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Therapeutic Potential of *Carica papaya* Leaves in Dengue Associated Thrombocytopenia

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Abstract

Dengue is a viral disease that today affects a vast number of people in over 128 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. In Pakistan 505,430 dengue cases reported. There is no specific treatment for dengue fever. Fever reducers and pain killers can be taken to control the symptoms of muscle aches and pains, and fever. The best options to treat these symptoms are acetaminophen or paracetamol. The first dengue vaccine, Dengvaxia but there are not properly beneficial for dengue disease. *Carica papaya* leave's juice is given to those who are effected with dengue fever they used their leaves as an herbal medicine. *Carica papaya* leaves juice significantly accelerates the rate of increase in platelet count among patients with dengue fever and dengue hemorrhagic fever.

Keywords: *Carica papaya* leaves, Dengue, Dengue treatment.

INTRODUCTION

Carica papaya is a juicy and tasty fruit belongs to the genus *Carica* and family *Caricacea*, and scientifically known to be *Carica papaya* Linn and it is a dicotyledonous, polygamous, plant and diploid species [1]. Nature has been considered as a source of various medicinal plants, which aids in the wide variety of human treatments. Papaya is a small evergreen tropical plant that bears papaya fruit throughout the year. Due to its medicinal properties and other nutraceutical activities, it is the most widely cultivated and best-known species [2].

Papaya plant has been identified with variety and considerable size and with quality and characteristics. C. papaya is an indigenous plant cultivated in almost all parts of the world, large scale in India, Sri Lanka, Tanzania, Florida, Philippines, South Africa, and Australia. Among these countries, India is the largest cultivar of papaya. In India, Maharashtra, Bihar, West Bengal, Haryana, Punjab, Delhi, Uttar Pradesh, and Andhra Pradesh are states involved in the cultivation of C. papaya plant [3].

Botanical Classification [4]

1. Domain	Flowering plant
2. Sub Kingdom	Tracheobionta
3. Class	Magnoliopsida
4. Subclass	Dilleniidae
5. Superdivision	Spermatophyta
6. Phyllum	Steptophyta
7. Order	Brassicales
8. Family	Caricaceae
9. Genus	Carica
10. Botanical Name	Carica papaya Linn

Its origin is Southern Mexico, Central America, and the northern part of South America. Now it is cultivated in many tropical countries such as Bangladesh, India, Indonesia, Sri Lanka, the Philippines, and the West Indies including Malaysia. Malaysia is known to be one of the top 5 papaya exporting countries [5].

Constituents of papaya plant

Carica papaya linn is one of the important plant used for numerous purposes in the field of medicine .Clinical make up of different parts of papaya plant are described in the table [6].

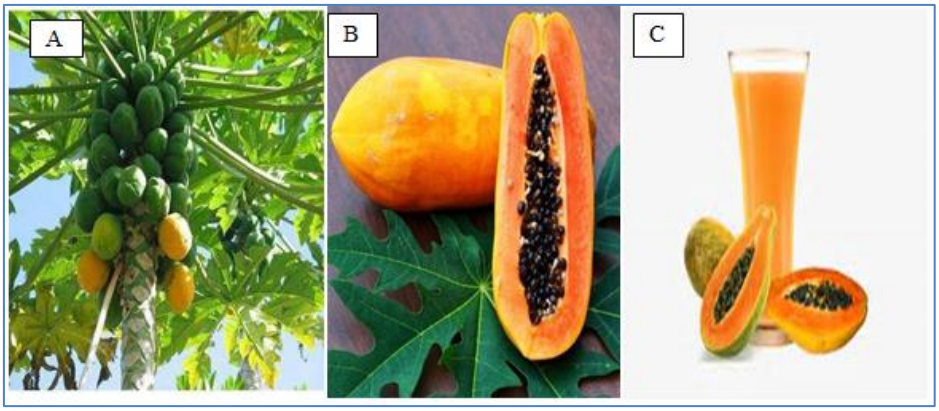

Fig: 01 A): Carcia papaya plant B) *Carcia papaya* fruit with seed C) *Carcia papaya* juice [7, 8].

Table-01: Chemical composition of various parts of *Carica papaya* Linn Plant [9, 10, 11].

