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PHARMACOLOGICAL AND CHEMICAL COMPOSITION OF CARICA PAPAYA: ON OVERVIEW

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ABSTRACT

Papaya (Carica papaya linn) is well known for its exceptional nutritional and medicinal properties throughout the world. From the times immemorial, the whole Papaya plant including its leaves, seeds, ripe and unripe fruits and their juice is used as traditional medicine. Nowadays, Papaya is considered as nutraceutical fruit due to its multifaceted medicinal properties. The prominent medicinal properties of papaya include Dengue, Anti-fertility, Diuretic, Uretonic, Anti-hypertensive, Hypolipidemic, Anti-helmintic, Wound healing, Anti -fungal, Antibacterial, Antitumor and free radical scavenging activities. Phytochemically, the whole plant contains enzymes (Papain), lycopene, carotenoids, alkaloids, monoterpenoids, flavonoids, mineral and vitamins. This important nutricious fruits feed the body and immune system. In present review article, a attempt is made to compile all the strange facts available about this tasty fruit. This tasty fruit of papaya is popular among family members of all ages for the delicious dishes derived from it.

KEYWORDS: Carica papaya Linn, Papaya, dengue, Nutraceutical, Wound healing.

INTRODUCTION

It is a mixture of proteolytic enzyme derived from the latex of unripe fruit of tropical melon tree, *Carica papaya,* belonging to family Caricaceae.[1] The medicinal effect of *C. Papaya* leaves extract can be recognized due to the presence of several active components such as papain, chymopapain, alkaloid, glycoside, tannin, saponin, L-tocopherol, ascorbic acid, riboflavin, Flavonoids and mineral(such as calcium, iron, magnesium, potassium, sodium, and zinc)etc. Carica papaya plant could be helped to increase the platelet levels in these patients.[2]

Table 1: Botanical Classification of Papaya.

Domain	Flowering plant
Kingdom	Plantae
Subkingdom	Tracheobionta
Class	Magnoliopsida
Subclass	Dilleniidae
Division	Magnoliophyta
Subdivision	Spermatophyta
Phylum	Steptophyta
Order	Brassicales
Family	Caricaceae
Genus	Carica
Botanical name	*Carica papaya* Linn.

Figure-1:Carica papaya tree[3]

Botanical Description

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. Papaya is a tree like a plant and it can be 16-33 feet tall. The leaves are 50-70 cm in diameter with deep seven lobes. *C. Papaya* tree comes into fruiting with in 5 months and lives for 4-5 year. Usually, male and female flowers are on different tree, but some flowers are bisexual. *C.papaya* leaves are spirally arranged. They are clustered near apex of the trunk; the petiole is up to 1m long, hallow, greenish and 25-75 cm in diameter.[4]

Phytochemical constituent of C. Papaya

Table 2: Chemical composition of various parts of Papaya plant.[5,6,7]

Part	**Constituents**
Fruits	Protein, fat, carbohydrates, minerals, vitamins, volatile compound, alkaloids, glycosides.
Juice	N-butyric, n-hexanoic and n-octanoic acid, lipid, myristic, palmitic, stearic linoleic, linolenic acid and oleic acid
Seed	Fatty acid, crude protein, crude fibres, papaiya oil, carpaine, benzyl isothiocyanate, benzylthiourea, β-sitosterol, caricin and enzyme myrosin.
Root	Caproside and enzyme myrosine
Leaves	Alkaloids carpain, pseudocarpain and dehydrocarpain 1,2, choline, caproside, vitamin C and E.
Bark	β-sitosterol, glucose, fructose, galactose and xylitol.
Latex	Proteolytic enzyme papain, chemopapain, glutamine cyclotransferase, chymopapain A,B,C, peptidase A and B, lysosome.

Table-3: Phytochemical constituent of *Carica papaya* leaves in mg/10 g residue of different solvents.[8,9]

Phytochemicals	Solvent extraction (ethanol) mg/10 g residue	Solvent extraction (hot water) mg/10 g residue	Solvent extraction (acetone) mg/10 g residue	Solvent extraction (chloroform) mg/10 g residue
Phenols	0.7	0.7	0.64	0.56
Flavonoids	10.0	0.0	0.21	0.22
Saponins	0.8	0.04	0.04	0.4
Alkaloids	0.6	0.01	0.02	0.54
Glycosides	0.7	0.01	0.3	1.6

Method of Papaya Leaf Extraction

Air dried papaya leaves of 250 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 demineralised water. All three washings we recollected and distilled under vacuum up to 20-30 TDS.[11] Resultant syrup mass was dried in vacuum oven. Crude papaya leaf extract of approx 45 gms was obtained.[12]

Therapeutic Properties/ Uses

1. 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.[13] 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.[14]

Figure-2: Infected mosquito.

