

POTENTIAL MEDICINAL PROPERTIES OF *CARICA PAPAYA LINN.* - A MINI REVIEW

NATARAJAN SUDHAKAR*, THEIVANAI @ VIDHYA RM.

Department of Biotechnology, Dr. M.G.R. Educational & Research Institute University, Maduravoyal, Chennai 600095, Tamilnadu, India.
Email: nudha79@gmail.com

Received: 05 Nov 2013, Revised and Accepted: 01 Feb 2014

ABSTRACT

Carica papaya Linn. is commonly called as paw-paw and it belongs to the family *Caricaceae*. Papaya possess excellent medicinal properties for treatment of different ailments. The different parts of the *Carica papaya* plant including leaves, seeds, latex and fruit exhibited to have medicinal value. The stem, leaf and fruit of papaya contain plenty of latex. The latex from unripe papaya fruit contain enzymes papain and chymopapain; other components include a mixture of cysteine endopeptidases, chitinases and an inhibitor of serine protease. Phytochemical analysis of *C.papaya* leaf extract revealed the presence of alkaloids, glycosides, flavonoids, saponins, tannins, phenols and steroids. This review focuses on different properties of papaya such as antioxidant and free radical scavenging activity, anticancer activity, anti-inflammatory activity, treatment for dengue fever, antidiabetic activity, wound healing activity and antifertility effects. Thus *C.papaya* acts as a multi faceted plant. It is also imperative to identify the mechanism of the plant compounds and studying the active principle of the extract. Thus, we should include the papaya in our diet as fruit salads, fruit juice, leaf extract, decoction prepared through papaya leaves, etc. However, including papaya seeds in any of the form should be avoided for young men and pregnant women, since it possess antifertility effects that was demonstrated well in animal models.

Keywords: Carica papaya, Papaya, Medicinal properties of papaya, Phytochemical analysis, Importance of papaya, Effects of papaya.

INTRODUCTION

Natural compounds isolated from various parts of the plant such as leaves, fruits, stem, roots, seeds have been shown to possess excellent medicinal value. Thousands of plant varieties used in folklore medicine have been studied for treatment of cancer, diabetes, arthritis, infectious diseases, etc. However, still it remains an area of research interest for unveiling the medicinal value of several plant species that is not studied thoroughly. *Carica papaya* Linn. is one such a plant with potential medicinal value and it is commonly called as paw-paw. *Carica papaya* belongs to the family *Caricaceae* and it has been cultivated in most of the tropical countries.

The edible part of papaya is widely used all over the world. The unripe fruit of papaya is used as mild laxative and abortifacient agent and leaves are used for treatment of pyrexia, diabetes, gonorrhea, syphilis, inflammation and as a dressing component for wounds[1]. This review focuses on potential medicinal properties of *Carica papaya* and its activity.

METHODS USED FOR LITERATURE COLLECTION

Literature survey was done in pubmed using key words *Carica papaya*; medicinal properties of *carica papaya*; phytochemicals in *Carica papaya*; antioxidants in *Carica papaya*; anticancer activity/antidiabetic activity/anti-inflammatory activity/wound healing activity/anti fertility effects of *Carica papaya*. The articles published only in pubmed indexed journals were primarily considered for writing this review.

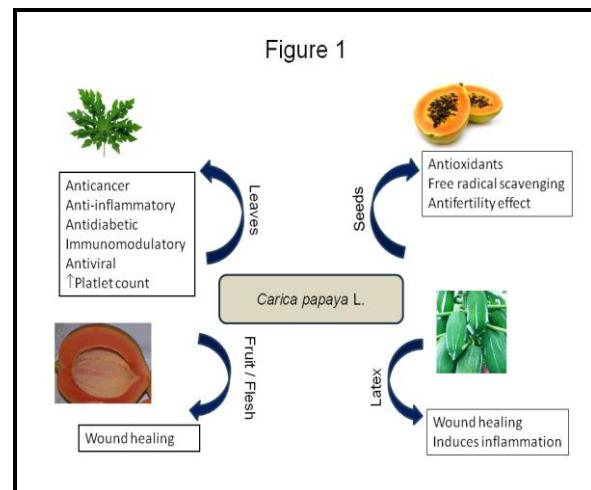
Medicinal properties of *Carica papaya* plant

