arranged leaves confined to the top of the trunk. The leaves are large, 50–70 cm in diameter, deeply palmately lobed, with seven lobes. The tree is usually unbranched, unless lopped. The flowers appear on the axils of the leaves which mature into a large fruit. The fruit feels soft when it is ripe and its skin has attained amber to orange hue.

These nutritional values of papaya help to prevent the oxidation of cholesterol. Papaya is rich in iron and calcium; a good source of vitamins A, B and G and an excellent source of vitamin C (ascorbic acid). The extracts of unripe *C. papaya* contain terpenoids, alkaloids, flavonoids, carbohydrates, glycosides, saponins, and steroids. [3],

Table 1: Papaya, raw Nutritional value per 100 g [5].

Energy	163KJ
Sodium	3 mg
Potassium	257
Phosphorus	5
Magnesium	10
Iron	0.10
Calcium	24
Vitamin C	61.8
Folate (vit. B ₉)	38
Vitamin B ₆	0.1
Niacin (vit. B ₃)	0.338
Riboflavin (vit. B ₂)	0.05
Thiamine (vit. B ₁)	0.04 mg
Vitamin A	328
Protein	0.61
Fat	0.14
Dietary fibre	1.8

Phytoconstituents	<i>Carica papaya part</i>
Enzyme	Unripe fruit
Papain, chymopapain	
Carotenoids	Fruits
B carotene, cryptoxanthin	
Carposide	Roots
Glucosinolates	Seeds
Benzyl isothiocynate, papaya oil	
Minerals	Shoots, leaves
Ca, K, Mg, Zn, Mn, Fe	
Monoterpenoids	Fruits
Linalool, 4-terpinol	
Flavonoids	Shoots
Myricetin, kaemferol	
Alkaloids	Leaves
Carpinine, carpaine, vitamin C and E	

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Pharmacological Activity of *Carica Papaya* leaves

Whole *Carica papaya* has a unique pharmacological uses

Leaves :-

Papaya leaf has a numberless of benefits. In some parts of Asia, the young leaves of the papaya are steamed and eaten like spinach. [3]

a. Dengue fever

Commencing on studies of Dr. SanathHettige, who conducted the research on 70 dengue fever patients, said papaya leaf juice helps increase white blood cells and platelets, normalizes clotting, and repairs the liver.

b. Cancer

*Cell Growth Inhibition*Recent research on papaya leaf tea extract has demonstrated cancer cell growth inhibition. It appears to boost the production of key signaling molecules called Th1-type cytokines, which help regulate the immune system. [5], [6],

c. Antimalarial and Antiplasmodial Activity

Papaya leaves are made into tea as a treatment for malaria.^[7] Antimalarial and antiplasmodial activity has been noted in some preparations of the plant,^[7] but the mechanism is not understood and not scientifically proven [7],[8],

d. Facilitate Digestion

Karpain is the chemical compounds present in the leaves of the papaya plants, this compound kills microorganisms that often interfere with the digestive function.[8],

Mechanism of Action of Carica Papaya Extract in Dengue

The papaya plant brings about its effect in dengue by treating the thrombocytopenia associated with the condition. Many studies has reported membrane stabilizing properties of *C. papaya* L. leaf extracts in *in vitro* studies. Studies found that *C. papaya* L. leaf extracts inhibited heat-induced and hypotonicity-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 of leaf. Thus, the extracts are likely to contain 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 prevent platelet lysis. The authors postulate that this effect is may be due to the presence of flavonoids and other phenolic compounds in the papaya leaves. [9]

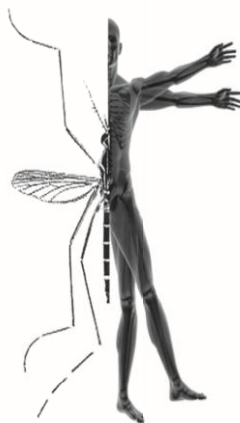
Studies in Humans

Treatment of dengue using *C. papaya* leaf extract in humans has been reported in few studies conducted in Asia. A pilot study was conducted in Sri Lanka on 12 patients suffering from dengue. The platelet count in patients was <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 hours. They were 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 hours of treatment with the extract.[10]

A case report from Pakistan described the effective treatment of dengue in a driver with papaya leaf extract. The patient received 25 mL of papaya leaf extract two times in a day for 5 days. Increase in the platelet and white blood cell count was observed after 2 days of treatment. However, the results of the study to be interpreted with caution, taking into consideration the vague and incorrect details mentioned in the report. For example, the report states that the driver was bitten by a “mosquito carrying Dengue virus”, 24 hours after which he started developing symptoms of dengue.[11],

