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A REVIEW ON MEDICINAL PROPERTIES OF CARICA PAPAYA

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ABSTRACT

The present paper deals with origin and distribution, brief morphological characters, nutritional value and medicinal properties of carica papaya plants. Papaya (*Carica papaya* Linn.) is commonly known for its food and nutritional values throughout the world. The medicinal properties of papaya fruit and other parts of the plant are also well known in traditional system of medicine. Since, each part of papaya tree possesses economic value; it is grown on commercial scale. During the last few decades considerable progress has been achieved regarding the biological activity and medicinal application of papaya and now it is considered as valuable nutraceutical fruit plant. It can be chosen as a source of papain for the development of various industrial and pharmaceutical products. In the present review nutritional value of the fruit and medicinal properties of its various parts have been discussed to provide collective information on this multipurpose commercial fruit crop. The present paper deals with origin and distribution, brief morphological characters, nutritional value and results of reported research findings on its medicinal properties

KEYWORDS: Papaya, *Carica papaya*, Medicinal plant, Fruit, Papain.

INTRODUCTION

Papaya belonging to the small family –caricaceae.it is a possible souce of breeding for inducing freezing and virus resistance in culvated papaya. The fruits, leaves, latex and bark obtained from papaya plantare used for medicinally and for various ourposes. The main active constituent present in papaya is papain. Papain is a major chemical compound extracted from fruit and stem latex is used in brewing and wine making and in the textile and tanning industries. Proteins in diet are essential for growth, repair and for regulating the homeostasis of the body functions. But many people are intolerant to such foods including milk, cheese, yogurt, baked beans, bean soup, eggs, chicken, fish, meat, etc. This intolerance

can lead to uncomfortable and embarrassing symptoms such as flatulence, bloating, belching, diarrhoea/constipation, malnutrition, food allergies, anaemia, undigested food in stool, chronic intestinal parasites and abnormal flora. These symptoms usually occur during achlorhydria and/or pancreatin insufficiency. So, the need of protein digesting supplement arises to overcome the deficiency manifestations. Now a day's demand of protein digesting aids has increased on the other hand supply of pepsin (prepared from hog mucosa) has decreased. Thus, the plant source derived proteases like papain can be used as supplement as there will be no scarcity relative to its supply.4) Papain is a food grade, highly active endolytic cysteine protease (EC 3.4.22.2) derived from Carica papaya. Its broad substrate specificity and the ability to hydrolyze small peptides as well as large proteins make papain an ideal enzymatic supplement. The optimum pH value for the activity of papain is in the range of 5.0-9.0, varying with different substrates. Papain is almost inactive at gastric pH of 1.2. Therefore, the ideal place for papain delivery is the intestine, where pH is in the range of 5.0-8.0. However, specific characteristics of papain (being a protein) like hydrophilic nature; complex structure and insufficient stability in gastrointestinal tract (GIT) are the major obstacles in oral delivery of papain. The key to the success of digestive proteins as pharmaceuticals is to have in place an efficient site specific pH dependent drug delivery system that allows the protein drug to gain access to the target site at right time and for the proper duration. pH sensitive polymers (water insoluble at low pH, water soluble at high pH) are of particular interest as the release rate of drug can be triggered by the pH of the environment. Enteric formulation of papain is more rational than immediate release commercial papain products since the former would protect the acid labile enzyme from gastric pH and deliver it to its site of action i.e., intestine. Enteric coated microspheres of pancreatin of 1.0 to 1.2mm in diameter showed 25% higher therapeutic effectiveness compared with 1.8- 2.0 mm microspheres. Stead et al.11) also stated that faecal fat excretion was reduced by 44% with increased coe‹cient of fat absorption with enteric coated microspheres of pancreatin compared to enteric coated tablet. Therefore, the design of microparticulate systems has received increasing attention for oral delivery of these biomolecules.12) Natural enzyme, papain extracted from plant *carica papaya* is an endogenous protein has proteolytic activity which cleaves collagen molecules affected in dental caries and digest of dead cells resulting in removal of infected dentine. Papain is reported as safe, non-cytotoxic as well as bio-compatible with oral tissues having bactericidal

and bacteriostatic effect. But low chemical stability of papain limits the use of papain in formulation.