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.[15] 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.[16] 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.[17]

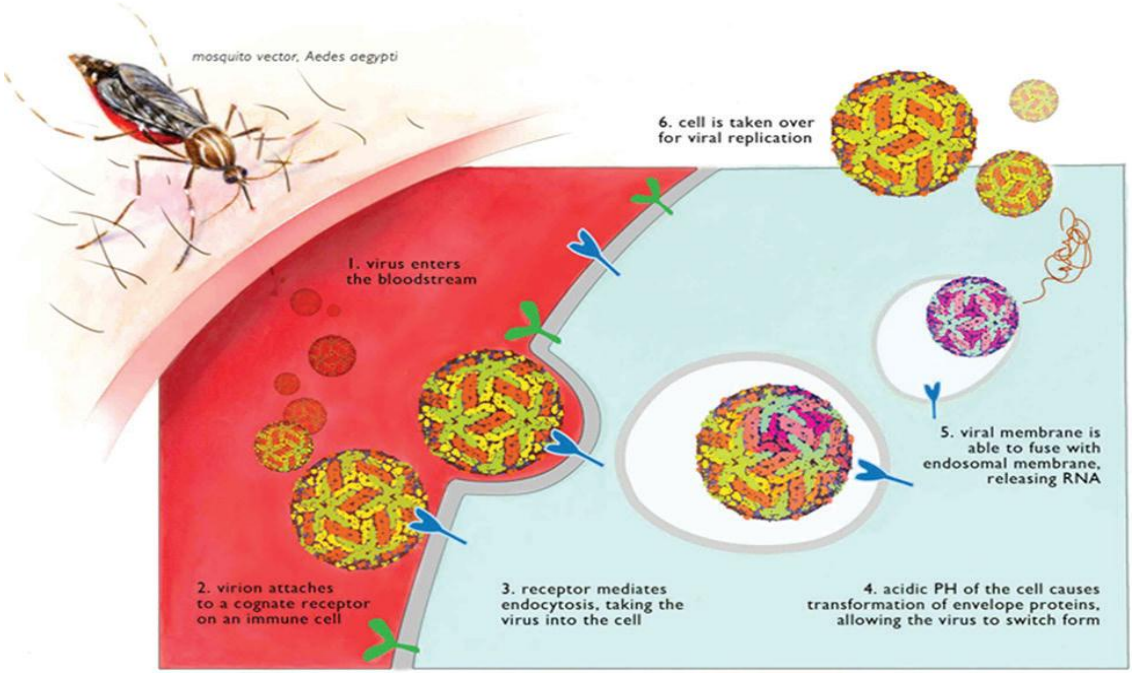

Figure-3: Primary Infection Pathway of the Dengue Virus.[15]

2. Anti-inflammatory activity

The anti-inflammatory property of plant cysteine proteinases were already noted in literature. In a clinical study, the histological severity of inflammatory bowel disease was determined for treatment of chronic inflammatory and related diseases papain has found to be safe and efficacious.[18] Anti-inflammatory activity of papaya seeds were also reported.[19] The anti-inflammatory effect of the leaves extract including the reference drug was very poor when using the carrageenan method, the 100 mg/kg extract produced its highest effect at 3 hr (2.7%) after carrageenan injection while the 200 mg/kg extract also produced its effects at 3

hr (6.7%) after injection. The reference drug indomethacin produced time dependant reduction as the effect was more pronounced at 3 hr (11.4%) of carrageenan administration. The results of this investigation revealed that the aqueous extract of the leaves was slightly less effective than that of indomethacin.[20]

3. Wound healing activity

The similarities between latex coagulation in papaya and the mammalian coagulation process led us to propose that some analogous factor may be present in both systems. If putative analogies do occur, it is possible that some plant metabolites intervening during plant healing may also act during the healing process ensuring clot formation in mammals.[21] The proliferative effect of papain attained 15% above control, suggesting that this properly is specific for some proteolytic enzymes.[22] Also one study showed that papain from C. papaya latex was effective in protecting histamine-induced ulcer in rat by blocking the acid secretion.[23] Papain major component of papaya latex is nonspecific cysteine proteinase that is capable of breaking down a wide variety of necrotic tissue substrates over a wide pH range from 3.0 to 12.0.[24] This factor may also have contributed to the faster wound healing and was facilitated by the action proteinases. Papain also known to be effective in disloughing necrotic tissue, prevention of infection and the antimicrobial and antioxidant properties related to hydroxyl scavenging and iron chelating properties.[25] Moreover, they decrease the risk of oxidative damage to tissue also they show burn healing properties as the increment in hydroxyproline content.[26]

