REVIEW

Anticancer activity of *Carica papaya*: A review

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Carica papaya is widely cultivated in tropical and subtropical countries and is used as food as well as traditional medicine to treat a range of diseases. Increasing anecdotal reports of its effects in cancer treatment and prevention, with many successful cases, have warranted that these pharmacological properties be scientifically validated. A bibliographic search was conducted using the key words "papaya", "anticancer", and "antitumor" along with cross-referencing. No clinical or animal cancer studies were identified and only seven in vitro cell-culture-based studies were reported; these indicate that *C. papaya* extracts may alter the growth of several types of cancer cell lines. However, many studies focused on specific compounds in papaya and reported bioactivity including anticancer effects. This review summarizes the results of extract-based or specific compound-based investigations and emphasizes the aspects that warrant future research to explore the bioactives in *C. papaya* for their anticancer activities.

Keywords:
Anticancer / Antitumor / Bioactivity / *Carica papaya* / Nutraceuticals

1 Introduction

Carica papaya belongs to the small family Caricaceae and is one of the major fruit crops cultivated in tropical and subtropical zones. Worldwide, the 2010 figures for papaya show that over 11.2 million tons of fruits were produced in an area of 438 588 Ha in 60 countries [1].

In traditional medicine, different parts of *C. papaya* including its leaves, barks, roots, latex, fruit, flowers, and seeds have a wide range of reputed medicinal application. In Jamaica, the ripe fruit is used as topical ulcer dressings to promote desloughing, granulation, healing, and reducing odor in chronic skin ulcers [2]. The green fruit is used for contraceptive purposes by traditional healers in Pakistan, India, and Sri Lanka and for various human and veterinary diseases in Nigeria such as malaria, hypertension, diabetes mellitus, jaundice, intestinal helminthiasis [3]. The leaves are used for colic, fever, beriberi, abortion, asthma in India [4], and cancer in Australia [5, 6]. The milky juice (latex) is employed as styptic and as debridement when applied as external applications to burns and scalds [3]. People in Lao, Cambodia, and Vietnam use the latex to treat eczema and psoriasis [7]. The seeds have been used as vermifuge, thirst quencher, or pain alleviator [4]. The main traditional uses of different parts of papaya in various localities around the world are summarized in Table 1.

Many of these traditional uses have been validated by scientific studies. Experiments have shown that *C. papaya* possesses anthelmintic, antiprotozoan, antibacterial, antifungal, antiviral, antiinflammatory, antihypertensive, hypoglycemic and hypolipidemic, wound healing, antitumor, free-radical scavenging, antisickling, neuroprotective, diuretic, abortifacient, and antifertility activities [3, 4, 8–10].

Among those conditions, it is interesting to note that there have been anecdotal reports of patients with different types of cancer achieving good results such as following consumption of parts of papaya plant [5, 6]. The utility of herbal medicines for cancer treatment and prevention is receiving increasing attention due to the cost and side effects of current radiation or chemotherapeutic agents used for cancer patients, and the continuing increase in new cancer cases as well as cancer deaths. Projections indicate that the deaths over the world from cancer will rise to more than 13.1 million in 2030 [11]. The purpose of this review is to conduct a literature search to unveil the scientific evidence that *C. papaya* may be of use in the treatment and prevention of cancer.

2 Method

Different databases including PubMed, SciFinder, Web of Knowledge, Scopus, and Embase were searched for studies

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Abbreviations: **BG**, benzyl glucosinolates; **BITC**, benzyl isothiocyanate; **IC_{50}**, the half maximal inhibitory concentration; **MPLC**, medium pressure liquid chromatography; **MTT**, (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide

Table 1. Traditional uses of different parts of papaya in various localities [2–7]