Origin

Papaya belongs to Caricaceae family and the plant is originated from Caribbean Coast of Central America. This small botanical family, native to tropical and subtropical America is represented by 31 species. Carica papaya is the most economically important and widely cultivated species. It is usually cultivated in the tropical and neo-tropical regions of the world between 32º North and South (Pantoja, Follett, & Villanueva-Jiménez, 2002). Even though papaya is believed to have been cultivated by early civilizations; no records are available prior to the arrival of Columbus in America (Morton, 1987). This herbaceous plant is also known as papaw, paw,kapaya, lapaya, tapaya, papayao, papaya, papaia, papita, lechosa, fruta bomba, mamon, mamona, and mamao and tree melon.

Morphology

The shape of papaya plant resembles palms leaves with large monoaxial palms. Young plants are single stemmed during the first 1-2 years of growth. However, in some highly fertile orchards, heavy lateral branch might also develop early on juvenile plants. Mature papaya leaves are palmate with deep lobes, supported by smooth, hollow petioles. This petiole gives highly textured leaf scars on the smooth, light tan, hollow stem. The persistent leaf scar enlarges as the plant grows in circumference. On the other hand, ripe papaya fruit resemble melons and are rich in vitamin A and C. The latex contains protease that is papain and is collected from unripe green fruit (Litz, 2004). Papain In the group of cysteine protease, papain family accounts the largest of it all. Papain may be obtained from bacteria, plant, vertebrates and invertebrates. Commercial papain available in the market is a plant derived preparation coming from the latex of papaya. Papain or cysteine protease hydrolase was first extracted from crude dried latex of papaya (Balls & Thompson, 1940). The term papain was first introduced by Wurtz and Brochut in describing the proteolytic principle in papaya latex (Boyer, 1971). Proteolytic enzyme is a group of enzyme capable of hydrolyzing the peptide bond in a protein molecule (Sandhya, Sumantha, & Pandey, 2008). Papain consists of a single polypeptide chain with three disulfide bridges and sulfuhydyl group necessary for activity of the enzyme. The molecular weight of papain is 23,406 Da and its optimum pH for maximum activity is around 6.0 to 7.0. It will digest most protein substrate more extensively than the pancreatic proteases. Papain exhibits broad specifity, cleaving peptide bonds of basic amino

acids, leucine or glycine. It also hydrolyzes esters and amino acids (IUBMB Enzyme Nomenclature, 2009).

Toxonamical Classification of Carica Papaya

DOMAIN: flowering plant

KINGDOM: plantae

SUBKINGDOM: Tracheobionta

CLASS: Magnoliopsida

SUB CLASS: Dilleniidae

SUPER DIVISION: Spermatophyta

PHYLLUM: Steptophyta

ORDER: Brassicales

FAMILY: Caricaceae

GENUS: Carica

BOTANICAL NAME: Carica Papaya Linn.[2]

Uses of Plant Parts

LEAF: To treat digestive disorders and other disturbances in gastrointestinal tract.

FRUIT: To treat high feaver, cough, and anoreia.

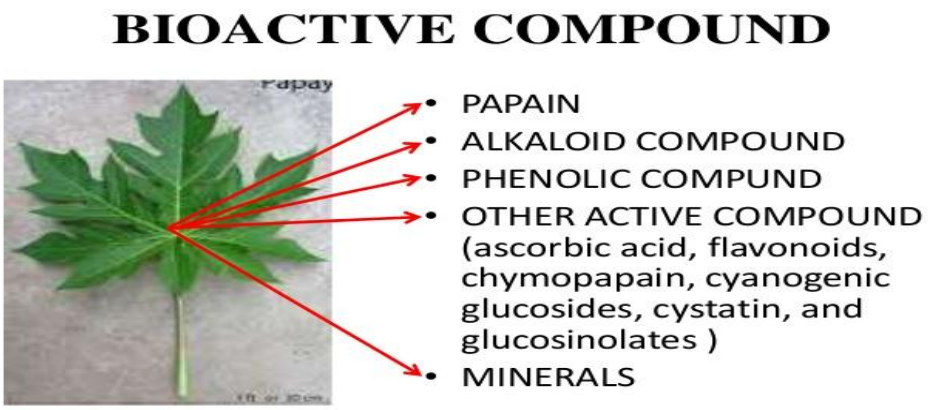
SEED: To improve protein digestion and to expel intestinal worms.

ROOT: To treat urinary disorders.

BARK: To treat toothache.

Phytochemical Constituents of C. Papaya Leaves

The medicinal effects of C.papaya leaves extracts can be recognized due to the presence of several active components such as papain, chymopapain, alkaloids, glycosides, tannins, saponin, L-tocopherol, ascorbic acid, riboflavin, flavinoids,and and minerals.



