



ISSN (E): 2277- 7695

ISSN (P): 2349-8242

NAAS Rating: 5.23

TPI 2021; 10(9): 45-49

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www.thepharmajournal.com

Received: 10-07-2021

Accepted: 23-08-2021

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An overview of papaya: Phytochemical constituents and its therapeutic applications

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Abstract

Papaya (*Carica papaya* Linn.) comes under a family *Caricaceae* and it is evergreen plant of tropical and subtropical regions. The various parts of the papaya plant have different uses, and it has been used for therapeutic purposes since ancient times. The review's goal is to describe some phytochemical constituents of papaya as well as their applications. Fruit, leaf, seed, bark, latex, and other components of the papaya plant play an important role in disease management. The active components of papaya extracts, such as alkaloids, glycosides, tannins, saponins, and flavonoids, are responsible for the therapeutic activity. In addition, in dengue fever patients, papaya leaf juice increases platelet counts. According to the findings different parts of papaya extracts have anti-inflammatory, anti-microbial, anti-malarial, anti-plasmodial, anti-dengue, anti-oxidant, anti-cancer, diuretic, and anti-diabetic properties.

Keywords: Overview, Phytochemical, therapeutic, applications, *Carica papaya* Linn

1. Introduction

Papaya (*Carica papaya* Linn.) comes under family *Caricaceae* and it is evergreen plant of tropical and subtropical regions. It is believed to be native to tropical America and subsequently got introduced in Australia, Hawaii, Philippines, Sri Lanka, South Africa and India (Marotta *et al.*, 2006) [18]. The fruit is cultivated all over the world, but exclusively in tropical and subtropical areas (FAO, 2019) [10]. It has been classified as a herbaceous laticiferous plant because of its hollow non-woody stem also known as *papaya melon tree*, *paw paw*, *papau*, *kapaya*, *lapaya*, *payas*, *papye*, *tapaya*, *papita* (Vyas *et al.*, 2014) [36], also pronounced differently in various localities. The Arabic name is babaya, in English, French, German, Hindi languages it is called as paw paw/ papaya, papailler, melonenbraum, and papeeta, respectively (Salas *et al.*, 2008) [29].

Papaya is considered as one of the medicinal plant which represents an important source of therapeutic remedies, on the basis of traditional or indigenous healing systems and widely used by the majority of populations in many countries (Sharifi-Rad *et al.*, 2018) [31]. Plants are the most naturally powerful and affordable medication sources (Van-Der-Watt and Pretorius 2001) [35]. Many *Caricaceae* species have been used to treat a variety of diseases (Alabi *et al.*, 2012). Every part of the plant can be economically used for nutritional and medicinal purpose (Nwofia *et al.*, 2012) [22]. Leaf extract is mainly used for the treatment of dengue fever, malaria (Deshpande *et al.*, 2021) [8]. It is cultivated for its young, matured leaves, shoots and fruits which can be processed into value added products (Neetu *et al.*, 2018) [21]. The fruit and other plant parts contain milky latex in which the two important proteolytic enzymes, papain and chymopapain that have been used as clarifying agent in beer and meat tenderizing agent (Wilson, 1994; Ayoola and Adeyeye, 2010) [38, 4]. Unripened fruits are commonly better source of papain than ripe fruits (Krishnaiah *et al.*, 2002; Scheldeman *et al.*, 2011) [16, 30]. Fruit is mainly used as desert, processed into jam, candy, puree, juice, preserves, pickles, and green fruits are also cooked as vegetables (Kumar *et al.*, 2019a) [17].

2. Materials and Method

Various electronic databases, such as Scopus, Google Scholar, Web of Science, and PubMed, were used to gather information for this review article about the phytochemical constituents and therapeutic applications of *Carica papaya*.

3. Chemical constituents present in different parts of papaya

Parts of papaya plant have vast application in food industry, pharmaceutical industry, cosmetics industry and also in non-food applications. It is one of the valuable plant of medicinal use. The different parts including leaves, fruits, root, bark, seeds and stem as shown in Table 1, contains many chemical constituents in different parts of plant (Krishna *et al.*, 2008).

