

## Anticancer activities of Papaya (*Carica papaya*): A Review

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### ABSTRACT

Cancer is considered one of the deadly diseases in the world. According to WHO cancer now causes more deaths than all coronary heart disease. The incidence and mortality of the worldwide major cancers are now available in the GLOBOCAN series of the International Agency for Research on Cancer. The transition of global demographic and epidemiologic shows that burden of cancer will increase particularly in low and middle income countries, with over 20 million new cancer cases expected annually as early as 2025. Medicinal plants made known to be prospective and useful job for the treatment of several diseases and disorders from prehistoric days to nowadays. One of the commonly used plants, which have supporting evidences from the recent scientific data for the different types of cancers, is *Carica papaya*. Papaya (*Carica papaya*) is widely used as folk caloric herbal medicine, being a powerhouse of nutrients and accessible throughout the year. It is a rich source of three powerful antioxidants, the minerals, vitamins and contains high content of fibre. *Carica papaya* has provided many remedies for various diseases from ancient days to nowadays, and is regarded as a Nutraceutical. Because of this comprehensive medicinal value of *Carica papaya*, we are trying here to convey the reports studied especially for the anticancer activities of the age-old fruit, which will help researchers to pull in concert data and may be a “lead” for the one of the dangerous disease in the world.

**Keywords:** *Carica papaya*, Anticancer, Traditional System of Medicine, Prostate cancer

### INTRODUCTION

In the present scenario, cancer is considered one of the deadly diseases in the world. After a huge number of drugs have been put in the market, yet there is very low feedback from the society as the available drugs are high cost and least effective for the disease. Estimates of the worldwide incidence and mortality from 27 major cancers and for all cancers combined for 2012 are now available in the GLOBOCAN series of the International Agency for Research on Cancer (Morimoto 2008; Siegel, Ma et al. 2014). On the basis of this study, the data clearly showed that there were 14.1 million new cases and 8.2 million deaths in 2012. The most commonly diagnosed cancers were lung (1.82 million), breast (1.67 million), and colorectal (1.36 million); the most common causes of cancer death were lung cancer (1.6 million deaths), liver cancer (745,000 deaths), and stomach cancer (723,000 deaths) (Morimoto 2008; Jemal, Bray et al. 2011; Siegel, Ma et al. 2014; Ferlay, Soerjomataram et al. 2015). According to WHO, cancer now causes more deaths than all coronary heart diseases. The transition of global demographic and epidemiologic shows that burden of cancer will increase

particularly in low and middle income countries, with over 20 million new cancer cases expected annually as early as 2025 (Jemal, Bray et al. 2011; Ferlay, Soerjomataram et al. 2015). The profile varies greatly in different populations, and the evidence suggests that this variation is mainly a consequence of different lifestyle (such as tobacco use, physical inactivity, excess body weight, and reproductive patterns) and environmental factors (Jemal, Bray et al. 2011; Siegel, Ma et al. 2014; Ferlay, Soerjomataram et al. 2015).

Medicinal plants made known to be prospective and useful job for the treatment of several diseases and disorders from prehistoric days to nowadays (TsouhFokou, Nyarko et al. 2015; Parray 2017). One of the commonly used plants, which have supporting evidences from the recent scientific data for the different types of cancers, is *Carica papaya*.

The plant *Carica papaya*, common name papaya tree is one amid the 22-acknowledged species in the genus *Carica* of the family Caricaceae (Gill 1992; Manohar 2013). Papaya, botanical name *Carica papaya*, is a lozenge tropical fruit, often seen in orange-red, yellow-green and yellow-orange hues, with a rich orange pulp. The communal names of *Carica papaya* are Papita, Papeeta, Papiitaa, Melon (Ayoola 2010) tree, Papaw, Paw paw. On the basis of ethno-medicinal literature, not only the fruit of papaya but root, bark, peel, seeds and pulp are also known to have medicinal properties (Milind 2011; Dikibo 2012; Aravind 2013), so we can say that it is the complete medicinal plant. Besides this, it is a perennial flowering tree, valued for its buttery fruit that is thought to offer many health benefit aids. The

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remarkable fruit of plant comprises enzymes and compounds that can avert cancer, ageing and can endorse healthier and sound heart (Ayoola 2010). Papaya (*Carica papaya*) is one of the all year-round preferred pudding fruits known for its sweet, juicy, melt on your mouth flesh. Being not only delicious fruit but it is equally crammed with minerals and vitamins that offer many health benefits for the typical papaya lover (Wall 2006).