The different parts of the *Carica papaya* plant proved to have medicinal value including leaves, seeds, latex and fruit. *C. Papaya* has a wide variety of medicinal properties including anticancer, antiviral, anti-inflammatory, antimicrobial, antidiabetic, antihypertensive, wound healing activity, free radical scavenging activity and increase in thrombocyte count, etc. The phytochemical constituents of *Carica papaya* and its medicinal properties are presented as follows.

Phytochemical Compounds and antioxidants present in *Carica papaya*

Phytochemical analysis of *C.papaya* leaf extracts revealed the presence of alkaloids, glycosides, flavonoids, saponins, tannins, phenols and steroids[1,2]. The stems, leaves and fruits of papaya contain plenty of latex. The latex of *Carica papaya* is a rich source of

four cysteine endopeptidases namely papain, chymopapain, glycyl endopeptidase and caricain – a papaya endopeptidase II [3]. As the fruit ripens, papain and chymopapain get degraded and not present in the ripe fruit[4]. Other components include a mixture of cysteine endopeptidases such as endopeptidase IV, omega endopeptidase, class-II & class-III chitinase and an inhibitor of serine protease[3,5,6,7]. Aqueous extract of unripe *C.papaya* administered orally in Wistar albino rats demonstrated no adverse effect on the histology of liver, kidney, heart and small intestine[8].

**Fig. 1: Medicinal properties of carica papaya****Antioxidants and free radical scavenging activity**

The leaves, seeds and juice of papaya shows free radical scavenging and antioxidants activity. The antioxidant activity of various fractions (ethanol, petroleum ether, ethyl acetate, n-butanol and aqueous extract) from seeds of *C.papaya* was evaluated and showed that ethyl acetate and n-butanol fractions demonstrated antioxidant and free radical scavenging activity than other fractions[9]. Papaya juice is an efficient scavenger of highly reactive hydroxyl radicals (OH^{\cdot})[10], which significantly decreased the lipid peroxidation levels and increased the antioxidant activity in rats[11]. The leaf extract of *C.papaya* evidenced significant antioxidant and free radical scavenging potential [12]. The peroxidase is present in the unripe fruit of *C.papaya* but it is gradually decreased after fruit ripening

[13]. Whereas, the pulp of papaya is rich in benzyl glucosinolate in the premature stage, which is present in the seed after fruit ripening [14]. The benzyl glucosinolate is hydrolyzed to benzyl isothiocyanate (BITC). The seed extract of *C.papaya* demonstrated rich source of BITC [15]. The nutrient value of papaya fruit per 100g of fresh papaya fruit along with the recommended daily allowance (RDA) is presented in **Table I** [16,17]. It shows that papaya is an excellent source of vitamin A, vitamin C and dietary fibre and a good source of vitamin E. There is not much information about the nutritive value of papaya leaves and seeds.

Table 1. Nutritive value of *Carica papaya* fruit per 100g (source: USDA National Nutrient database)

Vitamins	Nutrient Value	RDA/day for Indians
Energy	43 Kcal	2730Kcal
Water	88.06g	
Carbohydrates	10.82 g	
Protein	0.47 g	60g
Total Fat	0.26 g	
Cholesterol	0 mg	
Dietary Fiber	1.7 g	
Vitamins		
Folates	37 µg	200µg
Niacin	0.357 mg	18mg
Pyridoxine	0.038 mg	2.0mg
Riboflavin	0.027 mg	1.6mg
Thiamin	0.023 mg	1.4mg
Vitamin A	285µg	600µg
Vitamin C	60.9 mg	40mg
Vitamin E	0.30 mg	7.5 - 10mg
Vitamin K	2.6 µg	55µg

Reference: Nutrient value of *Carica papaya* followed from USDA National Nutrient Database and Recommended Daily Allowance (RDA) referred from 'Nutrient Requirements and Recommended Dietary Allowances for Indians' followed from Indian Council of Medical Research (ICMR), Draft Guidelines 2009 [16,17].

