

TRADITIONAL MEDICINAL USE OF PAPAYA (*CARICA PAPAYA* L.)

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Papaya (*Carica papaya* L.) is a perennial plant and widely cultivated in tropical and subtropical regions of the world. It is a rich source of antioxidants vitamin A, B, C, flavonoids, potassium, magnesium and low in calories. It contains proteolytic enzymes like papain and chymopapain. Papain is extracted from unripened fruit and used in industry for making toothpaste, shampoo, facial cream, chewing gum and in food processing as meat tenderiser and for coagulating the milk. In India, papaya is regarded as a medicinal plant in the Ayurvedic literature. All parts of papaya such as seeds, fruit, pulp, root and leaves have medicinal importance. Leaves extract used for the treatment of dengue fever, reduce blood glucose level, inhibit cancer cell growth, help in digestion and anti-inflammatory activity. Fruit pulp of papaya is used to cure ulcer, pimples, burns and reduce blood pressure. Seeds possess anti-fertility, anti-helminthic activity and used as a substitute for black pepper. Papaya peel is used to rebuild damaged skin. Papaya contains phenolic compounds, glucosinolates, alkaloids (carpain and pseudocarpain), flavonoids and tannins. In-vitro anti-diabetic, anti-cancerous, anti-inflammatory, anti-malarial and anti-hypoglycemia potential of papaya was determined by techniques such as flow cytometer, gas and high performance liquid chromatography, etc., to justify the traditional medicinal use of papaya plant.

Keywords: *Carica papaya*, Medicinal importance, Leaf extract, Fruit pulp, Seeds

Introduction

Papaya (*Carica papaya* L.) is a perennial edible fruit crop. It is cultivated in tropical and subtropical regions worldwide. It was originated from Central and South America (Morton, 1987). It belongs to the family Caricaceae (Ming *et al.*, 2008). It contains nine pairs of chromosomes (2n=9). It is a dicotyledonous plant with a small genome size of 372 Mbp (Arumuganathan and Earle, 1991; Damasceno *et al.*, 2009; Araujo *et al.*, 2010). It is short lived and semi-woody. Papaya can be grown upto 10 m in height.

Fruits are produced within nine to ten months from the germination period. The leaves are palmately-lobed and clustered at the top of plant (OECD, 2005).

According to the percentage of the US recommended daily allowances, papaya fruit ranked first among 35 commonly used fruits. Papaya fruit is highly nutritious and is a rich source of antioxidants vitamins (A, C and E), thiamine, folate, riboflavin, niacin, flavonoids, potassium, magnesium, iron, calcium and fibre (Chandrika *et al.*, 2003; Ming *et al.*, 2008). It contains no starch and is low in calories. The fruit contains proteolytic enzymes like

papain and chymopapain. Papain is extracted from unripened fruit and used for making toothpaste, shampoo, facial cream, chewing gum and in food processing to tenderise meat, milk coagulation, clarify beer and juice (Morton, 1987). (4 per cent plagiarism)

Traditional Medicinal Properties of Various Parts of Papaya

Papaya is regarded as a medicinal plant in the Ayurvedic literature. In different regions of India, the different parts of the papaya plant including leaves, seeds, fruit, peel and root are used as medicine. Papaya pulp was used by tribal women of Madhya Pradesh for easy abortion (Sahu, 1982). Leaves are ground and taken with salt to treat cough (Singh, 1986). Banerjee (1997) said that papaya is used to control diabetes. Unripe papaya and root were prescribed by *vaidyas* in Uttaranchal for the treatment of jaundice and kidney stones (Kala *et al.*, 2005). Papaya sap was used to cure tetanus by several *vaidyas* in Chhattisgarh (Ekka and Dixit, 2014). Various in-vitro studies of papaya were done to justify the traditional medicinal use of papaya plant.

Leaves

Papaya leaves are eaten like spinach in Asia. Leaves have several benefits (Aravind *et al.*, 2013).

Dengue Fever

The leaf extract of papaya is used for the treatment of dengue. Leaves extract increases platelets count and total white cell counts (Hettige, 2008, Ahmed *et al.*, 2011) studied that leaf extract increases platelets count from 55,000/ μ l to 1,68,000/ μ l in dengue patients.

The anti-dengue activities of papaya leaf extract was checked by using bioinformatics tools. Flavonoid quercetin was identified as possessing highest binding energy against NS2B-NS3 protease, which was confirmed by the formation of six hydrogen bonds with the amino acid residues at the binding site of the receptor. Flavonoid quercetin showed the antiviral activity by inhibiting the DENV2 virus assembly mechanism. These results showed that flavonoids of papaya have anti-dengue activities (Senthilvel *et al.*, 2013).