Papaya fruit is mainly consumed as salad, or in preparation of value added products like jam, pickles, tuty fruity, lether etc., it is known for common man's fruit with rich in nutrients and available at reasonable price (Pinnamaneni, 2017) [28]. Fruit has low carotene, due to which it reduces the damage caused by free radicals compared to other fruits. Fruits are rich in different enzymes excelled aid in digestion especially in celiac disease patients, helps in tenderizing meat (Philip and Chen, 1988). Consumption of fruits increases the absorption of iron from meal so called as antihaemolytic activity.

Papaya seeds are black in colour looks similar to pepper majorly adulterant in pepper. Seeds are edible, have sharp spicy flavour and unique aroma (Franke *et al.*, 2007) [11]. Seeds are good source of lipids (21-30 per cent), protein (16-32 per cent), carbohydrate (8-58 per cent) used as alternative energy sources which may complement the undernourished populations (Dotto *et al.*, 2021) [9]. Oil of papaya seeds are rich in essential fatty acids such as oleic acid, palmitic acid, arachidic acid, linoleic acid and stearic acid and widely used as an anti-inflammatory agent (Basu *et al.*, 2006; Dotto *et al.*,

2021) [6, 9]. Seeds are also good source of phytochemicals such as phenolics, tocopherols, polysterols, and carotenoids. These have the properties from anti-proliferatiion of carcinogenic cells to protective against cellular oxidative injury, also reduces the threat of non-communicable diseases (Olcum *et al.*, 2020) [24]. Phenolic compounds act as scavenge reactive molecules thus protecting the cellular environment against the damaging impacts of oxidative and inflammatory activities of carcinogens (Wang *et al.*, 2020) [37].

Papaya leaf are bitter in taste, contains more than 50 phytochemical constituents some of them are mentioned in table 1. Leaf extract reduces the alcohol prompted acute gastric ulcers and oxidative trauma in rats (Indran *et al.*, 2008) [12]. Extract of leaves used to treat dengue fever, works to combat RBC sickling. The presence of phytochemicals enhances the antioxidant activity which improves the body immune system, improves gastrointestinal disorders and controls the issues like bloating, burning of heart, constipation and bowel movement.

Stem trunk is hollow, delicate; it's a single stemmed tree. Stem bark acts as antifungal, antihaemolytic and helps in sore teeth. The roots which are blended used as antibacterial action. Boiled roots decoction used for abortifacient, diuretic, checking irregular bleeding from the uterus, piles, antifungal activity also contains Nicotine, Carposide, Myrosine they have antibacterial effect (Krishna *et al.*, 2008; Aravind *et al.*, 2013).

Table 1: Nutritional constituents of different parts of papaya (Krishna *et al.*, 2008; Pinnamaneni, 2017) [28]

Part	Constituent	Medicinal use
Fruit	Protein, fat, fiber, carbohydrates, mineral: calcium, phosphorous, iron, vitamin C, thiamine, riboflavin, niacin and carotene, amino acids, citric and malic acids (green fruit)	Reduce human urine acidity, rheumatism, weight loss, thrombosis
Juice	N-butyric acids, n-hexanoic and n-octanoic acids, lipids, Myristic, planets, stars, linolec, linolenic and cis-vaccenic and oleic acid	Stomachic, digestive, carminative diuretic, dysentery and chronic diarrhoea, expectorant, sedative and tonic, relieves obesity, bleeding piles, wound of urinary tract, ringworm and skin disease psoriasis
Seed	Fatty acids, crude protein, crude fiber, papaya oil, carpaine, benzylisothiocynate, benzylglucosinolate, glucotropacolin, bemzylthiourea, hentriacontane, β -sitosrol, caressing and enzyme myrosin	Carminative, emmenagogue, vermifuge, abortifacient, counter irritant, as paste in the treatment of ringworm and pasoriasis, anti-fertility agent in malic
Root	Carposide and enzyme myrosin	Abortifacient, diuretic, checking uneven bleeding from the uterus, piles, antifungal activity
Leaves	Alkalodis carpain, pseudocarpain and dehyrocarpaine I and II, choline, methyl derivatives, glucosinolates, carposide vitamin C and E	Cures asthma, increases platelets count, cardiac stroke, anti-malaria, anti-cancer, anti-tumor, dressing wound, antibacterial
Stem, bark	β -sitossterol, glucose, fructose, sucrose and xylitol	Jaundice, anti-haemolytic activity
Latex	Proteolytic enzymes, papain and chemopapain, glutamine, cyclortransferase, Chymopapains A, B and C, Peptidase A and B and lysozymes.	Helps in digestion, arthritis, dyspensia, digestive disorder

