

Experimental Evidences Showing Nutritional and Medicinal Property of Carica Papaya Plant

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Abstract: *Papaya plant is popular in all over world for its various nutritional values and medicinal properties. Papaya fruit contains ample amount of carbohydrates, protein, fat, mineral, iron, calcium, phosphorous, vitamin C, thiamine, riboflavin, niacin and carotene, amino acids, citric and malic acids (green fruit). Its leave is major source of alkaloids carpain, dehyrocarpaine, choline, carposide vitamin C and E. Studies show that papaya plant may be helpful in treatment of cancer, dengue, asthma, microbial infection and skin related diseases as well as in cosmetics. Because of such huge nutritional and pharmaceutical properties it may be considered as a nutraceutical plant. In last twenty years scientists and researchers trying to know about numerous compounds obtained from various extraction processes of papaya leave which could be helpful to explain its huge number of medicinal properties. In the present review we have focussed on the nutritional benefits and clinical significances as well as harmful effects.*

Keywords: Nutritional value, nutraceutical, antithrombocytopenic, antioxidant and clinical significance

1. Introduction

Compounds isolated from various parts of Carica Papaya Linn such as leaves, fruits, stem, roots, seeds have been shown to possess excellent nutritional value. Carica papaya Linn. is of potential medicinal value. Carica papaya belongs to the family Caricaceae and it is grown in various parts of the world, including India, Europe and tropical America. The edible part of papaya is widely used all over the world throughout the year. These days, Papaya is considered as nutraceutical fruit due to its various medicinal properties. The well-known medicinal properties of papaya include, antithrombocytopenic, antioxidant, immunostimulant, antimicrobial, antifungal, antihelminthic, antidiabetic, antiparasitic and abortifacient property. It is a rich source of multiple vitamins including Vitamin C, Vitamin A and Vitamin E the B vitamin pantothenic acid and folate; minerals, magnesium and potassium; and fiber. In addition to all this, it contains a digestive enzyme- Papain the effectively treats causes of trauma, allergies and sports injuries[1], [2]. The fruit is an excellent source of beta carotene that prevents damage caused by free radicals that may cause some forms of cancer. It is reported that it helps in the prevention of diabetic. Papaya lowers high cholesterol levels as it is a good source of fiber. Papaya effectively treats and improves all types of digestive and abdominal disorders. Ripe fruit consumed regularly helps in reducing constipation. It is also reported that papaya prevents premature aging. With the presence of the above mentioned properties it can be safely said that this is excellent fruit enriched with protein, carbohydrate, mineral, vitamins and antioxidant with such a huge medicinal properties without any known side effect.

2. Methods Used For Literature Collection

Literature survey was done in PubMed and Google's using keywords, Carica papaya; nutritional properties of Carica papaya; antioxidants in Carica papaya; nutraceuticals of Carica papaya; medical, pharmacological potentials of

Carica papaya, effect of papaya on dengue fever /platelet/bacteria / pathogenic bacteria /fungus / helminthes, parasites / diabetes and also harmful / side effect of Carica papaya and analgesic activity of papaya etc.

Nutritional value

Papaya is a very common fruit with high nutritive value. It is low in calories and rich in natural vitamins and minerals. Papaya places first among the fruits for vitamin C, vitamin A, riboflavin, folate, calcium, thiamine, iron, niacin, potassium and fibre. It is preferred fruit of obese people because of low calories content (32 kcal/100g of ripe fruit). Papaya has more carotene than other fruits (apples, guavas, sitaphal and plantains) which help to prevent damage by free radicals. Unripe green papaya is used as vegetable, it does not contain carotene but all other nutrients are present (Table 1 and 2). The fruit is a rich source for different types of enzymes. Papain, vegetable pepsin present in good amount in unripe fruit is an excellent aid to digestion, which helps to digest the protein in food at acid, alkaline or neutral medium. Thus, it can be prescribed for dyspeptic patients, as papain may help in the digestion of proteins. Papaya has the property of tenderizing meat. This knowledge is being put to use by cooking meat with raw papaya to make it tender and digestible. The fermented papaya fruit is a promising nutraceutical as an antioxidant. It improves the antioxidant defence in elderly patients even without any overt antioxidant deficiency state at the dose of 9g/day orally. The papaya lipase, a hydrolase enzyme tightly bonded to the water insoluble fraction of crude papain, is considered as a "naturally immobilized" biocatalyst.