Plant part	Method of use	Medicinal use and locality
Ripe fruit	Fruit juice, topical ulcer dressings, cosmetic (ointment, soap)	Warts, corns, sinuses, and chronic forms of skin induration (scaly eczema, cutaneous tubercles) in Caribe, Philippines; chronic skin ulcers in Jamaica
		Stomachic, digestive, diuretic, expectorant, sedative and tonic, bleeding piles, and dyspepsia in India
Green fruit	Juice	Contraceptive and abortifacient in Pakistan, India, and Sri Lanka
		Malaria, hypertension, diabetes mellitus, hypercholesterolemia, jaundice, intestinal helminthiasis in Nigeria
Latex	Topical use	Dermatitis and psoriasis in Africa, Asia, Europe
		Abortion in India, Malaysia
Seeds	Chewing, juice, powdered, paste, pessaries	Abortifacient, anthelmintic, thirst quencher, pain alleviator, bleeding piles, and enlarged liver and spleen in West Indies and India
Leaves	Fine paste, smoke, juice, infusion, decoction	Heart tonic, febrifuge, vermifuge, colic, fever, beriberi, abortion, asthma in India
		Rheumatic complaints in Philippines
		Stomach troubles, cancer in Australia
Flowers	Infusion, decoction	Jaundice, cough, hoarseness, bronchitis, laryngitis, and tracheitis in Asia
Roots/barks	Decoction, poultice, infusion	Digestive, tonic, abortifacient in Australia, sore teeth in India, syphilis in Africa

investigating anticancer activities of *C. papaya*. The search terms used were "papaya" and "anticancer" or "antitumor". The reference lists of related articles were also reviewed for additional relevant studies.

It is important to note that *C. papaya* is also known as "pawpaw". Searching in some databases with the keyword "papaya" also gave the results for "pawpaw"; however, there are many reports of anticancer effect for a totally different species–pawpaw *Asimina triloba* in the family of *Annonaceae*. Therefore, the bioactive compounds and the anticancer properties of *C. papaya* from the family *Caricaceae* (Fig. 1A) need to be well distinguished from that of pawpaw *A. triloba* (Fig. 1B). Several articles have been found to include annonaceous acetogenins–effective chemotherapeutic agents in *A. triloba* as bioactive compounds in *C. papaya* [12–14].

3 Results and discussion

In our search, no human clinical trials were identified 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 [15]. Case 1 was a 47-year old female with stomach cancer that had 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-day break between two periods. The pancreatic metastases disappeared, the tumor marker, carcinoembryonic 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 reported 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.

More surprisingly, the number of in vitro cancer studies for *C. papaya* was also limited to only seven cell culture-based studies. This review briefly details these studies and summarizes the scientific evidence derived from them. In addition, some important phytochemicals found in *C. papaya* with previously reported cytotoxicity and anticancer activities are also included with their proposed mechanism of actions.

3.1 In vitro studies

The cytotoxic effect of *C. papaya* extract has been tested in various cancer cell lines in in vitro studies summarized in Table 2 [5, 15–20].

In 2002, Rahmat et al. [16] had screened the antiproliferative activity 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). They reported that papaya juice and pure lycopene caused cell death in the liver cancer cell line Hep G2 with the half maximal inhibitory concentration (IC_{50}) of 20 mg/mL and 22.8 μg/mL, respectively. However, neither papaya juice nor pure lycopene showed any effect 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. The lack of action of the extracted lycopene was explained by multiple potential factors such as the