Part	Constituents
1. Fruit	protein, fat, fibre, carbohydrates, minerals, calcium, phosphorus, iron, vitaminc ,thiamine, riboflavin, niacin, and caroxene, amino acid, citric acids and molic acid (green fruits), volatile compounds : linalol, benzylisothiocynate, cis and trans 2, 6-dimethyl-3,6 expoxy-7 octen-2-ol. Alkaloid, α; carpaine, benzyl-β-d glucoside, 2-phenylethl-β-D-glucoside, 4- hydroxyl -phenyl-2 ethyl-B-D glucoside and four isomeric malonated benzyl-β-D glucosides
2. Juice	N-butyric, n-hexanoic and n-octanoic acids, lipids; myristic, palmitic, stearic, linoleic, linolenic acids-vaccenic acid and oleic acids
3. Seed	Fatty acids, crude proteins, crude fibre, papaya oil, carpaine, benzylisothiocynate, benzylglucosinolate, glucotropacolin, benzylthiourea, hentriacontane, β-sistosterol, caricin and an enzyme nyrosin
4. Root	Arposide and an enzyme myrosin
5. Leaves	Alkaloids carpain, pseudocarpain and dehydrocarpaine I and II, choline, carposide, vitamin C and E
6. Bark	β-sitosterol, glucose, fructose, sucrose, galactose and xylitol
7. Latex	proteolytic enzymes, papain and chemopapain, glutamine cyclotransferase, chymopapain A, B and C, peptidase A and B and lysozymes

Table-02: Medicinal and pharmacological properties of various parts of *carcia papaya* plant

Parts	Benefits
01:leaves	1. Papaya leaf juice helps to increase white blood cells and platelets, normalizes clotting and also helps to repair the liver. 2. Recent research shows that papaya leaf tea extract inhibits growth of the cancer cell. it helps to enhance the production of key signaling molecules called Th1-Typ. 3. Car-pain the constituent of papaya leaves kills microorganisms which affects the digestive function. It helps to increase appetite, relieve nausea and ease menstruation.[12] 4. The leaves of C. papaya have been used in folk medicine for centuries. Recent studies have shown its beneficial effect as an anti- inflammatory agent [10], for its wound healing properties [11], antitumor as well as immunomodulatory effects and as an antioxidant [13]. 5. A toxicity study (acute, sub acute, and chronic toxicity) conducted on Sprague Dawley rats administered with *Carica papaya* leaves juice (CPLJ) of the sekaki variant revealed that it was safe for oral consumption.[14]
2.Papaya fruit	1. Papaya fruit is laxative in nature and helps to maintain regular bowel movement. 2. Folic acid in papaya is required to convert homocysteine into cysteine. This cysteine helps to avoid heart attack ot stroke .[9] 3. The papaya fruit is globally used in different form such as fresh or the form of juices, jams, and crystallized dry fruit [15]. 4. The ripe C. papaya fruit is the rich source of vitamin A, C, and calcium [16].
03:seeds	1. Papaya seeds have an antibacterial property which helps to play affective role against infections of E.coli Salmonella and Staphylococcus.

	2. Papaya seeds help to protect kidney from toxins and also detoxify the liver.[10]
04:peel	01- Papaya peal can be use as skin lightening agent. 02- Papaya peal with the honey is used as a skin moisturizer. 03- Papaya, Orange, lavender and rosemary oil along with vinegar added to bath water which helps to relax muscles and relieve pain.[11]

Dengue fever

Dengue viruses, mosquito-borne members of the *Flaviviridae* family, are the causative agents of dengue fever [16]. Dengue is an arboviral infection transmitted by mosquitoes of the Aedes species. It is a disease with global implications, resulting in considerable morbidity and mortality. Transmission occurs in at least 128 countries, and almost 4 billion people are at risk [17]. According to the survey of World Health Organization every year 50 million people across the world are infected by dengue fever and about 2/5 of the world population are at risk from this dreadful disease which spread over about 100 countries [18].

Dengue fever occurs due to infection by four distinct serotypes (DEN 1–4), and has diverse manifestations, ranging from an uncomplicated febrile illness to serious disease with organ dysfunction. In the more severe forms, plasma leakage gives rise to shock and organ failure; life threatening haemorrhage can also occur. Unusual organ manifestations of dengue are also increasingly reported, and comprise the expanded dengue syndrome [19]. The mosquito gets the virus by biting an infected person [20]. The first symptom of the disease appears in about 5-7 days after the infected mosquito bites a healthy person. It is possible to become infected by dengue multiple times because the virus has four different serotypes [21].

Dengue is a viral disease which is carried by an arthropod that is the mosquito *Aedes aegypti* is the vector, caused by 4 possible viral serotypes, namely, serotype 1, 2, 3, and 4. In Malaysia, dengue cases have been on the rise since 2002. Total 9l of 18,371 cases of dengue fever (DF) and dengue hemorrhagic fever (DHF) were reported last year and had claimed 33 lives in the same year [18]. In pakistan 505,343 dengue cases reported. Dengue Hemorrhagic Fever (DHF), a potentially lethal complication, was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand. Today DHF affects most Asian countries and has become a leading cause of hospitalization and death among children in the region [19].