Anticancer activity

An *in vitro* study using extract of the papaya seed homogenate was highly effective in inhibition of super oxide generation and inducing apoptosis in acute promyelocytic leukemia cell line HL-60 and the activity was mainly contributed by benzyl isothiocyanate [BITC] [15]. The BITC isolated from papaya fruit extract induced cytotoxic effect in proliferating human colon CCD-18Co cells to the quiescent state [18]. The aqueous extract of *Carica papaya* exposed to onion bulbs disturbed the mitotic cell division of *Allium cepa* by affecting the spindle formation and hence shows its cytotoxic effect [19]. The aqueous extract of papaya flesh (0.01% - 4% v/v) treated with breast cancer cell line MCF7 revealed significant inhibition of cell proliferation [20]. Aqueous extract of papaya leaves in an unrevealed composition shown to possess anticancer activity and inhibition of cell proliferation in a variety of cancer cell lines, which has been patented by Morimoto et al [21]. Likewise, the aqueous extract demonstrated antitumor activity and immunomodulatory activity in tumor cell lines and it proved upregulation of immunomodulatory genes by microarray studies [22]. However, further investigation using cell culture studies, animal studies and clinical trials are needed for proving the chemoprevention and therapeutic potential of different parts of papaya and check the adverse effects if any in consumption of some parts of papaya [23].

Anti-inflammatory activity

The *C.papaya* leaf extract was examined in rats using edema, granuloma and arthritis models. The extract showed significant reduction in paw edema, granuloma formation and reduced inflammation in rats. Thus it proved the anti-inflammatory activity of *C.papaya* [2]. Intake of papaya fruits in healthy individuals alleviated anti-inflammatory response mediated through regulatory T-cells (Tregs) [24]. However, the latex obtained from unripe fruit has the property of inducing inflammation and it is proved in rat as a model for testing the anti-inflammatory activity of compounds [25].

Treatment for dengue fever

A case report from Pakistan [26] documented that aqueous extract of *C.papaya* leaves administered to a patient affected with dengue fever twice daily for 5 consecutive days exhibited elevated platelet count from $55 \times 10^3/\text{ul}$ to $168 \times 10^3/\text{ul}$. Another study in murine model also evidenced increase in platelet and RBC count without any acute toxicity after oral administration of *C.papaya* extract [27]. The juice prepared from *C.papaya* leaves recorded significance increase of platelet count in randomized controlled trial conducted on patients with dengue fever and dengue hemorrhagic fever [28].

Antidiabetic activity

The aqueous extract of *C.papaya* leaves significantly reduced plasma blood glucose level and serum lipid profile in diabetic rats [29,30]. The ethanolic extract of *C.papaya* leaves demonstrated significant reduction in blood glucose level and regeneration of the beta cells of pancreas in diabetic mice [3]. Aqueous extract of unripe papaya fruit significantly inhibited the key enzymes α -amylase and α -glucosidase involved in type 2 diabetes and also inhibited the lipid peroxidation in rat pancreatic cells studied *in vitro* [32].

Wound healing activity

Aqueous extract of *C.papaya* significantly enhance the wound healing that make it an ideal dressing component for treatment of wounds [33]. Fruits and seeds of *C.papaya* were evaluated for wound healing activity using wound excision model in diabetic rats showed significant reduction in the wound area compared to untreated diabetic control. It also showed increased granulation, elevated hydroxyproline content and deposition of collagen in the wound area [34,35].

Papaya latex prepared in carbopol gel for treatment of burns demonstrated significant increase in hydroxyproline content as well as wound contraction in swiss albino mice [36]. Diabetic mice supplemented with fermented papaya preparation (FPP) showed effective recruitment of monocytes and proangiogenic response by the macrophages at the wound site resulting in wound closure [37].