Table 1: Nutritional composition of ripe and unripe pawpaw fruits (Source: Krishna et al. 2008)

Constituents	Ripe papaya	Unripe papaya
Protein	0.6 g	0.7 g
Fat	0.1 g	0.2 g
Minerals	0.5 g	0.5 g
Fibre	0.8 g	0.9 g
Carbohydrates	7.2 g	5.7 g
Energy	32 kcal	27 kcal

Total carotene	2,740µm	0
Beta carotene	888 µm	0

Table 2: Nutritive Value of Papaya fruit (Source: USDA National Nutrient data base)

Principle	Nutrient Value(Per 100g)	Percentage of RDA
Energy	43 Kcal	2%
Carbohydrates	10.82 g	8%
Protein	0.47 g	1%
Total Fat	0.26 g	1%
Cholesterol	0 mg	0%
Dietary Fiber	1.70 g	4%
Vitamins		
Folates	37 µg	9%
Niacin	0.338 mg	2%
Pantothenic acid	0.218 mg	4%
Pyridoxine	0.038 mg	3%
Riboflavin	0.027 mg	2%
Thiamin	0.023 mg	2%
Vitamin A	950 IU	32%
Vitamin C	60.9 mg	102%
Vitamin E	0.30 mg	2%
Vitamin K	2.6 µg	2%

3. Clinical Importance of Papaya Plant

Antithrombocytopenic activity

A study was conducted by S. Subenthiran *et al.*, in 2013 to investigate the platelet increasing property of *Carica papaya* leaves juice in patients with dengue fever. They enrolled 228 patients with dengue fever and dengue haemorrhagic fever. Approximately half the patients received the juice, for 3 consecutive days while the others remained as controls and received the standard management. They observed significant increase in mean platelet count observed in the intervention group ($P < 0.001$) but not in the control group 40 hours since the first dose of juice. Comparison of mean platelet count between intervention and control group showed that mean platelet count in intervention group was significantly higher than control group after 40 and 48 hours of admission ($P < 0.01$). Hence they concluded that *Carica papaya* leaves juice does significantly increase the platelet count in patients with dengue fever and dengue haemorrhagic fever[3]. To identify the active compound responsible for antithrombocytopenic activity Vishwanath Zunjar *et al.*, has isolated. Phenolics, and alkaloids from *Carica papaya* leaves. They used busulfan induced thrombocytopenic wistar rats model to test effect of leave extract on platelet counts (Table-3).

Table 3: Platelet count of different groups at 1 day before busulfan treatment and 20th day of busulfan treatment(source :Vishwanath Zunjar *et al.*[4])

Groups	Platelet count (Mean ± SEM)
Normal (1 day before busulfan treatment)	623.30 ± 37.64 × 10 ⁹ /L
Disease control animals (1 day before busulfan treatment)	749.75 ± 78.39 × 10 ⁹ /L
Normal (20th day of busulfan treatment)	701.03 ± 20.53 × 10 ⁹ /L.
Disease control animals (20th day of busulfan treatment)	78.00 × 10 ⁹ /L
Petroleum extract (20th day of busulfan treatment)	662.25 ± 33.12 × 10 ⁹ /L
ethyl acetate extract	584.02 ± 29.20 × 10 ⁹ /L

(20th day of busulfan treatment)	
Carpaine	555.5 ± 27.77 × 10 ⁹ /L
(20th day of busulfan treatment)	

They found only alkaloid fraction showed good biological activity, further Carpaine isolated from the alkaloid fraction exhibited potent activity in sustaining platelet counts upto 555.50 ± 85.17 × 10⁹ /L with no acute toxicity. The alkaloid group contains carpaine, pseudocarpaine-I pseudocarpaine-II and choline (Tang, 1979) one may have anti-thrombocytopenic activity. In seek of the main active component in alkaloidal group, petroleum ether extract and ethyl acetate extract based screening was done. Both having very good anti-thrombocytopenic activity, with petroleum ether extract giving better activity over ethyl acetate extract. Finally the principal component of the alkaloid, Carpaine, was isolated and tested which showed higher activity than petroleum ether extract and ethyl acetate extract. In order to confirm the findings LC-MS method for quantitative analysis of carpaine was performed. The amount of carpaine in water, petroleum ether and ethyl acetate extract was found to be 16.79 ± 0.09 mg/g 117.10 ± 0.59 mg/g and 99.47 ± 0.53 mg/g respectively. As petroleum ether and ethyl acetate extract containing higher amount of carpaine, exhibited much higher efficacy. A pure sample of carpaine showed highest anti-thrombocytopenic activity than other groups of extracts. So, it was concluded that Carpaine present in the leaves to be responsible for the antithrombocytopenic activity of *Carica papaya* leave.[4] Another study was in 2016 carried out on dengue patient by Gadhwal AK *et al.*, they divided all participants randomised into two groups, study group and control group. The study group was given papaya leaf extract capsule of 500 mg once daily and platelet was analysed at different time points (Table.4) and routine supportive treatment for consecutive five days and control was given only routine supportive treatment. They found average platelet transfusion requirement in study group was significantly less than control group (0.685 units per patient v/s 1.19 units per patient) (p value <0.01).

