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Extraction and effects of papain obtained from leaves of *carica papaya*: A remedy to dengue fever

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Abstract
Aim: In this study we will see about the source, extraction, co-constitutes of papain especially from *Carica papaya* which is actively used nowadays to get symptomatic relief from dengue fever. We will also discuss about the extracts and formulations that can be done using *Carica papaya* leaves so that we get a maximum extent of papain activity. We focus on papain because of its broad range of activity than other constituents which have lesser activity that are found in *Carica papaya*.

Keywords: papain, *carica papaya*, dengue treatment, nutritional value, chemical constituents, papaya leaf extract, pharmacological uses

Introduction

Overview about dengue

Dengue is a mosquito-borne infection which in recent decades has become a major international public health problem. Dengue is prevalent in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban areas[3]. It has become a major public health problem. Dengue Heamorrhagic 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. There are four distinct types, but closely related viruses which cause dengue. Recovery from infection by one type provides lifelong immunity against that virus but confers only partial and transient protection against subsequent infection by the other three types of viruses. There is evidence that sequential infection increases the risk of developing DHF. Up to date there is no specific treatment for dengue fever. Lack of adequate global interest and funding has greatly restricted the development of treatment regimes. Ayurvedicliterature reveals that papaya *(Carica Papaya)* leaf extract has haemostatic and other medicinal properties that could be utilized very much in treatment of dengue.

Carica papaya

The origin of *Carica Papaya*[1] is in Tropical America. Its seeds were distributed from the Caribbean to Malacca and India by travelers and botanists in the eighteenth century. The distribution was continued throughout Asia and Pacific. *Carica Papaya* is grown in all tropical countries and many subtropical countries.

Fig 1: Papaya fruit

Fig 2: Papaya plant

Synonym: papaw
Biological source: *Carica Papaya* Linn.
Family: *Caricaceae*

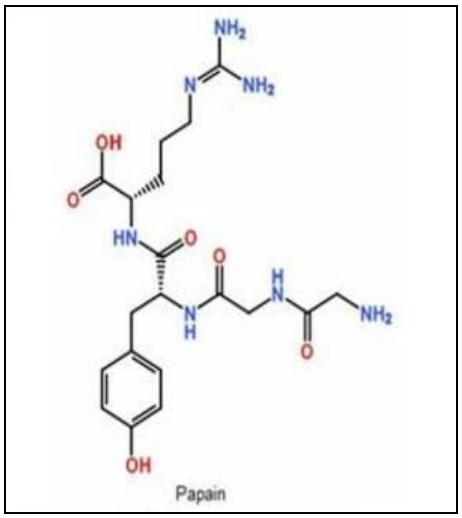

Fig 3

Structure of papain[7]

Papain is a sulfhydryl protease from the latex of the papaya fruit. Its molecules consist of one polypeptide chain with 212 amino acid residues. The chain is folded into two domains with the active site in a groove between the domains[7].

Table 1: Nutritional value of *carica papaya*

Nutrients	Mg	Percentage
Folates	38 µg	9.5 %
Nicain	0.338 mg	2 %
Pantothenic acid	0.218 mg	4 %
Pyridoxine	0.019 mg	1.5 %
Riboflavin	0.032 mg	2.5 %
Thiamin	0.027 mg	2 %
Vitamin A	1094 IU	36 %
Vitamin C	61.8 mg	103 %
Vitamin E	0.73 mg	5 %
Vitamin K	2.6 µg	2 %
Sodium	3 mg	0 %
Potassium	257 mg	5 %
Calcium	24 mg	2.5 %
Iron	0.10 mg	1 %
Magnesium	10 mg	2.5 %
Phosphorous	5 mg	1 %
Zinc	0.07 mg	0.5 %

Table 2: Chemical constituents[2]

Phytoconstituents	Carica Papaya Part
Enzyme	Unripe fruit
Papain,	
Chymopapain	
Carotenoids	Fruits
B-carotene,	
Crytoxanthin	
Carposide	Roots
Glucosinolates	Seeds
Benzyl isothiocynate,	
Papaya oil	
Minerals	Shoots,
Ca, K, Mg, Zn, Mn, Fe	Leaves
Monoterpenoids	Fruits
Linalool,	
4-terpinol	
Flavonoids	Shoots
Myricetin,	
Kaemferol	
Alkaloids	Leaves
Carpinine	
Carpine,	
Vitamin C and E	