Antifertility effects of *C.papaya*

The papaya seeds were shown to have antifertility properties in male albino rats. Papaya seed extract treated in male albino rats reduced the cauda epidymal and testicular sperm counts [38]. Male Wistar rats treated orally with papaya seed extract (200mg/kg) demonstrated hypertrophy of pituitary gonadotrophs and gradual degeneration of germ cells, sertoli cells and leydig cells of testis thereby drastically affects the male reproductive functions [39]. The aqueous extract of papaya seed administered to male Sprague-Dawley rats suppressed the steroidogenic enzymes in the testis and reversible changes occurred when the extract was withdrawn after 30-45 days of treatment [40]. So that the papaya seed extract can be used as an effective male contraceptive [41].

CONCLUSION

Thus *C.papaya* acts as a multi faceted plant. It is also imperative to identify the mechanism of the plant compounds and studying the active principle of the extract. *C.papaya* possesses rich source of vitamins, antioxidants, flavonoids, 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.

Thus, intake of papaya as fruit salads, fruit juice, leaf extract, decoction prepared through papaya leaves, etc. should be a part of our diet. However, including papaya seeds in any of the form should be avoided for young men and pregnant women since, it possess antifertility effects that was demonstrated well in animal models.

Conflict of Interest

The authors do not have any conflict of interest to declare.