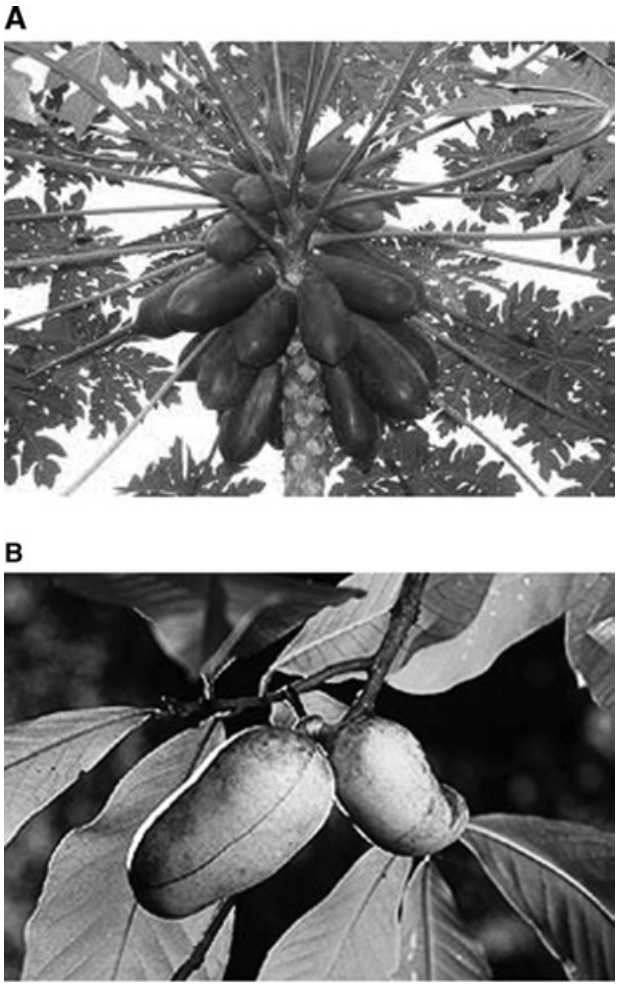

Figure 1. Papaya–pawpaw *Carica papaya, Caricaceae* (A) and Pawpaw *Asimina triloba, Annonaceae* (B).

unsuccessful extraction process, the sensitivity of lycopene to light and oxidation or microbial contamination during treatment.

Although papaya is a significant source of glucosinolates and benzyl isothiocyanate (BITC) [17,21–25], which have been extensively studied for their anticancer activities, there was only one in vitro study conducted by Nakamura et al. in 2007 [17] for apoptosis induction and inhibition of superoxide generation of *n*-hexane extract from papaya seed and pulp in comparison with authentic BITC. Biological effects similar to BITC, in inhibiting the superoxide generation and the viability of acute promyelotic leukemia HL-60 cells, were exhibited by the papaya seed extract (IC_{50} was 10 μg/mL for generation of superoxide and 20 μg/mL for viability) but not by papaya pulp extract even at a concentration of 100 μg/mL. The experimental results suggested that these effects of papaya seed extract may be due to electrophilic compounds such as benzyl isothiocyanate.

The effects of papaya flesh extracts on the viability of breast cancer cell line MCF-7 were examined concurrently with extracts from other fruits in two studies by Garcia-Solis et al. [18] and Jayakumar et al. [19]. In these studies, the authors also evaluated antioxidants such as β-carotene, polyphenols, and flavonoids in the fruits to focus on the contribution of these antioxidants in the inhibition of proliferation. Among 14 plant foods commonly consumed in Mexico (avocado, black sapote, guava, mango, prickly pear cactus (nopal), pineapple, grapes, tomato, pear, grape, tomato, and papaya), Garcia-Solis found that only papaya had a significant inhibitory effect on breast cancer cell growth. The extracts from papaya flesh at all five tested concentrations (0.01, 0.5, 1, 2, 4%) resulted in inhibition of proliferation of MCF-7 cells after a 72-h treatment, in which the extract at concentration of 2 and 4% caused 30 and 53% inhibition of cell proliferation, respectively. Interestingly, they found that the antiproliferative effect in cancer cells did not correlate with total phenolic content or with antioxidant activity of the fruit extracts [18]. In contrast, Jayakumar concluded that among 13 fruits analyzed, chiku, pomegranate, dragon fruit, lichi, durian, grape and apple, with higher sources of polyphenols and flavonoids showed more protective effects against nitric oxide-induced proliferation of MCF-7 cells. In this study, an ethanolic extract from papaya pericarp inhibited cancer cell growth and scavenged nitric oxide (about 35% of nitric oxide was scavenged by the extract at concentration of 640 μg/mL) [19].

In a study of Rumiyati et al., cytotoxicity was observed when another breast cancer cell line, T47D, was treated with a protein fraction containing ribosome-inactivating proteins isolated from *C. papaya* leaves with an IC_{50} of 2.8 mg/mL [20]. The authors used immunocytochemistry to show the induction of apoptosis via the mitochondrial pathway: in breast cancer cells treated with the protein fraction, the tumor suppressor gene p53 expression was increased by about 59.4% and antiapoptotic factor Bcl-2 protein expression was decreased by approximately 63% in comparison to control cells.