Anti-HIV Activity

Methanol and aqueous extracts of papaya aerial parts were tested for their anti-HIV-1 activity. Aqueous extract was more active as an anti-HIV-1 agent than methanol extract. This anti-HIV-1 activity may be because of the presence of flavonoids, triterpenes, tannins, alkaloids and carbohydrates in the extracts (Rashed *et al.*, 2013).

Anti-cancer Activity

The leaf extract of papaya has been shown to prevent the cancer cell growth. Leaf extract increased the production of Th1-type cytokines that regulate the immune system (Aravind *et al.* 2013). Gurudatta *et al.*, (2015) showed that papaya leaf extract in a dose of 200 mg/kg body weight was effective to inhibit the progression of cancer growth. Rashed and Fouche, (2013) analysed the phytochemical composition of petroleum ether extract of papaya aerial parts using silica gel column chromatography. β -sitosterol and stigmasterol were the major constituents of petroleum ether extract of papaya aerial parts. Extract of aerial parts were tested for their anti-cancer activity on three cancer cells TK10 (renal), UACC62 (melanoma) and MCF7

(breast) cancer cells using a Sulforhodamine B (SRB) assay. The use of extract at the concentration of 100 µg/ml showed most significant anti-cancer effect on MCF7 (breast) cancer cells while other two cancer cells showed less anticancer effect.

Anti-tumour activity

Otsuki *et al.* (2010) showed the effect of papaya extract on tumour cell lines and human peripheral blood mononuclear cell (PBMC). The cell viability of PBMC checked by flow cytometry showed that leaf extract has not affected the viability of PBMC. Increased antitumour cytokine production IL12p40, IL12p70, TNF- α and INF- γ which inhibits the growth of tumour was assessed by ELISA. Microarray analysis showed that 23 immunomodulatory genes were increased after the treatment with papaya leaf extract. The upregulation of these genes was confirmed by real-time RT-PCR. This analysis showed that mRNA expression of CCL2, CCL7, CCL8 and serine protease inhibitor type 2 (SERPINB2) enhanced the survival of tumour cell line.

Anti-hypertensive Activity

Brasil *et al.* (2014) determined the chemical composition in the methanolic leaf extract of papaya and their anti-hypertensive effect in rats. The flavonoids, rutin, maghaslin, clitorin, and nicotiflorin were identified by electrospray ionisation mass or mass spectrometry in methanol extract of papaya. The presence of these substances and the total flavonoids content may have contributed to the reduction of angiotensin converting enzyme (ACE) inhibitory activity and improved baroreflex. ACE is a component of the RAS, which is responsible for the long-term control of blood pressure.

Hypoglycemic effect

Maniyar and Bhixavatimath (2012) reported that the leaf extract of papaya decreased blood glucose levels and cured diabetes. Anti-diabetic efficiency of methanolic leaf extract of papaya was measured colorimetrically by estimating the degree of non-enzymatic haemoglobin glycosylation. Leaf extract increased the inhibition of glycosylation and α -amylase, which decreases the formation of glucose in blood (Ogundele *et al.*, 2017). It also lowers cholesterol, triacylglycerol and amino-transferases blood levels (Juarez-Rojop *et al.*, 2012).

Anti-inflammatory Activity

Extract of papaya leaves reduces oedema and granuloma in arthritis (Owoyele *et al.*, 2008). Gammulle *et al.* (2012) scientifically validated the anti-inflammatory activity of the leaf extract. High dose of mature leaf concentrate of papaya given to thrombocytopenic rats increased platelets, WBC and RBCs. The carrageenan-induced paw edema test is a tool for determining the potential anti-inflammatory agents. Mature leaf concentrate of papaya inhibited careegenan induced rat paw oedema and reduced vascular permeability in mice suggested effective anti-inflammatory activity.

Fruit

Ripe fruit pulp can be used for the treatment of indigestion, diarrhoea, dysentery (Singh, 1986). Fruit with unripe seeds cause abortion in pregnant women (Sahu, 1982). Unripe fruit can be used for the treatment of gastric and urinary bladder disorders (Rao and Jamir, 1982). Papaya fruit juice also contains antihypertensive agent (catecholamine-like blocking agent), which exhibits alpha adenoreceptor activity and cure the blood pressure (Eno *et al.*, 2000). Unripe fruit used

to cure gastric ulcer. The presence of alkaloid in fruit extract is a major account for the anti-ulcer property (Ezike *et al.*, 2009).

Skin Burn

Fruit pulp is mashed and applied daily on burn area to cure burn wound (Starley *et al.*, 1999). In vitro study was performed for wound healing. Fermented papaya fruit was applied on rats with burn trauma to study the wound healing effect. The antioxidant activity was measured by chemiluminescence assay. This fermented preparation reduced production of free radicals, which changes in the general inflammatory reaction. Myeloperoxidase activity reduced in the wound and serves as a marker of local inflammatory reaction. These results suggested that the local inflammation reduced in rats with burn trauma (Mikhailchik *et al.*, 2004).