Symptoms of Dengue Fever

Following are the symptoms of Dengue hemorrhagic fever, the most serious form of dengue fever, are hypotension, increased vascular permeability, thrombocytopenia and hemorrhagic manifestations [7, 8]. Thrombocytopenia is blood disorder and it is very rare and affects the platelets of the blood. Characteristics include low platelet count (100000 cells per mm [20] of blood or less) and low platelet survival time. Other symptoms include a tendency to bleed excessively into mucous membranes, especially during menstruation. [21]. Dengue patient are identical on some signs and symptom high fever, headache, muscle pain, joint pain, red rashes, bleeding from nose and mouth including itching and allergy [3]. In this fever virus required a host and then replicate [6].This make it difficult to eradicate the virus without harming the host organism's cells [7].

Treatment

There is no specific treatment for dengue fever [21]. The first dengue vaccine, Dengvaxia (CYD-TDV) developed by Sanofi Pasteur was licensed in December 2015 and has now been approved by regulatory authorities in 20 countries. Developing a safe and effective antiviral drug is difficult, because viruses use the host's cells to replicate. That makes it difficult to eradicate the virus without harming the host organism's cells [22]. Recently, *Carica papaya* leaves have been successfully employed in folk medicine for the treatment of dengue infections with hemorrhagic manifestations, using suspensions of powdered leaves in palm oil [23]**.** In the current study, the ability of *Carica papaya* leaf aqueous extract in increasing the platelet count in cyclophosphamide induced thrombocytopenic rat model was evaluated [24].

***Carica papaya* & Dengue**

Carica papaya has widely been used in history as a form of cure for Dengue. It is a herb and is commonly easy treatment. It has the ability to increase the number of platelets in dengue patient to help him fight the virus. *Carica papaya* leave's juice is given to those who are effected with dengue fever they used their leaves as a herbal medicine. They have ability to recover dengue fever and dengue hamorrhagi Fever [25].

Before papaya flowers appear or just as they appear, preventative fungicides may help control papaya anthracnose. Use a fungicide containing Copper hydroxide, after crushing and squeezing one leaf of a papaya gives about one tablespoon of papaya juice .to test the effectiveness of papaya juice two table sppons of papaya leaf juice is administered to dengue patient three times per daya after every 6 hours interval [26]. A study was conducted to identify the effects of papaya leaf juice as an herbal medicine for the treatment of dengue fever .fresh leaves of papaya plant collected and then their juice is extracted by crushing and squeezing

them. The extracted juice is strained to separate uncrushed fibers of papaya [27].

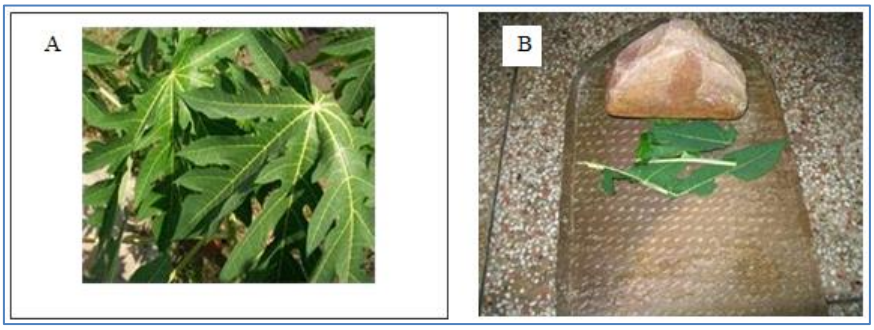

Fig-02: A) circa papaya leaf B) crushing material of leaf [28]

After crushing and squeezing one leaf of a papaya gives about one tablespoon of papaya juice to test the effectiveness of papaya juice two table spoons of papaya leaf juice is administered to dengue patient three times per day after every 6 hours interval. [29] Before papaya flowers appear or just as they appear, preventative fungicides may help control papaya anthracnose. Use a fungicide containing Copper hydroxide [30].

Table-03: Effects of papaya leaf juice in improving the blood platelets. [31, 32]

No of Patients	Age of patients	Platelets before using papaya leaf juice	Platelets after using papaya leaf juice (After 24 hrs)
1	38 yrs	28000	36000
2	52 yrs	80000	91000
3	41 yrs	143000	151000
4	23 yrs	46000	55000
5	19 yrs	67000	78000

After this herbal treatment improvement in platelets counts is observed this provides an evidence of positive effects of papaya on the dengue fever [33].

CONCLUSION

Dengue is a viral disease in all over the world large no. of people affected by this disease. In dengue fever no. of platelets are rapidly fall in lowest rate. basically this fever have three day cycle and show different symptoms in different People some time show low Bp rate, Allergy, bleeding from nose. Papaya leaves are used for the treatment of Dengue fever. Their leaves are used for the recovery of Disease. basically this fever have three day cycle and show different symptoms in different People some time show low Bp rate, Allergy, bleeding from nose. Papaya leaves are used for the treatment of Dengue fever. Their leaves are used for the recovery of Disease. Mannose, Azoxystrobin or Bacillus, Spray the orchard with the fungicide every two to four weeks. *Carica papaya* leaves juice significantly accelerates the rate of increase in platelet count among patients with dengue fever and dengue hemorrhagic fever.

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