In 2008, Morimoto et al. (15) patented the extremely high effectiveness of a brew/extract of different parts of papaya in water for the prevention, treatment, or improvement of many types of cancer: stomach, lung, pancreatic, colon, liver, ovarian, neuroblastoma, and other solid cancers or lymphoma, leukemia, and other blood cancers. Although only data that tested papaya leaf extract (1.25–27 mg/mL) in an MTT assay and ^{3}H-thymidine incorporation were shown, the anticancer effects were concluded for many other parts (roots, stems, and fruit) of papaya plant. The authors carried out gel filtration chromatography to fractionate papaya leaf extract according to molecular weight and measured the antitumor effect of the different fractions. They found two fractions that were capable of suppressing the proliferation of the tested cancer cell lines; one fraction containing components with molecular weights of 1700, 1000, 700, and 300; and another fraction containing compounds with molecular weights of 1700, 100, 600, 400, and 200. The compounds with molecular weights of

Table 2. In vitro studies of extracts of different parts of *Carica papaya*

Cancer cell lines	Treatment	Results	Reference
Breast cancer cell line (MDA-MB-231) Liver cancer cell line (Hep G2) Chang liver cell line (normal cell)	Papaya fruit juice(0.28–28 mg/mL), Lycopene extracted from papaya juice,Pure lycopene (3–30 μg/mL)	Pure lycopene and papaya juice inhibited viability of liver cancer cell line Hep G2 (IC_{50} = 22.8 μg/mL and 20 mg/mL, respectively) but had no effect on breast cancer cells or normal cells. Lycopene extracted from papaya juice did not show any effect on either cell line.	[16]
Acute promyelotic leukemia HL-60 cells	*n*-hexane extract of papaya seed or pulp (0.1–100 μg/mL),Pure benzyl isothiocyanate (10 μM)	Extract of seed: Dose dependently inhibited the superoxide generation (IC_{50} = 10 μg/mL) and the viability of cells (IC_{50} = 20 μg/mL), comparable to that of pure benzyl isothiocyanate. Extract of pulp had no effects at 100 μg/mL.	[17]
Breast cancer cell line (MCF-7)	Aqueous extract of papaya flesh (0.01–4% v/v)	Significant inhibitory effect on proliferation of MCF-7 cells ($p < 0.05$)	[18]
Breast cancer cell line (MCF-7) treated with sodium nitroprusside, a nitric oxide donor	Ethanolic extract of papaya pericarp (50–640 μg/mL)	Inhibited cell growth in MCF-7 cells (decrease in cell viability). Scavenged nitric oxide in dose-dependent manner (about 35% of nitric oxide was scavenged by extract at 640 μg/mL)	[19]
Breast cancer cell line (T47D)	Protein fraction containing RIPs isolated from leaves	The protein fraction possessed cytotoxicity: IC_{50} = 2.8 mg/mL). Induction of apoptosis by regulation of p53 and BCl-2 protein expression ((increased by 59.4% and decreased by 63%, respectively).	[20]
Stomach cancer cell line (AGS) Pancreatic cancer cell line (Capan-1) Colon cancer cell line (DLD-1) Ovarian cancer cell line (Dov-13) Lymphoma cell line (Karpas) Breast cancer cell line (MCF-7) Neuroblastoma cell line (T98G) Uterine cancer cell line (Hela) T-cell leukemia cell line (CD26 negative or negative Jurkat)	Aqueous extract of papaya leaves(1.25–27 mg/mL)	Papaya leaf extract showed a concentration-dependent anticancer effect on each of the cancer cell lines and suppressed DNA synthesis by suppressing the incorporation of ^{3}H-thymidine.	[15]
T-cell lines (H9, Jurkat, Molt-4, CCRF-CEM, and HPB-ALL) Burkitt's lymphoma cell lines (Ramos and Raji) Chronic myelogenous leukemia cell line (K562) Cervical carcinoma cell line (Hela) Hepatocellular carcinoma cell lines (HepG2 and Huh-7) Lung adenocarcinoma cell line (PC14) Pancreatic epithelioid carcinoma cell line (Panc-1) Mesothelioma cell lines (H2452, H226, and MESO-4) Plasma cell leukemia cell line (ARH77) Anaplastic large cell lymphoma cell line (Karpas-299) Breast adenocarcinoma cell line (MCF-7) Mesothelioma cell line (JMN) Pancreatic adenocarcinoma cell line (Capan1)	Aqueous extract of papaya leaves (0.625–20 mg/mL)	Inhibited the proliferative responses of both haematopoietic cell lines and solid tumor cell lines.In peripheral blood mononuclear cells, papaya extract reduced the production of IL-2 and IL-4 whereas increased the production of Th1 types cytokines such as IL-12p40, IL-12p70, INF-γ, and TNF-α.The expression of 23 immunomodulatory genes was enhanced by the addition of papaya extract.	[5]