Latex is rich in unripe fruits, followed by bark, fruits, leaves, which are rich in proteinaceous enzymes such as papan, chymopapain, papain proteinase known for the industrial, nutritional and therapeutic applications (Azarkan *et al.*, 2003) [5]. Cysteine proteinases may constitute as abundant as 80% of the enzyme portion in papaya latex. These have anxiolytic activity (Kebebew and Shibeshi 2013) [14], antioxidant, antifungal, anthelmintic, warts, sinusitis, eczema, cutaneous tubercles, bleeding piles and enlarged liver and pectoral properties, anathematic, relieves dyspepsia, cures diarrhea, burning pain and topical use, bleeding hemorrhoids, stomachic, whooping cough (Aravind *et al.*, 2013).

4. Pharmacological properties

Many pharmacological properties and bioactive components have been identified by different extraction methods from different parts of papaya were studied for their action and medicinal uses for the treatment of various diseases. The plant *Carica papaya* is known to have various activities like antioxidant, antihypertensive, wound healing, hepatoprotective, anti-inflammatory, antimicrobial, antifungal, antifertility, histaminergic, diuretic, anti-amoebic, anti-tumour, anthelmintic, the effect on smooth muscles, immunomodulatory activity, anti-ulcer activity, anti-sickling activity.

a) Antiinflammatory activity

The presence of secondary metabolites such as alkaloids, tannins, flavonoids, saponins which are effective against chronic inflammatory reaction. The enzymes papain and chymopapain showed antiinflammation and immunomodulatory effect (Nafiu *et al.*, 2019) [20]. Ethanolic extract of leaf has effective inflammatory actions on carrageenan induced paw edema in rats. The effect of inflammation showed wound healing properties and reduces the intractable inflammation. The oxidative stress involvement mechanism in living and pathological methods including ageing, cancer, CVD and Treatment with free-radical scavengers and antioxidants may be able to regulate processes in neurodegenerative diseases, according to new research. It's also shown to help with oxidative inflammatory damage in cirrhosis caused by the hepatitis C virus. (Marotta *et al.*, 2007). Papaya seed extract is sold as a dietary supplement with the claim of rejuvenating the body and increasing energy to improve immunity against infection and body functioning for its immunomodulatory and anti-inflammatory action (Mojica-Henshaw *et al.*, 2004).

b) Antimicrobial activity

The various extracts a solvent from the roots and leaves was evaluated for their antibacterial property using some pathogenic bacteria's by the agar diffusion method. The root extracts from organic solvents exhibit significant activity against tested pathogens in which methanolic extract shows superior activity. The gram positive bacteria's show highest sensitivity than the gram negative to the root extracts where *Pseudomonas aeruginosa* shows higher sensitivity. The leaves extracts exhibited better inhibition activity against tested pathogens compared to organic root extracts. For all extracts, the temperature is directly proportional and alkaline pH is inversely proportional to the antibacterial activity (Yogiraj *et al.*, 2015) [39]. Both dried and fresh leaves extracts has Antimicrobial activities against fungi and bacteria. The result indicated a very important broad-spectrum antibacterial activity against gram positive and gram negative bacteria (Anibijun and Udeze 2009) [3].