Table 4: Platelet count in study and control group from 1 to 7 day (Source: Gadhwal AK *et al* 2016) [5] .P value is significant if < 0.01, has been indicated as *.

Test Day	Study group	Control group	P value
1 st day	59.82±18.63 (× 10 ³)	61.06±20.03 (× 10 ³)	0.36
2 nd day	61.67±19.46 (× 10 ³)	59.93±19.52 (× 10 ³)	0.20
3 rd day	82.96±16.72 (× 10 ³)	66.45±17.36 (× 10 ³)	< 0.01*
4 th day	122.43±19.36 (× 10 ³)	88.75±21.65 (× 10 ³)	< 0.01*
5 th day	112.47±17.49 (× 10 ³)	102.59±19.35 (× 10 ³)	< 0.01*
7 th day	124.47±12.35 (× 10 ³)	122.46±19.76 (× 10 ³)	0.08

Carica papaya leaf extract increases the platelet count significantly in dengue fever without any side effect and prevents the complication of thrombocytopenia[5].

Antioxidant and immunostimulant

Carica papaya is widely used as herbal remedy to prevent, protect against, and cure several diseases. These curative properties are based on the presence in different parts of the plant of phytochemical nutrients with antioxidant effect. Oxidative stress is a normal even occur in cell due to formation of reactive oxygen species (ROS) e.g.- superoxide radical (•O⁻²) and hydroperoxyl (HO•⁻²). ROS may damage

plasma membrane, important enzyme, protein and DNA and also apoptosis of cell. Low level of ROS is maintained by various enzyme systems participating in the in vivo redox homeostasis. Hence, oxidative stress is consequence of imbalance between the prooxidants and antioxidants in the body. Superoxide dismutases (SOD), Catalase, and Glutathione peroxidase are the major enzyme of antioxidant enzyme system. Plasma malondialdehyde(MDA) is a biomarker for oxidative stress.[6] K. M. Sadek et al., showed that acrylamide increases MDA and decrease of GSH level, SOD and Catalase activity due to the oxidative stress induced by acrylamide on membrane polyunsaturated fatty acids in rat's stomach, liver and kidney. Administration of Carica papaya fruit aqueous extract was significantly ameliorated the increased levels of MDA and decline of GSH, SOD and Catalase activity in all tissue caused by acrylamide toxicity. It also increases immune functions (IgG and IgM) while acrylamide significantly decrease it specially IgG. Thus, this study suggests that papaya fruit has potent antioxidant and immunostimulant activity[7].

C. papaya seeds water extract act as antioxidant against hydrogen peroxide (H₂O₂) oxidative stress in human skin Detroit 550 fibroblasts. C. papaya seeds water extract is not toxic and acts as a potent free radical scavenger, providing protection to Detroit 550 fibroblasts that underwent H₂O₂ oxidative stress[8]. So, it is potentially useful for protection against oxidative stress.

Antimicrobial activity

Papaya leaf is beneficial against pathogenic bacteria. Recently, It was reported that treatment of Carica papaya leaf ethyl acetate extract could inhibit *B. stearothermophilus*, *L. monocytogenes*, *Pseudomonas* sp., and *E. coli*. The extract activity was influenced by pH heating process it was more effective in low pH. The extract activity was influenced by NaCl against *B. stearothermophilus* and *E. coli* [9]. Antibacterial activity against some human pathogenic bacteria were also tested method by I.I. Anibijuwon et al, in 2009. They reported methanol root ethanol extracts have highest activity against the test bacteria. The root extracts demonstrated higher activities against all the gram-positive bacteria than the gram-negative bacteria tested by them and aqueous leaf extract showed pronounced inhibition demonstrating higher activities against the test bacteria than the organic solvents. This also have higher activities against all the gram-positive bacteria than the gram-negative bacteria tested. Increase in temperature increases while alkaline pH decreased the extract activity[10].

Antifungal activity

Pedro Chavez-Quintal et al., in 2011, reported that papaya leaf extract exhibited the broadest action spectrum. The MIC₅₀ (minimum inhibitory concentration to inhibit the growth of 50% of organisms) for the leaf extract was 0.625 mg ml⁻¹ for *Fusarium* spp. and >10 mg ml⁻¹ for *C. gloeosporioides*, both equal to approximately 20% mycelial growth inhibition. Ethanolic extracts from *Carica papaya* L. cv. Maradol leaves are a potential source of secondary metabolites with antifungal properties[11]. Papaya leaf Crushed and boiled extract have inhibitory action against 6 saprophytic fungi *Penicillium* sp, *Aspergillus flavus*,

Aspergillus niger, *Fusarium* sp, *Rhizopus* and *Helminthosporium*, 5 dermatophytic fungi *Microsporum canis*, *Microsporum gypseum*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans* and 6 yeasts including *Candida albicans*, *Candida albicans* ATCC 0383, *Saccharomyces cerevisiae*, *Candida galbrata*, *Candida tropicalis*, *Candida kruzei*. But anti-fungal activity was greater in case of crushed leaf extract as compared to boiled[12].