4. Anti-fertility activity

The anti-fertility effects of Carica papaya were investigated by feeding adult and pregnant rat with different components of the fruit. No attempt was made to force feed the animal and the result indicated that the unripe fruit interrupted the estrous cycle and induced abortion. This effect vanished as the fruit became stale or over riped. Chloroform extract of Carica papaya seeds induced long term azoospermia in languor monkey.[27] Papaya also showed the anti-implantation and abortifacient effect.[28]

5. Antihelmintic activity

A wide range of plants and plant extracts has been used traditionally for the treatment of helminthes infections including papaya, which is rich in proteolytic enzymes known to digest nematode cuticles, have low toxicity and have been used in traditional medicine against gastrointestinal nematodes for decades.[29] In 1940, the worm digesting activity of a

preparation of papain from *C.papaya* latex was described as they rapidly digest the ascaris cuticle.

5. Anticancer activity

Initially pharmaceutical preparations containing various proteolytic enzymes (papain) have been used as adjuvant in the treatment of malignant diseases, despite lack of knowledge of their mode of action. Experiments indicate that the effects after oral administration of polyenzymes preparations are related to the induction of cytokines production by human peripheral blood mononuclear cells.[30] Papaya *in vitro* study shows that it will treat many cancer cell line and they have anticancer activity. Papain enzyme from papaya effective against cancer. Papain breaks down the fibrin cancer cell wall and protein into amino acid form. Other than papain it also contain lycopene which highly reactive towards oxygen and free radical. Isothiocyanate effective against breast, lung, colon, pancreas, prostate as well as leukemia. These enzymes capable of inhibiting both formation and development of cancer cell.[31]

6. Antifungal activity

The latex of papaya and fluconazole has synergistic action on the inhibition of Candida albicans growth.[32] This synergistic effect results in partial cell wall degradation due to lack of polysaccharides constituents in the outermost layers of fungal cell wall and release of cell debris into the cell culture. Latex proteins appear to be responsible for antifungal action and minimum protein concentration for producing a complete inhibition was reported as about 138 mg/dl.[33]

7. Antibacterial activity

The seeds of Carica papaya were found to possess bacteriostatic activity against several enteropathogens such as bacillus subtilis, enterobacter cloacae, escherichia coli, salmonella typhi, staphylococcus, proteas vulgaris, pseudomonas aeruginosa and klebsiella pneumonia. Among the gram-positive and gram-negative bacteria tested the gram negative bacteria were more susceptible to the extract.[34,35,36]

8. Anti-hypertensive activity

Papaya leaves decoction can be used as an anti-hypertensive agent. A study on villagers of Agboville located at 80 km of Abidjan (West Africa), showed the hypotensive activity of papaya plant when administered orally.[37]

9. Anti-amoebic activity

The cold macerated aqueous extract of matured papaya seeds has shown anti-amoebic activity against Entamoeba histolytica.[38,39]

10. Immunomodulatory activity

Papain induces human eosinophils to degranulate and to produce superoxide anion. The E-64 inhibitors abolished the activation by papain suggesting that the protease activity is required to trigger eosinophil response. It is likely that this action in eosinophils is mediated by protein G linked receptor. As it stands it appears that bromelaine and papain depending on the target cell display opposite effects.[40,41]

11. Anti- sickling activity

Sickle cell disease (SCD) results from a mutation in hemoglobin inside the red blood cells, where a glutamic acid at 6th position is replaced by valine. Recent studies showed that unripe papaya fruit extract has anti-sickling activity.[42] Another study showed the potent anti-sickling property of Carica papaya leaf extract in a dose- dependent manner.[43] Aqueous root extract of papaya when given orally at a dose of 10 mg/kg to rats produces significant increase in urine output and shows similar profiles of urinary electrolyte excretion to that of hydrochlorothiazide.[44,45]

12. Hypoglycemic and hypolipidemic activity

Study show that oral treatment with 0.1 mg/kg/day of glibenclamide and 100-400 mg/kg/day of aqueous seed extract of Carica papaya induced significant, steady and progressive hypo-glycemic and hypo-lipidemic effect.[46]

CONCLUSION

Papaya (*Carica papaya* Linn.) is well known for its exceptional and medicinal properties throughout the world. The whole Papaya plant including its leaves, seeds, ripe and unripe fruits and their juices is used as traditional medicine. The available literature does not reveal any adverse/toxic effects upon consumption. Quite a significant amount of work has been done on the biological activity and hence extensive investigation on its pharmacodyanamics, kinetics and proper standardization and clinical trials is needed to exploit their therapeutic utility to combat various diseases.

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