Advantages of Carica Papaya

- Papaya leaves juice helps to heal fever, malaria and chikungunya.
- Increases appetite.
- Streamming digestion.
- Treat menstrual pain.
- As an acne medicine.
- Treat high blood pressure.
- Streamlining breast milk.

Nutritional Value of Carica Papaya

Nutrients Mg Percentage Folates 38µg 9.5% Nicain 0.338mg 2 % Pantothenic acid 0.218mg 4% Pyridoxine 0.019mg 1.5% Riboflavin 0.032mg 2.5% Thiamin 0.027mg 2% Vitamin A 1094IU 36% Vitamin C 61.8mg 103% Vitamin E 0.73mg 5% Vitamin K 2.6µg 2% Sodium 3mg 0% Potassium 257mg 5% Calcium 24mg 2.5% Iron 0.10mg 1% Magnesium 10mg 2.5% Phosphorous 5mg 1% Zinc 0.07mg 0.5% Table 2: Chemical constituents2 Phytoconstituents Carica Papaya Part Enzyme Papain, Unripe fruit Chymopapain Carotenoids B-carotene, Fruits Crytoxanthin Carposide Roots Glucosinolates Benzyl isothiocynate, Seeds Papaya oil Minerals Shoots, Ca, K, Mg, Zn, Mn, Fe Leaves Monoterpenoids Linalool, Fruits 4-terpinol Flavonoids Myricetin, Shoots Kaemferol Alkaloids Leaves Carpinine Carpine, Vitamin C and E.

Table 1: Chemical composition of various parts of Papaya plant.[1, 3, 4]

Part	Constituents
Fruits	Protein, fat, fibre, carbohydrates, minerals: calcium, phosphorous, iron, vitamin C, thiamine, riboflavin, niacin, and carotene, amino acids, citric and malic acids (green fruits), volatile compounds: linalool, benzylisothiocyanate, *cis* and *trans* 2, 6-dimethyl-3,6 epoxy-7 octen-2-ol, Alkaloid, α; carpaine, benzyl-β-D glucoside, 2-phenylethyl -β-D-glucoside, 4-hydroxy-phenyl-2 ethyl-β-D-glucoside and four isomeric malonated benzyl-β-D-glucosides.
Juice	N-butyric, n-hexanoic and n-octanoic acids, lipids; myristic, palmitic, stearic, linoleic, linolenic and *cis*-vaccenic and oleic acids.
Seed	Fatty acids, crude protein, crude fibre, papaya oil, Carpaine, benzylisothiocyanate, benzylglucosinolate, glucotropacolin, benzylthiourea, hentriacontane, -sitosterol, caricin and an enzyme myrosin.
Root	Carposide and an enzyme myrosin.
Leaves	Alkaloids carpain, pseudocarpain and dehydrocarpaine I and II, choline, carposide, vitamin C and E.
Bark	-Sitosterol, glucose, fructose, sucrose, galactose and xylitol.
Latex	Proteolytic enzymes, papain and chemopapain, glutamine cyclotransferase, chymopapains A, B and C, peptidase A and B and lysozymes.

Table No 2: Nutritive value of 100g of Papaya fruit.[5]

Constituents	Ripe Papaya	Green Papaya
protein	0.6g	0.7g
minerals	0.5g	0.5g
fibre	0.8g	0.9g
fat	0.1g	0.2g
carbohydrates	7.2 g	5.7g
energy	32kcal	27kcal
total carotene	2.740µm	0
beta carotene	888µm	0

Therapeutic Uses of Carica Papaya

- The chymopapain and papain extracts of the leaves are useful in the treatment of digestive disorders.
- The extracts from fruits and seeds have bactericidal properties.
- The fruit juice and leaf extract have been demonstrated to have anticancer, anti-bacterial, antioxidative, anti-inflammatory, nephroprotective, hepatoprotective, hypoglycemic and hypolipidemic effects.
- Anti-sickling effect in sickle cell disease.