Anthelmintic activity

Ameen, S. A et al., recently check the anthelmintic efficacy of the aqueous and crude extract of *Carica papaya* seeds in 40 Isa Brown commercial layers infected naturally with nematodes. Their results showed that the powdered and aqueous extract of *C. papaya* after its administration, produced a significant increase (P < 0.001) in packed cell volume, red blood cells, haemoglobin concentration, lymphocyte counts and significant decrease in eosinophil counts. The faecal egg counts also showed a remarkable and significant reduction in the levels of the identified helminths. The decline in faecal egg counts was more mark able with the aqueous extract than crude extract administered[13]. *Hymenolepis diminuta* infections in rats was papaya seed to check the anthelmintic activity it was found that it have good anthelmintic infection [14].

Antiparasitic Activity

The tropical fruit *Carica papaya* and its seeds have proven anthelmintic and anti-amoebic activities. Air-dried *C. papaya* seeds are efficacious in treating human intestinal parasites and without significant side effects. Okeniyi JA et al in 2007, to investigate the effectiveness of air-dried *C. papaya* seeds on human intestinal parasitosis, 60 asymptomatic Nigerian children with stool microscopic evidence of intestinal parasites received immediate doses (20 mL) of either an elixir composed with air-dried *C. papaya* seeds and honey (CPH) or honey alone (placebo) in two randomized treatment groups. Repeat stool microscopic examinations were conducted 7 days post intervention for intestinal parasites. Significantly more subjects given CPH elixir than those given honey had their stools cleared of parasites [23 of 30 (76.7%) vs. five of 30 (16.7%); z = 4.40, P = .0000109]. There were no harmful side effects. The stool clearance rate for the various types of parasites encountered was between 71.4% and 100% following CPH elixir treatment compared with 0-15.4% with honey. Thus, Air-dried *C. papaya* seeds consumption offers a cheap, natural, harmless, readily available monotherapy and preventive strategy against intestinal parasitosis, especially in tropical communities[15]. Further, in 2014 Sabaa Tahier Mohammed evaluate the efficacy of *Carica papaya* seeds against *Entamoeba histolytica* infection compared with metronidazole in mice model. They found that even a single oral dose of *Caricapapaya* seeds water extracts of up to (0.1ml /mice/day) decreases parasite appearance in feces and disappear completely at eighth day compared with metronidazole which takes ten days. They also found that histomorphology of intestine tissue return to normal in the group which was given *Carica papaya* seeds[16]. So, *Carica papaya* seeds may be effective in treating *Entamoeba histolytica*.

Antidiabetic effect

Several studies have reported that some parts of the C. papaya plant exert hypoglycemic effects in both animals and humans. Juárez-Rojop et al., in 2012 performed a study in which they induced diabetes STZ and treated with aqueous extract of C. papaya was administered as drinking water to both diabetic and non-diabetic animals during 4 weeks. They investigated that aqueous extract of C. papaya have both hypoglycemic and antioxidant activity. Furthermore, it improved the lipid profile in diabetic rats. In addition, the leaf extract improves integrity and function of liver and pancreas[17].

Analgesic activity

Analgesic activity of extract of papaya leaves (*Carica papaya* L.) to male mice has been evaluated by Afrianti et al., they analyses that analgesic effect of an ethanolic extract of *Carica papaya* leaves in mice was of similar potency as paracetamol[18].

Abortifacient property

Oderinde O et al in 2002 reported that low dose (100 mg/kg body weight)aqueous crude extract of *Carica papaya* (Linn) seeds does not have any adversely affect in prenatal development of SD rat. But it has abortifacient property, if high dose (800 mg/kg body weight) of aqueous crude extract of *Carica papaya* seeds was administered. The results indicate that *Carica papaya* toxicity can adversely affect the fetus at high dose[19].

4. Conclusion

Carica papaya is a well known nutraceutical plant having a wide range of pharmacological activities. C.papaya possesses rich source of vitamins, antioxidants, flavanoids, polyphenols, etc. and hence, regular intake of papaya will improve our health by quenching the free radicals generated in the body and enhance our immune system to fight against the foreign pathogens. The whole Papaya plant including its leaves, seeds, ripe and unripe fruits and their juices is used as traditional medicine. As evident from various experiments it accelerates the increase in the platelet count and shortens the hospitalization period. The available literature does not reveal any negative, adverse and toxic effects upon consumption of papaya. Thus, intake of papaya as fruit, salads and fruit juice regularly should be a part of our diet.

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