c) Antimalarial and anti-plasmodial activity

Malaria is a mosquito-borne infectious illness that is widespread in tropical and subtropical areas. Malaria has become the most common cause of sickness, with an annual death rate of over 1 million children under the age of five. (Okpe *et al.*, 2016) [23]. Kovendan *et al.* (2012) [15] reported the ethanolic extract of leaf has antimalarial property against *P. falciparum* as target species, the results indicated that leaf extracts has potential to be utilized as an ideal environmental friendly for control of mosquitoes and it also showed reasonable anti-parasitic effect.

d) Anti-dengue activity

Traditional extraction method of papaya juice in clinical studies suggested that leaf extracts improves the platelet count in dengue patients and faster recovery. Within 24 hours of therapy, leaf juice induces a substantial increase in platelet counts. (Pinnamaneni, 2017) [28]. After 40-48 hours of receiving the first dosage of papaya leaf juice, a new open-label experiment from Malaysia revealed a considerably increased platelet count (Subenthiran *et al.*, 2013) [34]. Dengue fever is a largely self-limiting illness with a spontaneous rise in platelets

after recovery, according to small size research. Another study demonstrated the corresponding and alternative medicine use among dengue fever was high. A higher level of education was known to be the factor associated with corresponding and alternative medicine use. Isotonic drinks, crab soup, and papaya leaf extract were the most commonly used complementary and alternative medicines for dengue fever (Ching *et al.*, 2015) [7].

e) Antioxidant and anticancer activity

The methanolic extract of unripe fruits of papaya has been reported to shows antioxidant activity. The antioxidant activity of the extract was evaluated in mice, treated with an oral dose of 100 mg/kg. The researchers conclude that there is a substantial increase in the activities of glucose-6-phosphate dehydrogenase, GPx, glutathione reductase, GST, due to the ethyl acetate fraction. A substantial decrease in GPx was observed in the kidney following administration of ethyl acetate fraction. The quercetin and β -sitosterol are responsible for the antioxidant potential of the extract (Oloyede 2005) [25]. In the Asian Journal of Pharmaceutical and Clinical Research, Sianipar *et al.* (2018) [32] demonstrated antioxidant and anticancer properties of the hexane fraction from papaya flower. The antioxidant activity was completed utilizing the α, α -diphenyl $-\beta$ -picrylhydrazyl technique and potential movement of the anticancer was completed utilizing 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide examines to check the cytotoxic movement on WiDr (colon malignancy cell) and Vero cell (typical cell). The IC₅₀ of cancer prevention agent esteem was 100.81 ± 1.180 g/ml cytotoxic effect shows that the hexane component of papaya male blossom exhibited selectivity to WiDr cell.

f) Diuretic activity

The aqueous root extracts of Papaya was evaluated for their diuretic activity at the dose rate of 10 mg/kg which is an equivalent dose of standard diuretic hydrochlorothiazide. The results show a 74 % reduction in urine output when compared to the control group (Sripanidkulchai *et al.*, 2001) [33].

i) Antidiabetic activity

Diabetes mellitus is increase in the blood sugar level whereby causing damage of other organs such as kidney, liver and so on. *C. papaya* has been widely used in some local communities in African to treat *Diabetes mellitus* (Abisola and Wahab 2012) [1]. Different researchers had revealed that some parts of the *C. papaya* tree showed reduction in blood sugars level in both humans and animals. A study reported the hypoglycaemic property of leaf extracts of *C. papaya* against streptozotocin-induced in diabetic rats. In this study, the diabetic rats were treated by oral administration of chloroform extracts at a dose of 0, 31, 62 and 125 mg/kg and non-diabetic rats were given 0 and 62.0 mg/kg for about 20 days. The biochemical studies revealed a significant reduction in blood glucose, transaminase, and triglyceride levels in diabetic rats after oral administration of *C. papaya* leaf extract. These findings also demonstrated *C. papaya*'s antidiabetic potential and beneficial effects in the treatment of any diabetic symptom (Juarez-Rojopa *et al.*, 2014) [13].

5. Conclusion

Several parts of the papaya plant have been used for medicinal purposes since prehistoric days. The phytochemical

constituents of papaya play a significant role in disease management. This review paper provides the information of active components of papaya, such as alkaloids, glycosides, tannins, saponins, and flavonoids, are responsible for its therapeutic activity,

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