Medicinal Properties

Papaya has been known as a food or quasi drug .it is used as a folk remedy for various disorders and wide consumption to its pharmacological properties. It contains different kinds of immuno-stimulating agents and antioxidants. Papaya pulp is utilized in African hospital

for wounds healing and curing burns because management of chonic non-healing ulcers pases difficulty and many clinical problems. Papaya latex is very useful for curing dyspepsia and is externally applied to burns and scalds, it also cures diarrhea, bleeding, haemorrhoids and whooping cough. Juice of papaya helps in alleviating infections of colon by clearing away infection, pus, and mucus, and prescribed to cure gastrointestinal maladies. Its ripe fruit is a carminative, diuretic, expectorant, sedative and has preventive action against dysentery, skin diseases, psoriasis, and ringworm. Unripe fruit has ability to exhibit bacteriostatic activity against human enteric pathogens.it aids in reducing menstrual irregularities and natural menstruation flow in women. Green leaves present an essential nutrients while yellow one provides iron. Papaya fruit is contain some immuno-stimulating and antioxidant agent. However, apart from these, there are several reports on the therapeutic properties and pharmacological actions of papaya based on modern scientific investigations. Some have been discussed below.

Antimicrobial

The seeds of papaya has antimicrobial activity against Trichomonas vaginalis trophozoites. The report suggests the use of papaya seed in urogenital disorder like trichomonas's with care to avoid toxicity. The seed and pulp of papaya was shown to be bacteriostatic against several enter pathogens such as Bacillus subtilis, Enterobacter cloacae Escherichia coli, Salmonella typhi Staphylococcus aureus, Proteus vulgaris pseudomonas aeruginosa and klebsiella pneumoniae by the agar cup plate method. Purified extracts from ripe and unripe fruits also produces very significant antibacterial activity on S. Aureus, Bacillus cereus, E.coli, Aeruginosa and Shigella flexneri.

Anthelmintic

The air dried papaya seeds given as elixir with honey has shown significant effect on the human intestinal parasites, without significant side effects. It is reported that their consumption offers a cheap, natural, harmless, readily available monotherapy and preventive strategy against intestinal parasitotic, especially in tropical communities. Benzylisothiocyanate, present in seeds is the chief or sole anthelmintic.

The latex of papaya has anthelmintic efficacy against Heligmosomoides polygyrus in experimentally infected mice, which suggests its potential role as an anthelmintic against potent intestinal nematodes of mammalian hosts.

Anti-Amoebic

The cold macerated aqueous extract of matured papaya seeds has shown anti-amoebic activity against Entamoeba histolytic a.

Antimalarial

The petroleum ether extract of the rind of raw papaya has exhibits significant antimalarial activity. There may be significant commercial potential in extracting the active element from this plant, which grows abundantly throughout the tropics and the rind of which is discarded as waste, can be exploited for antimalarial activity.

Antifungal

The latex of papaya and Fluconazole has synergistic action on the inhibition of Candida albino's growth. This synergistic effect results in partial cell wall degradation (it indicated by transmission electron microscopy observation).

Diuretic

Aqueous root extract of papaya when given orally at a dose of 10mg/kg to rats produces significant increase in urine output and shows similar profiles of urinary electrolyte excretion to that of Hydrochlorothiazide.

Female Anti-Fertility

Sharma and Mahatma have reported that the composite root extract containing papaya root extract as one of the constituent, induces morphological changes in the endometrial surface epithelium in albino rat uterus. The characteristic smooth regular pattern of normal epithelium appears to have changed at places by haphazardly oriented groups of cells and loss of microvilli indicating a disorganised picture. Normal consumption of ripe papaya during pregnancy may not pose any significant danger. However, the unripe or semi-ripe papaya (which contains high concentration of the latex that produces marked uterine contractions) could be unsafe in pregnancy.

Histaminergic

Crude latex causes contraction of the isolated guinea pig ileum strips, which is mediated via H1-receptor and dependent on extracellular Ca2+ influx. Papaya flower pollen is able to induce respiratory IgE-mediated allergy. The existence of common allergens among papaya flower pollen, fruit and papain has been demonstrated by RAST inhibition.

Dengue

Dengue is a severe arthropod-borne viral disease. It occurs in tropical areas. In human, it causes mortality as well as morbidity. The main vector which spreads dengue in humans is Flavivirus belongs to family flaviviridae that uses mosquitoes (aedes aegypti) has its host organism.[12] According to world health organization (WHO) degue has affected 40%of the total world"s population. Dengue can treated by both symptomatic and supportive. Dengue can be controlled with only proper supportive care and vigilant fluid administration during different phases due to absence of any particular therapeutic treatment.[8] Recently, carica papaya leaves etract has +become popular among the dengue suffering patients due to increasing platelet activity of leaves. Various active phytochemicals (papin, flavanoids, phenols, saponins, alkaloids, ascorbic acid, etc.) have been identified by phytochemical screenig process in carica papaya.[8] The carica papaya leaf extract has a wide variety of pharmacological properties including anticancer, antioidant, anti-inflammatory, antibacterial, hepatoprotective, hypoglycemic and hypolipedmic effects and increases platelet count.[9] the first symptoms appears in about 4-5 days after bite , and include high feaver,severe headache,nausea, vomiting and body rashes,joint or muscle pain.Dengue virus has four different serotypes or subspecies (DEN-1, DEN-2, DEN-3, and DEN-4). Although each infection provides lifelong immunity to that specific serotype, a subsequent infection at a later stage with a different serotype increases the risk of a more etreme version of disease called dengue hemorrhagic fever (DHF).