Papaya is widely used as folk caloric herbal medicine, being a powerhouse of nutrients and accessible throughout the year. It is a rich source of three powerful antioxidant i.e., vitamin C, vitamin A and vitamin E respectively; the minerals includes; magnesium and potassium; the B vitamins includes pantothenic acid and folate; contain high content of fibre (Wall 2006; Ayoola 2010; Nwofia 2012). Besides all, it comprises a digestive enzyme-papain that effectually treats causes of trauma, allergies and sports injuries. All the nutrients of papaya improve cardiovascular system, protect against heart diseases (heart attacks and strokes) and prevent colon cancer. The fruit of tree is an estimable source of beta carotene that averts damage triggered by free radicals that may be the basis of some forms of cancer (Tietze 2003; Morimoto 2008; Nguyen, Shaw et al. 2013). It is conveyed that it aids in the prevention of diabetic heart disease. In addition papaya lowers high cholesterol levels as it is a good source of fibre and the plant can be used for treatment of a numerous diseases (Tietze 2003; Krishna 2008; Aravind 2013). *Carica papaya* has provided many remedies for various diseases from ancient days to nowadays like warts, corns, sinuses, acne and skin infections, eczema, cutaneous tubercles, glandular tumors, wound healing, blood pressure, dyspepsia, constipation, amenorrhea, general debility, , anti-aging, anthelmintic, prevents atherosclerosis, heart diseases and dengue fever; extracts from the plant roots are practiced for aborting early pregnancy, boosts the immune system, expel worms, improves and preserves good vision and stimulate reproductive organs, as a upshot *C. papaya* is regarded as a Nutraceutical (Daly 2011; Milind 2011). Because of this comprehensive medicinal value of *Carica papaya*, we are trying here to convey the reports studied especially for the anticancer activities of the age-old fruit, which will help researchers to pull in concert data and may be a “lead” for the one of the dangerous disease in the world.

## REPORTED ANTI-CANCER ACTIVITIES OF CARICA PAPAYA

### Cancer cell growth inhibition:

The papaya fibre is capable to bind with toxins which cause cancer in the colon and keep them away from the healthy colon cells. These nutrients provide synergistic shield for colon cells from free radical damage to their DNA. Papaya leaf tea extract has demonstrated cancer cell growth inhibition. It seems to boost the production of key signaling molecules called Th1-type cytokines, which help regulate the immune system (Milind 2011; Aravind 2013).

Currently, scientific investigations have demonstrated the inhibitory action of this decoction on the proliferation of both solid tumor cell lines and hematopoietic cell lines (Morimoto 2008; Morimoto 2008; Otsuki, Dang et al. 2010). The decoction was equipped by brewing *Carica papaya* leaves with water in a glass beaker or wooden vessel for a period (varying from 5 minutes to 12 hours in various reports). The heating procedure to prepare the decoction can potentially affect temperature-sensitive compounds, leading to likely changes in bioactivity.

This type of effect has been described for other herbal medicines such as ginseng root and ginger, where steaming preparation has been observed to increase the anti proliferative effect compared to unprocessed materials (Wang, Zhang et al. 2006; Qi, Wang et al. 2010; Cheng, Liu et al. 2011). The study was used to test the hypothesis that the preparation of *Carica papaya* leaves following an Aboriginal remedy alters the chemical pattern and thus the anticancer effect of *Carica papaya* leaf (Nguyen, Parat et al. 2016). *Carica papaya* leaf decoction, an Australian Aboriginal remedy, has been used widely for its healing capabilities against cancer, with numerous anecdotal reports.

The study investigated in vitro cytotoxicity on human squamous cell carcinoma cells followed by metabolic profiling of *Carica papaya* leaf decoction and leaf juice/brewed leaf juice determines the effects imparted by the long heating process typical of the Aboriginal remedy preparation. Also, MTT assay results showed that in comparison with the decoction, the leaf juice not only exhibited a stronger cytotoxic effect on SCC25 cancer cells, but also produced a substantial cancer-selective effect as shown by tests on non-cancerous human keratinocyte HaCaT cells. Additionally, evidence from testing brewed leaf juice on these two cell lines suggested that the brewing process markedly reduced the selective effect of *Carica papaya* leaf on SCC25 cancer cells (Nguyen, Parat et al. 2016). In traditional medicine, *Carica papaya* leaves have been used for treatment of cancer in Vietnam and Australia (Lucas 1914; Tietze 2003; Vien 2013). *Carica papaya* leaf decoction, an Australian Aboriginal remedy, has been reported widely for its healing capabilities against cancer, with numerous anecdotal reports (Nguyen, Shaw et al. 2013).