Skin Disorders

The sun protection factors in papaya fruit extract was analysed by ultraviolet (UV) spectrophotometer irradiated with UVB lamp. The analysis showed that the major antioxidant of papaya was stable when exposed to UVB irradiation, therefore, used as anti-solar formulation (Shenekar *et al.*, 2014). Paste of crushed fruit is applied on the face used to cure pimples (Saikia *et al.*, 2006). Kardono *et al.* (2013) used papaya fruit and latex extract to develop skin lightening lotion based on tyrosinase inhibition and antioxidant activities. Antioxidant activity of fruit and latex extract was evaluated using DPPH free radical scavenging activity method. Papaya latex showed the highest antioxidant activity (32.01 per cent) followed by fruit extract (26.09 per cent). Latex extract showed (68.42 per cent) tyrosinase inhibitory activities followed by latex extract (36.80 per cent). These results

suggest that papaya latex and fruit extract used as natural source for skin whitening.

Seeds

Papaya seeds are black in colour and edible. Seeds have spicy taste and pungent smell. Seeds have various other medicinal importance. (Yogiraj *et al.*, 2014).

Ulcer treatment

Gas chromatography coupled mass spectrometer profiling of aqueous seed extract of papaya observed the presence of acacic acid, genistein, phorbol ester, cryptolepinone, brusatol, α -ionone and paclitaxel. The presence of these compounds (paclitaxel and betulonic acid) in seed extract may be responsible for decreased gastric pH, acid secretion, acid output, secretion volume and ulcer index in indomethacin-induced ulcer rats. Acidity in the stomach secretions of rats with indomethacin-induced ulcers decreased with the seed extract treatment. Decrease in glutathione levels in rats pretreated with aqueous extract of papaya seed may be responsible for the enhancement of antioxidant enzymes resulted in anti-ulcerogenic activity (Oloyed *et al.*, 2015).

Anti-fertility

The biochemical (ascorbic acid, ascorbigen, ascorbic acid utilisation, ascorbic acid macromolecular complexing, ascorbic acid free radical formation, total ascorbic acid and glutathione, cholesterol, protein and glycogen) changes in rat ovaries and uterus was studied after 7 days and 15 days of treatment with aqueous seed extract. The decrease in glycogen level in uterine resulting made changes in uterine secretion, which unsuitable for fertilised ovum implantation. Seed extract treatment showed antifertility,

antiimplantation and abortifacient in rat (Chinoy *et al.*, 1995). The uterine contraction was increased. Papaya seed extract lower testosterone level which leads to infertility in males (Sinha and Nathawat, 1989; Hasim *et al.*, 2013). Lakshman and Changamma, (2013) reported that seed extract of papaya reduced the cholesterol levels in testes that leads to decreased steroidogenesis and inhibit spermatogenesis. The antifertility agents interfere with biosynthesis of steroid hormone, which results in infertility in albino rat.

Anti-helminthic activity

Seeds of papaya were extracted in an aqueous buffer or in organic solvents and fractionated by chromatography on silica. The anthelmintic activity of seed extract aliquot was tested against *Caenorhabditis elegans*. Benzyl isothiocyanate was responsible for anthelmintic activity that was found in seed extract of papaya (Kermanshaia *et al.*, 2001). Okeniyi *et al.* (2007) reported that dried papaya seeds effectively removed intestinal helminth (*Ascaris lumbricoides*). Seeds were also very effective against *Hymenolepis diminuta* infection (Sapaat *et al.*, 2012).

Peel and root

Peel of papaya helps to rebuild damaged skin due to the presence of vitamin A. It is also used to lighten the skin. Papaya peel mixed with honey acts as moisturiser for the skin

(Aravind *et al.*, 2013). Papaya root extract has greater wound healing activity (Tiwari *et al.*, 2011).

Conclusion

Papaya fruit is ranked first among 35 commonly used fruits. It contains high amount of antioxidants (vitamins A, B and C), thiamine, folate, riboflavin, niacin, flavonoids, potassium, magnesium, iron, calcium and fibre. Unripened fruits possess proteolytic enzymes like papain and chymopapain. Papain is utilised in industry for making toothpaste, shampoo, facial cream, chewing gum and in food processing to tenderise meat, milk coagulation, clarify beer and for juice. All parts of papaya— fruit, roots, peel, seeds and pulp— have medicinal importance. Papaya is used for the treatment of various diseases such as ulcer, indigestion, dengue, skin lightening, wound healing, burn and cancer cell inhibition. It is also used to lower blood glucose level and reduce blood pressure. Flow cytometer, gas and high performance liquid chromatography, mass spectrometer and colorimeter analysis showed the presence of phenolic compounds such as glucosinolates, alkaloids (carpain and pseudocarpain), flavonoids and tannins in papaya, which is responsible for anti-diabetic, anti-cancerous, anti-inflammatory, anti-hypoglycemia and anti-hypertensive activity.

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