Action of papain on platelet count 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 preinfected 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

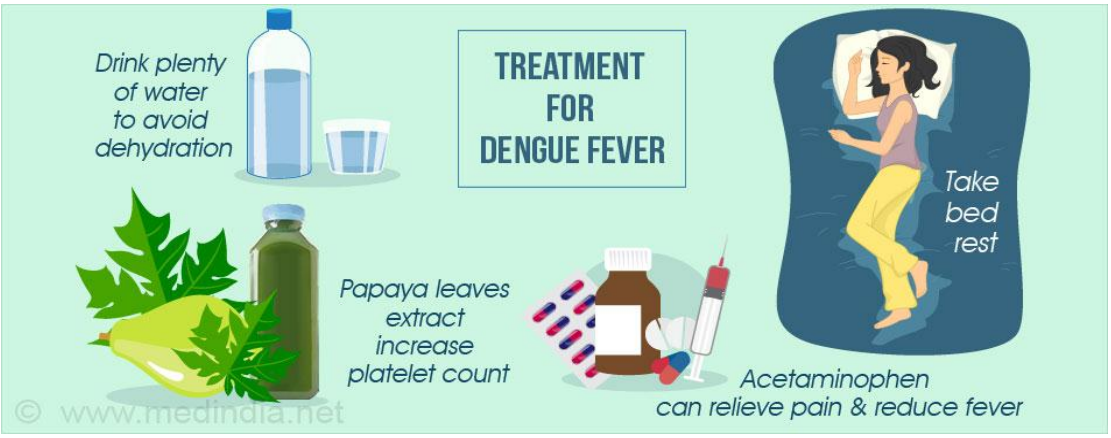
course of recovery with increasing the platelet count and prevents the complication of thrombocytopenia without any side effects.

Method of Extraction

Preparataion of extract of papaya leaf 4Air dried papaya leaves of 250grams 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 45grams was obtained.

According to the properties of papaya leaves the following method is generally used Fresh leaves of carica papaya are collected during july. The leaves are washed thoroughly under tap water and then with distilled water then wiped to remove dust with a clean cloth. Leaves are shade dried at room temperture and powdered using amixergrider. 25ml of aqueous etract of carica papaya leaves was administered to patient infected with dengue fever.The same dose was repeated daily i.e. morning and evening for five consecutive days.

Treatment for dengue fever



Marketed Formulation of C. Papaya Leaves

Papaya leaf extract formulations are available on the global market as supplements under Rochway, Iowa Select Herbal. Herbal papaya and Sido Muncul Hervbal. However, they are formulated using micronization, fermentation and liquid extraction.

CARIPILL- THE DRUG FROM PAPAYA LEAF EXTRACT

No specific treatment for dengue. But suggests that the juice of papaya leaves may be a cure for dengue.

It suggest that the dengue virus works in reducing the platelet count according to immune response of the individual.

The marketed preparations are tablets, and syrups.

Dosage: 1 tablet of caripill (1100mg) should be taken 3 times a day for 5 days.[13]

Caripill Syrup

Caripill syrup increases the platelet count in patient suffering from dengue. Caripill tablet has been approved by the scientific and regulatory authority. The primary ingredient in caripill syrup is carica papaya leaf extract and the efficacy and safety is well documented. Caripill syrup can be given to children 2 years and above.it works by stimulating the genes responsible for production of platelets.

Dosage

For children more thatn 1year and less than 5years: 275mg (5ml) three times a day for 5days.
For children more than 5 years and less than 18 years: 550mg (10ml) three times a day for 5days.
For children weighing more than 40kgs: 1100mg tablet three times a day for 5days (14).

CONCLUSION

Carica papaya known as food. This article mainly focus on the biological activity and possible medicinal applications of papaya and hence extensive investigation on its pharmacodynamic and clinical trials is needed to exploit their therapeutic utility to fight against various diseases. 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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