REFERENCES

1. Gill, L.S. (1992): Ethnomedical Uses of Plants in Nigeria, Uniben Press, Benin, Nigeria.

2. Owoyele BV, Adebukola OM, Funmilayo AA, Soladoye AO. Anti-inflammatory activities of ethanolic extract of *Carica papaya* leaves. *Inflammopharmacology*, 16(4): 168-73, (2008).
3. Azarkan M, El Moussaoui A, van Wytswinkel D, Dehon G, Looze Y. Fractionation and purification of the enzymes stored in latex of *Carica papaya*. *J Chromatogr B Analyt Technol Biomed Life Sci*, 790(1-2): 229-238, (2003).
4. Oloyede Ol. Chemical profile of unripe pulp of *Carica papaya*. *Pak J Nutr*, 4(6): 379-381, (2005).
5. Odani S, Yokokawa Y, Takeda H, Abe S, Odani S. The primary structure and characterization of carbohydrate chains of the extracellular glycoprotein proteinase inhibitor from latex of *Carica papaya*. *Eur J Biochem*, 241(1): 77-82, (1996).
6. Azarkan M, Amrani A, Nijs M, Vandermeers A, Zerhouni S, Smolders N, Looze Y. *Carica papaya* latex is a rich source of a class II chitinase. *Phytochemistry*, 46(8): 1319-25 (1997).
7. El Moussaoui A, Nijs M, Paul C, Wintjens R, Vincentelli J, Azarkan M, Looze Y. Revisiting the enzymes stored in the laticifers of *Carica papaya* in the context of their possible participation in the plant defence mechanism. *Cell Mol Life Sci*, 58(4): 556-70 (2001).
8. Oduola, T.; Bello, I.; Idowu, T.; Awwioro, G.; Adeosun, G.; Olatubosun, L.H. Histopathological changes in Wistar albino rats exposed to aqueous extract of unripe *Carica papaya*. *N. Am. J. Med. Sci.* 2: 234-237 (2010).
9. Zhou K, Wang H, Mei W, Li X, Luo Y, Dai H. Antioxidant activity of papaya seed extracts. *Molecules*, 16(8): 6179-92, (2011).
10. Webman EJ, Edlin G, Mower HF. Free radical scavenging activity of papaya juice. *Int J Radiat Biol*, 55(3): 347-51 (1989).
11. Mehdipour S, Yasa N, Dehghan G, Khorasani R, Mohammadirad A, Rahimi R, Abdollahi M. Antioxidant potentials of Iranian *Carica papaya* juice in vitro and in vivo are comparable to alpha-tocopherol. *Phytother Res*, 20(7): 591-4 (2006).
12. Okoko T, Ere D. Reduction of hydrogen peroxide-induced erythrocyte damage by *Carica papaya* leaf extract. *Asian Pac J Trop Biomed*, 2(6): 449-53 (2012).
13. Pandey VP, Singh S, Singh R, Dwivedi UN. Purification and characterization of peroxidase from papaya (*Carica papaya*) fruit. *Appl Biochem Biotechnol*, 167 (2): 367-76, (2012).
14. Li ZY, Wang Y, Shen WT, Zhou P. Content determination of benzyl glucosinolate and anti-cancer activity of its hydrolysis product in *Carica papaya* L. *Asian Pac J Trop Med*, 5(3): 231-3, (2012).
15. Nakamura Y, Yoshimoto M, Murata Y, Shimoishi Y, Asai Y, Park EY, Sato K, Nakamura Y. Papaya seed represents a rich source of biologically active isothiocyanate. *J Agric Food Chem*, 55(11): 4407-13, 2007.
16. USDA National Nutrient Database for Standard Reference; <http://ndb.nal.usda.gov>
17. Indian Council of Medical Research (ICMR), Draft Guidelines 2009 for Nutrient Requirements and recommended Dietary Allowances for Indians.
18. Miyoshi N, Uchida K, Osawa T, Nakamura Y. Selective cytotoxicity of benzyl isothiocyanate in the proliferating fibroblastoid cells. *Int J Cancer*, 120(3): 484-92, (2007).
19. Akinboro A, Bakare AA. Cytotoxic and genotoxic effects of aqueous extracts of five medicinal plants on *Allium cepa* Linn. *J Ethnopharmacol*, 112(3): 470-5, (2007).
20. García-Solís P, Yahia EM, Morales-Tlalpan V, Díaz-Muñoz M. Screening of antiproliferative effect of aqueous extracts of plant foods consumed in México on the breast cancer cell line MCF-7. *Int J Food Sci Nutr*, 60, Suppl 6: 32-46 (2009).
21. Morimoto, C., Dang, N. H., Dang, N., YS Therapeutic Co Ltd (YSTH-Non-standard) Toudai Tlo Ltd (TOUDNon-standard) Morimoto C (MORI-Individual) Dang N H (DANG- Individual), Cancer prevention and treating composition for preventing, ameliorating, or treating solid cancers, e.g. lung, or blood cancers, e.g. lymphoma, comprises components extracted from brewing papaya. Patent number- WO2006004226-A1; EP1778262- A1; JP2008505887-W; US2008069907-A1, 2008.
22. Otsuki N, Dang NH, Kumagai E, Kondo A, Iwata S, Morimoto C. Aqueous extract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effects. *J Ethnopharmacol*, 127(3):760-7, (2010).