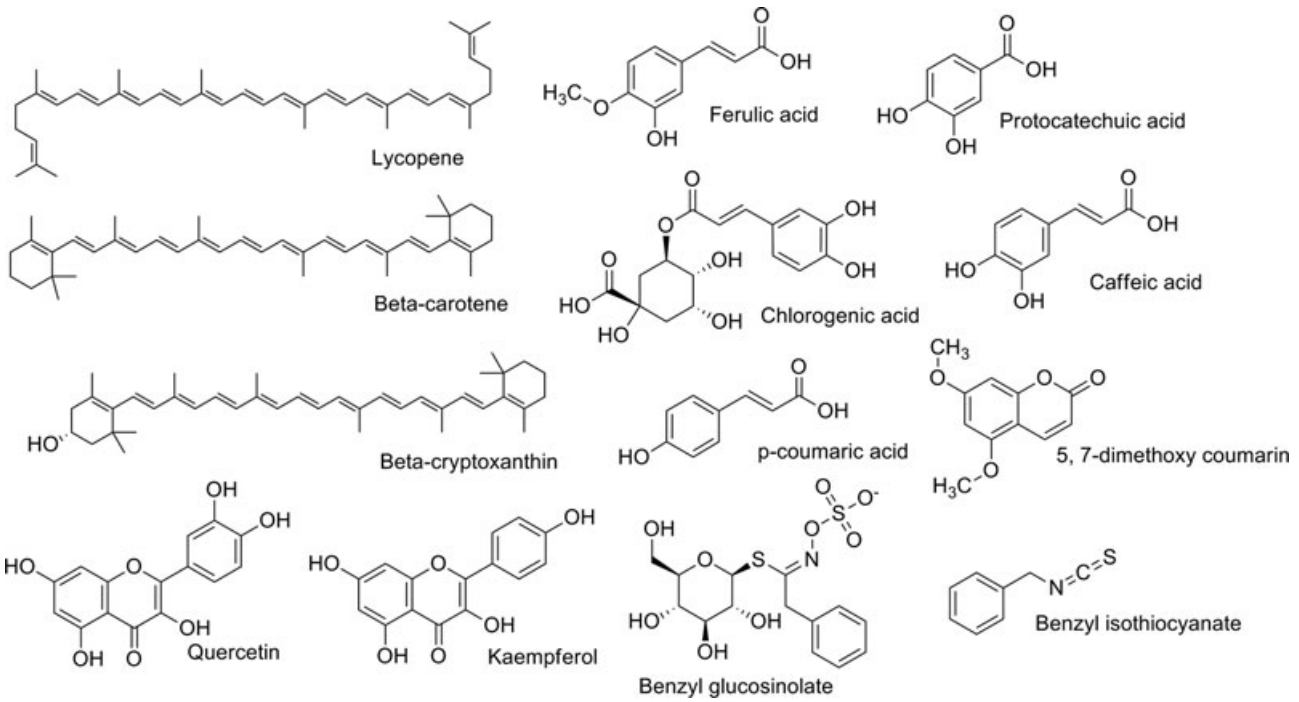

Figure 2. Important phytochemicals found in *Carica papaya*.

1700, 1000, and 700 to 300 absorb UV with absorption peaks detected at 260 nm.