### Effect on Prostate cancer:

Prostate cancer (PCa) is the second most common cancer in men worldwide and the mortality of prostate cancer is very high and is listed as the sixth leading cause of cancer-related deaths in men (Jemal, Bray et al. 2011; Siegel, Naishadham et al. 2012; Siegel, Ma et al. 2014). Prostate cancer is common in men which is one of foremost cause of cancer-related deaths in men with very high mortality. Androgen deprivation and chemotherapeutic agents are the main treatment tactics for metastasized prostate cancer. Docetaxel and taxane are the frequently chemotherapeutic agents for the treatment of prostate cancer but consequences of using these drugs have not been adequate. Consequently, it becomes compulsory to find better treatment tactics for prostate cancer and to search for compounds that are active against prostate cancer preclusion. Lycopene extracted from tomato and other fruits or plants such as watermelon, pink grapefruit, pink guava, red carrot and papaya has been publicized to be effective for prostate cancer preclusion and treatment. The benefit of lycopene for its anti-prostate cancer activity is that lycopene can reach much higher concentration in prostate tissue than other tissues. Several mechanisms have been suggested to describe the lycopene effect on prostate cancer (Guns and Cowell 2005; Trejo-Solis, Pedraza-Chaverri et al. 2013). A potentially central mechanism is the modification of the phosphatidylinositol 3- kinase (PI3K)/protein kinase B (Akt) pathway (Elfiky and Jiang 2013; Qiu, Yuan et al. 2013). The effect of lycopene on PI3K/Akt pathway is summarized, which could be one of major mechanisms for anti-cancer activity of lycopene has been reviewed (Chen, O'Donoghue et al. 2014). Lycopene, the principal red carotenoid pigment of tomatoes, has been shown to inhibit the PI3K/Akt pathway in several studies, which plays a

significant role in cancer risk (Giovannucci 1999; Chan 2002; Renehan 2004)

IGF-1 can stimulate cancer cell proliferation and decrease apoptosis via activation of PI3K/Akt pathway in many cancers including prostate cancer (Chan 2002; Huang and Chen 2009; Chen 2011; Elfiky and Jiang 2013). Increasing incidental reports of its effects in cancer treatment and prevention, with many efficacious cases, have accepted that these pharmacological assets from the plant be scientifically validated. Using the key words “papaya”, “anticancer”, and “antitumor” along with cross-referencing, a bibliographic search was conducted. No medical and clinical or animal cancer studies were recognized and only seven in vitro cell-culture-based studies were reported; which indicated that *C. papaya* extracts may alter the growth of some types of cancer cell lines. Though, many studies focused on specific compounds in *C. papaya* and reported its bioactivity including anticancer effects (Nguyen, Shaw et al. 2013).

#### Effect on Human breast and liver cancer cells:

In 2002, the anti-proliferative activity was screened on human breast and liver cancer cell lines of pure lycopene and of both juice and extracted lycopene from papaya and watermelon (two fruits with high lycopene contents) (Rahmat 2002). The reports showed that papaya juice and pure lycopene triggered cell death in the liver cancer cell line Hep G2 with the half maximal inhibitory concentration (IC<sub>50</sub>) of 20 mg/mL and 22.8 mg/mL, respectively. Though, neither papaya juice nor pure lycopene displayed any upshot on the cell viability of breast cancer cell MDA-MB-21. The extracted lycopene from papaya juice did not display any effect on proliferation of either cell line (Nguyen, Shaw et al. 2013). No human clinical trials were known and no in vivo cancer studies have been conducted with extracts from any part of *C. papaya*. Only several case studies have been reported in a patent as experimental examples with very limited data (Morimoto 2008). The Case 1 was a 47-year old female with stomach cancer metastasized to the pancreas. She drank about 750 mL of papaya leaf extract everyday (one dried papaya leaf was boiled in a wooden vessel with 3000 mL of water until concentrated to 750 mL) for two 90-day periods with a 90 days break between two periods. The pancreatic metastases were seen disappeared, the tumor marker, carcino-embryonic antigen, dropped from 49 to 2.3, and the alpha-fetoprotein dropped from 369 to 2.0, with no relapse found after. The other cases were testified without any specific data; however, long-term survival was observed for five lung cancer patients, three stomach cancer patients, three breast cancer patients, one pancreatic cancer patient, one liver cancer patient, and one blood cancer patient after drinking papaya leaf extract (Oduola 2006; Oduola 2007; Oduola 2010). More unexpectedly, the number of in vitro cancer studies for *C. papaya* was also limited to only seven cell culture based studies. The effects of papaya flesh extracts on the viability of breast cancer cell line MCF-7 were examined simultaneously with extracts from other fruits in two studies by Garcia-Solis et al. (Garcia-Solis, Yahia et al. 2009) and Jayakumar et al. (Jayakumar 2011). The authors in these studies also assessed antioxidants such as polyphenols, carotene, and flavonoids in the fruits to focus on the contribution of these antioxidants in the inhibition of proliferation (Nguyen, Shaw et al. 2013).

#### CONCLUSION

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Cancer is considered as a one of the deadly diseases in the present scenario. As per WHO, cancer has reported to cause more deaths than all coronary heart disease in the world. The recent reports are suggesting that the burden of cancer will increase particularly in low and middle income countries and new cancer cases are annually as early as 2025. Medicinal plants have always played an imperative role in providing health care to large section of population, especially in developing countries from prehistoric days to nowadays. One of the commonly used plants, which have supporting evidences from the recent scientific data for the different types of cancers, is *Carica papaya*, was discussed in the above review paper. The main aim of this review is to provide the reports studied especially for the anticancer activities of the age-old fruit, which will help researchers to pull in concert data and may be a “lead” for the one of the dangerous disease in the world. There are lot of other well-known scientific researches and the surprises conceal in the fruit will be materialized.

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#### CONFLICT OF INTEREST

None

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