23. Nguyen TT, Shaw PN, Parat MO, Hewavitharana AK. Anticancer activity of *Carica papaya*: a review. *Mol Nutr Food Res*, 57(1):153-64, (2013).
24. Abdullah M, Chai PS, Loh CY, Chong MY, Quay HW, Vidyadarshini S, Seman Z, Kandiah M, Seow HF. *Carica papaya* increases regulatory T cells and reduces IFN-γ+ CD4+ T cells in healthy human subjects. *Mol Nutr Food Res*. 55(5): 803-6 (2011).
25. Gupta OP, Sharma N, Chand D. A sensitive and relevant model for evaluating anti-inflammatory activity-papaya latex-induced rat paw inflammation. *J Pharmacol Toxicol Methods*, 28(1): 15-9 (1992).
26. Ahmad N, Fazal H, Ayaz M, Abbasi BH, Mohammad I, Fazal L. Dengue fever treatment with *Carica papaya* leaves extracts. *Asian Pac J Trop Biomed*, 1(4): 330-3, (2011).
27. Dharmaratna SL, Wickramasinghe S, Weduge RN, Rajapakse RP, Kularatne SA, Halim SZ. Does *Carica papaya* leaf-extract increase the platelet count? An experimental study in a murine model. *Asian Pac J Trop Biomed*, 3(9): 720-4, 2013.
28. Subenthiran S, Choon TC, Cheong KC, Thayan R, Teck MB, Muniandy PK, Afzan A, Abdullah NR, Ismail Z. *Carica papaya* Leaves Juice Significantly Accelerates the Rate of Increase in Platelet Count among Patients with Dengue Fever and Dengue Haemorrhagic Fever. *Evid Based Complement Alternat Med*, 2013: 616737 (2013).
29. Juárez-Rojop IE, Díaz-Zagoya JC, Ble-Castillo JL, Miranda-Osorio PH, Castell-Rodríguez AE, Tovilla-Zárate CA, Rodríguez-Hernández A, Aguilar-Mariscal H, Ramón-Frías T, Bermúdez-Ocaña DY. Hypoglycemic effect of *Carica papaya* leaves in streptozotocin-induced diabetic rats. *BMC Complement Altern Med*, 12: 236, (2012).
30. Maniyar Y, Bhixavatimath P. Antihyperglycemic and hypolipidemic activities of aqueous extract of *Carica papaya* Linn. leaves in alloxan-induced diabetic rats. *J Ayurveda Integr Med*, 3(2): 70-4, (2012).
31. Sasidharan S, Sumathi V, Jegathambigai NR, Latha LY. Antihyperglycaemic effects of ethanol extracts of *Carica papaya* and *Pandanus amaryfolius* leaf in streptozotocin-induced diabetic mice. *Nat Prod Res*, 25(20): 1982-7, (2011).
32. Oboh G, Olabiyi AA, Akinyemi AJ, Ademiluyi AO. Inhibition of key enzymes linked to type 2 diabetes and sodium nitroprusside-induced lipid peroxidation in rat pancreas by water-extractable phytochemicals from unripe pawpaw fruit (*Carica papaya*). *J Basic Clin Physiol Pharmacol*, 30:1-14 (2013).
33. Mahmood A A, Sidik K, Salmah I. Wound healing activity of *Carica papaya* L. Aqueous leaf extract in rats. *International Journal of Molecular Medicine and Advance Sciences*, 1(4): 398-401 (2005).
34. Nayak SB, Pinto Pereira L, Maharaj D. Wound healing activity of *Carica papaya* L. in experimentally induced diabetic rats. *Indian J Exp Biol*, 45(8): 739-43 (2007).
35. Nayak BS, Ramdeen R, Adogwa A, Ramsuhag A, Marshall JR. Wound-healing potential of an ethanol extract of *Carica papaya* (Caricaceae) seeds. *Int Wound J*, 9(6): 650-5, (2012).
36. Gurung S, Skalko-Basnet N. Wound healing properties of *Carica papaya* latex: in vivo evaluation in mice burn model. *J Ethnopharmacol*, 121(2):338-41, (2009).
37. Collard E, Roy S. Improved function of diabetic wound-site macrophages and accelerated wound closure in response to oral supplementation of a fermented papaya preparation. *Antioxid Redox Signal*, 13(5): 599-606, (2010).
38. Lohiya NK, Goyal RB. Antifertility investigations on the crude chloroform extract of *Carica papaya* Linn. seeds in male albino rats. *Indian J Exp Biol*, 30(11):1051-5, (1992).

39. Udoth P, Essien I, Udoth F. Effects of Carica papaya (paw paw) seeds extract on the morphology of pituitary-gonadal axis of male Wistar rats. **Phytother Res**, 19(12): 1065-8, (2005).
40. Uche-Nwachi EO, Mitchell CV, McEwen C. Steroidogenic enzyme histochemistry in the testis of Sprague Dawley rats following the administration the water extracts from Carica papaya seed. **Afr J Tradit Complement Altern Med**, 8(1): 69-78, (2011).
41. Chinoy NJ, D'Souza JM, Padman P. Effects of crude aqueous extract of Carica papaya seeds in male albino mice. **Reprod Toxicol**, 8(1): 75-9, (1994).