Soon after, in 2010, Otsuki et al. [5] studied the effect of similar aqueous papaya leaf extract (0.625–20 mg/mL) on the growth of various tumor cell lines, including solid tumor cell lines and haematopoietic cell lines. They found the proliferation of those cell lines was inhibited with no statistical difference between solid and haematopoietic tumor cell lines and proposed the induction of apoptosis as one of the mechanisms involved in the growth inhibitory activity. In addition to this antitumor effect, the authors also reported the ability of papaya extract to increase the production of Th1-type cytokines, such as IL-12p40, IL-12p70, INF-γ, and TNF-α as well as the expression of 23 immunomodulatory genes in peripheral blood mononuclear cells. This study also attempted to identify the functional fraction in the papaya leaf extract by performing molecular weight cut off selection with a cellulose membrane tube. The active components with growth inhibitory effect on tumor cells and immunomodulatory effects were identified to be located in the fraction with molecular weight lower than 1000 [5].

3.2 Phytochemicals in *C. papaya* with reported anticancer activities

In a review about major Australian tropical fruit biodiversity, Pierson et al. [26] noted that although papaya is a major tropical fruit, only a few pharmacological studies have been conducted for *C. papaya* in comparison to other fruits. As mentioned above, no in vivo and limited in vitro studies have been done to evaluate the effects of papaya extracts on cancer. In addition to these limited data, by indirect means, several studies claimed health benefits including protection against cancer of *C. papaya* due to the antioxidant properties of papaya extract [27–31]. However, there is continuous debate about whether a high antioxidant activity is a good indicator of high anticancer activity, and no conclusive proof has been drawn thus far [32, 33]. Therefore, further investigation is required to assess the underlying mechanism of action rather than attributing the putative anticancer effects to antioxidant properties of bioactive compounds in papaya.

Carica papaya contains a broad spectrum of phytochemicals including enzymes (in the latex), carotenoids (in fruits and seeds), alkaloids (in leaves), phenolics (in fruits, leaves, shoots), glucosinolates (in seeds and fruits) [4, 8]. Some important phytochemicals found in *C. papaya* are presented in Fig. 2. In the literature, among more than 5000 compounds from plants that have been identified to be associated with anticancer properties [34], three groups of bioactive compounds—phenolics, carotenoids, and glucosinolates—have attracted considerable interest in anticancer studies. Pure compounds of these three groups have been extensively researched in in vivo and in vitro studies on many types of cell lines for their potential effects in cancer treatment and prevention. These bioactives act via multiple mechanisms such as cancer cell signaling, proliferation, apoptosis, migration, invasion, as well as angiogenesis and carcinogen elimination [34, 57–61, 78, 79, 108, 109] to exhibit in vitro and in vivo anticancer activities. Their reported anticancer activities

Table 3. Glucosinolates, phenolics and carotenoids in *Carica papaya* and their potential mechanisms for anticancer activities