A case study conducted in Indonesia used *C. papaya* L. leaves extract capsules (CPC), which contained 70% ethanol extract of *C. papaya* leaves. 80 patients included in the study had high continuous fever for 2-7 days, thrombocyte count of <150,000/ μ L and hematocrit of 20% or more. This patients were randomized into two groups; one group received CPC in addition to standard treatment, whereas the other group received only standard treatment for dengue. The study found that platelets in dengue patients increased faster in those who were administered the CPC. The authors thus conclude that treatment with CPC can hasten the recovery of patients and therefore reduce hospitalization. However, there is no clear explanation mention if any of the patients including those in the control group died due to dengue. The study also does not confirm the presence of dengue in these patients.[12]

A report in the British Medical Journal website described the fast recovery of platelet counts in two children suffering from dengue. These cases were proved to be positive for dengue infection by the demonstration of the dengue antigen in the serum. The boys, aged 10 years and 14 years, were administered a spoonful of ground papaya leaves paste every 4 hour. A dramatic increase in platelet counts was observed; in one case within 12 hours of initiating treatment, the count increased to 100,000. In the second case, it increased within 2 days to 250,000 platelet count. The duration of treatment was not mentioned in the British Medical Journal report.[13], A study in the journal of Medicinal and Aromatic Plants reported an increase in platelet counts in five patients within 24 hours who had taken papaya leaf extract for dengue. However, no other details have been provided- whether the dengue was confirmed in these patients, what other treatment was given and whether the increase in platelet count is significant. Furthermore, the response in platelet count beyond 24 hours has not been described.[14],



A study conducted in Malaysia had more systematic approach in evaluating the use of papaya leaf juice in the treatment of dengue. The juice was obtained from the papaya leaves under hygienic conditions from trees that were grown without the use of insecticides or pesticides. An open-labeled randomized controlled trial was conducted on 290 patients between the age of 18 and 60 years with platelet counts of $\leq 100,000/\mu\text{L}$. The patients were confirmed that they were suffering from dengue using a rapid dengue bedside test. Patients in the intervention group were administered fresh juice from 50 gm of *C. papaya* leaves once in a day 15 min after breakfast for 3 days. In addition, they received the standard treatment for dengue infection. The controls only received the standard treatment. The final analysis was conducted on 111 patients from intervention group and 117 controls. The study found that there was a significant increase in the platelet counts in the intervention group at the end of 40 hours when compared to the counts 8 hours after the intervention began. This significant increase of platelet count was not observed in the control group. An increase in arachidonate 12-lipoxygenase and the platelet-activating factor receptor gene expression was also observed in this intervention group. These genes are associated with the increased platelet production.[15],

DISCUSSION

From the various reports published in scientific literature, it appears that *C. papaya* L. leaf extract has beneficial properties in dengue. It has been shown to bring about a rapid increase in the platelet count. This could be attributed to its membrane-stabilizing property. The flavonoids and other phenols which were present in the extract have been suggested to provide the beneficial effects. One study also found that the leaves of papaya plant are rich in several minerals. The researchers suggested that these minerals may also balance the mineral deficiency caused by the dengue virus and strengthen the immune cells against it. [16],

However, it is not entirely clear. First of all, there are very few cases reported. Many of the reports have presumed that the patients suffer from dengue virus due to the presence of thrombocytopenia and have not confirmed the diagnosis. This may be due to the high cost of the test, which is often unaffordable to people in the underdeveloped and developing countries, where most of these studies were conducted. Therefore, it cannot be proved based on these case reports that the extract is effective in dengue. It is possible that the extract may be beneficial in other cases of thrombocytopenia also. Thus, it is important to diagnose the cases correctly and prove beyond doubt that the patient indeed suffers from dengue.

Most of the cases were given a crude papaya leaf extract prepared by grinding the papaya leaves. The amount of extract given was also different among the studies. Thus, the active principle is needed to be identified and the dosage standardized to conduct clinical studies on it to prove its efficacy in dengue beyond doubt. It is also very necessary to conduct pharmacokinetic studies to ensure that the active principle is absorbed from the digestive tract.

In addition to its effect against the dengue virus, the papaya plant also appears to be effective against the *Aedes* mosquito. Thus, if proved to be effective, this plant could control dengue at two levels- at the level of transmission as well as the host level. Papaya extract no doubt offers a cheap and effective treatment for dengue infection. However, it is also necessary not to rely entirely on the leaf extract and ignore standard treatment for dengue virus until the benefits are established. Large scale randomized clinical trials in dengue virus-confirmed patients is necessary to establish their usefulness.

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