Table 3: pharmacological uses[3]

Part	Uses
Latex	▪ Anthelmintic, ▪ Dyspepsia, ▪ Diarrhoea, ▪ Pain of burns and topical use, ▪ Bleeding haemorrhoids, ▪ Stomachic, ▪ Whooping Cough.
Ripe fruits	▪ Stomachic, ▪ Digestive, ▪ Carminative, ▪ Diuretic, ▪ Dysentery and Chronic diarrhoea, ▪ Expectorant, ▪ Sedative and tonic, ▪ Relieves obesity, ▪ Bleeding piles, ▪ Wounds of the urinary tract, ▪ Ringworm, ▪ Skin diseases and Psoriasis.
Unripe fruit	▪ Laxative, ▪ Diuretic, ▪ Dried fruit ▪ Reduces enlarged spleen and liver, ▪ used in snakebite to remove poison, ▪ Abortifacient, ▪ Anti-implantation activity, ▪ Antibacterial activity.
Seeds	▪ Carminative, ▪ Emmenagogue, ▪ Vermifuge, ▪ Abortifacient, ▪ Counter irritant, ▪ Ringworm and Psoriasis, ▪ Antifertility agents in males.

Seed juice	▪ Bleeding piles, ▪ Enlarged liver and spleen.
Root	▪ Abortifacient, ▪ Diuretic, ▪ Checking irregular bleeding from the uterus, piles, ▪ Antifungal activity.
Young leaves and vegetable	▪ Jaundice (fine paste), ▪ Urinary complaints &Gonorrhoea(infusion), Dressing wounds (fresh leaves), ▪ Antibacterial activity, ▪ Vermifuge, in colic, fever, beriberi, abortion (infusion), asthma (smoke).
Stem bark	▪ Jaundice, ▪ Anti-haemolytic activity, ▪ STD, ▪ sore teeth (inner bark), ▪ Antifungal activity.
Flowers	▪ Jaundice, ▪ Emmenagogue, ▪ Febrifuge, ▪ Pectoral properties.

Preparataion of extract of papaya leaf[4]

Air dried papaya leaves of250 grams were crushed and charged for extraction in a round bottom flask of glass. It was extracted at 80°C thrice with triple volume of de-mineralized water. All three washings were collected and distilled under vacuum up to 20-30TDS. Resultant syrup mass was dried in vacuum oven. Crude papaya leaf extract of approximately 45 grams was obtained.

Action of papain on platelet count[5]

Thrombocytopenia is a characteristic feature of dengue fever. Dengue virus induces bone marrow suppression; it can bind to human platelets in presence of virus specific antibody and immune mediated clearance of platelets, spontaneous aggregation of platelets to vascular endothelial cells pre-infected by virus inducing aggregation, lysis and platelet destruction. Anti-platelet antibody generated after dengue virus infection causes destruction of platelets.

A study for evaluation of platelet augmentation activity of *Carica Papaya* leaf aqueous extract in mice with cyclophosphamide induced thrombocytopenia by Patil *et al.*, showed significant increase in platelet count and decreasing clotting time.

Many active components of papaya carica extract such as papain, chymopapain, cystatin, tocopherol, ascorbic acid, flavonoids, cyanogenic-glucosides and glucosinolates inhibit immune mediated platelet destruction, bone marrow suppression by virus and stabilize the membrane of infected cells in dengue fever, so fasten the natural course of recovery with increasing the platelet count and prevents the complication of thrombocytopenia without any side effects.

Other pharmacological uses

- Antimicrobial
- Anti-amoebic
- Anthelminitic
- Antimalarial
- Antifungal
- Hepatoprotective
- Diuretic
- Immunomodulatory
- Female antifertility

Result

From our study we can conclude that papain can be actively used to give symptomatic relief from dengue haemorrhagic fever. The papain extract obtained from *Carica Papaya* leaves enable quick recovery from platelet destruction by inhibiting the immune mediated destruction of platelets. Currently *Carica Papaya* tablets and syrups are available in the market. In future probably *Carica Papaya* extract consisting of all other constituents other than papain can be used to treat not only dengue but a broad range of diseases.

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