Compound group	Method of determination	Compounds extracted	Reported anticancer activities and mechanism of action of pure compounds
Glucosinolates	HPLC-UV at 230 nm for BG and 254 nm for BITC	Benzyl glucosinolate (BG): 12.7 μmol/g seed, <0.03 μmol/g pulp Benzyl isothiocyanate (BITC): 4.6 μmol/g seed, <0.003 μmol/g pulp [17]	In vivo animal studies in rat, mouse, or hamster for inhibitory effect on: Intestinal carcinogenesis [35] Hepatocarcinogenesis [36] Lung tumorigenesis and metastasis [37–39]
	HPLC-UV at 228 nm for BGGC with mass selective detector for BITC	BG: Approximately 4 μmol/g seed, approximately 0.04 μmol/g pulp, approximately 2 μmol/g peel (decreases during development) BITC (decreases in peel and increases in pulp during development) [21]	Pancreatic carcinogenesis [40] Urinary bladder carcinogenesis [41] Mammary carcinogenesis [42] In vitro studies on: MDA-MB-231 breast cancer cells [43] MCF-7 breast cancer cells and HCT-116 (colon) cancer cells [44] Prostate cancer cells [45, 46]
	UV at 520 nm HPLC-UV at 235 nm	Total glucosinolates: 18.7 ± 0.8 μmol/g seed [22]	Human leukemia HL-60 cells [47] A375.S2 human melanoma cancer cells [48]
	HPLC-UV at 214 nm	BG: 6–8 μmol/g seed 0.4–0.6 μmol/g pulp (in young stage) Not detected in mature pulp [62]	Human pancreatic cancer [49–52] Human osteogenic sarcoma U-2 OS cells [53] AGS human gastric cancer cells [54] Human colon cancer HT29 cells [55]
	GC	BITC: 141.7–342.7 ppm in seed, 23.3–45.1 ppm in pericarp, 21.2–43.1 ppm in pulp [24]	SK-Hep1 human hepatocellular carcinoma cells [56] Proposed mechanism [57–61]: - Inhibition of carcinogen - activating P450 enzymes
	GC	BITC: 2910 ppm in seed (ripe papaya) 4 ppm in pulp [25]	- Induction carcinogen detoxifying enzymes - Modulation of oxidative stress - Depression of activation of carcinogens - Acceleration of carcinogen disposal - Induction of apoptosis - Arrest of cell cycle progression - Inhibition of angiogenesis - Inhibition of histone deacetylation - Regulation of translation initiation - Inhibition of cell invasion and metastasis - Inhibition of nuclear factor kappa B (NF-κB) pathways
Phenolics	HPLC-DAD at 250–380 nm HPLC-ESI-MS	Peel: ferrulic (1.33–1.62 mg/g)- caffeic (0.46–0.68 mg/g) rutin (0.1–0.16 mg/g) quercetin, myricetin, isorhamnetin: detected Flesh: only traces of caffeic, gallic, protocatechuic [63]	In vivo animal studies on rat or mouse for inhibitory effect on: Hepatic cancer [64] Prostate carcinoma [65] Colorectal carcinoma [66] Colon carcinogenesis [67, 68] Mammary cancer [69, 70]
	HPLC- DAD at 280 and 320 nm	Peel at four different ripeness stages (RS1-RS4) (phenolics decrease during ripening): Ferrulic acid 2.78 mg/g in RS1 – 1.87 mg/g in RS4	Lung cancer [71] In vitro studies on: Human lung cancer cell line [72] Human prostate adenocarcinoma cell line [73, 74]

Table 3. Continued

Compound group	Method of determination	Compounds extracted	Reported anticancer activities and mechanism of action of pure compounds
		Caffeic: 1.76 mg/g in RS1–1.13 mg/g in RS4; *p*-coumaric acid: 2.23 mg/g in RS1–1.36 mg/g in RS4 [80]	Human monocytic cell line U937 [75] Human glioblastoma cell line T98G [76] Human pancreatic carcinoma cell [77] Proposed mechanism [34, 78, 79]:
	GCMS	Leaf: 5,7-dimethoxy coumarin (0.14mg/g) Protocatechuic acid: 0.11 mg/g *p*-coumaric acid: 0.33 mg/g Caffeic acid: 0.25 mg/g Kaempferol: 0.03 mg/g Quercetin: 0.04 mg/g [81]	-Inhibition of cell proliferation -Induction of tumor suppressor gene expression -Enhancement of immune functions and surveillance -Inhibition of phase I and phase II enzymes -Inhibition of cell adhesion and invasion -Induction of cell-cycle arrest and induction of apoptosis -Inhibition of signal transduction pathways -Inhibition of formation of possible carcinogens
	HPLC-UV at 450 nm	Ripe fruit (different cultivars): Kaempferol: 350.32–605.20 μg/100 g Quercetin: 82.74–257.09 μg/100 g Total flavonoid: 961.00–1515.18 μg/100 g [82]	-Suppression of angiogenesis
Carotenoids	HPLC-DAD at 430, 450, 471 nm HPLC-APCI-MS	Mature green flesh: Lycopene: 1.5–12 μg/g β-cryptoxanthin: 3.1–8.0 μg/g β-carotene: 2.3–3.1 μg/g [63]	In vivo human studies for prevention effects in lung, prostate, pancreatic cancer [83–91] In vivo animal studies in rat, mouse, or hamster for inhibitory effect on:
	HPLC-DAD at 430, 450, 471 nm HPLC-APCI-MS	Fruit at four different ripeness stages (RS1-RS4) Total carotenoid: 0.92 mg/100 g in RS1–3.27 mg/100 g in RS4	Skin cancer [92] Respiratory tract cancer [93] Mammary cancer [94]
	UV-VIS at 450 and 470 nm for total carotenoids	Lycopene increases ten times during ripening: 0.35 mg/100 g RS1–3.5 mg/100 g RS4 β-cryptoxanthin: 0.29 mg/100 g RS1–1.06 mg/100 g RS4 β-carotene: 0.24 mg/100 g RS1–0.5 mg/100 g RS4 [80]	Colon cancer [95, 96] Prostate cancer [97, 98] Gastric cancer [99] Breast cancer [100] Liver cancer [101] In vitro studies on:
	HPLC-DAD at 450 nm	Fruit: β-carotene: 10.6 mcg/g α-carotene: 5.6 mcg/g β-cryptoxanthin: : 24.3 mcg/g α-cryptoxanthin: 16.5 mcg/g Lutein: 7.1 mcg/g 9-cis β-carotene: 7.0 mcg/g Neoxanthin, violaxanthin, zeaxanthin: detected [110]	Human colon carcinoma (HuCC) [102] B chronic lymphocytic leukemia (EHEB) [102], Human erythroleukemia (K562) [102] Prototype of Burkitt lymphoma cell (Raji) [102] HepG2 human hepatocellular carcinoma cell [103] Prostate cancer cells [104] Colon cancer cells [104]

Table 3. Continued

Compound group	Method of determination	Compounds extracted	Reported anticancer activities and mechanism of action of pure compounds
	UV-VIS for total carotenoid at 450 nm	Fruit:	Lung cancer cells [104]
		Total carotenoid: 3.4mg/100g	MCF-7 breast cancer cell [105, 106]
	HPLC at 450, 350 and 290 nm,	β-carotene: 0.38 mg/100g	Human lung adenocarcinoma cell line A549 [107]
		Lycopene: 2.07 mg/100g	Proposed mechanism [108, 109]:
		[111]	- Immunomodulation
	MPLC	Fruit:	- Modulation of phase I and phase II enzyme
		Yellow fleshed papaya:	- Induction of cell differentiation
		β-carotene: 1.4 ± 0.4 μg/g	- Modulation of growth factor signaling
		β-cryptoxanthin: 15.4 ± 3.3 μg/g	- Antiangiogenesis
		Lycopene: not detected	- Antiproliferation- Induction of apoptosis
		Red-fleshed papaya:	- Enhancement of gap junction communication
		β-carotene: 7.0 ± 0.7 μg/g	- Inhibition of cell invasion and metastasis
		β-cryptoxanthin: 16.9 ± 2.9 μg/g	
		Lycopene: 11.5 ± 1.8 μg/g	
		[112]	

and proposed mechanisms of action are highlighted in column 4 of Table 3. Concurrently, Table 3 summarizes the results of the studies in which glucosinolates, phenolics, and carotenoids have been determined in *C. papaya* plant parts by different analytical methods. The availability of carotenoids, phenolics, and glucosinolates in papaya is listed in column 3 of the table. Although the occurrence of these bioactives is not restricted to papaya; for example, glucosinolates are found in several vegetables including *Brassica* species, phenolics, and carotenoids are abundant in many tropical fruits such as mango, strawberry, tomato, passion fruit; the availability and anticancer activities of the bioactives recapitulated in Table 3 indicate that there are opportunities for new research to evaluate the anticancer potential of these phytochemicals in *C. papaya*.

4 Conclusion

The available evidence from the literature, although limited, indicates that *C. papaya,* with abundant bioactive phytochemicals, has the potential to be of use in combating cancer. However, there is a great need for more scientific investigations to improve our understanding of how papaya may exert its anticancer effects. Further work is needed to explore which bioactive compounds have anticancer effects and their mechanism of actions. Cell culture and animal studies as well as clinical trials are needed to determine doses as well as the adverse effects for the consumption of different parts of papaya for cancer treatment and prevention.

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