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AN OVERVIEW FOR PHYTOCHEMICAL ACTIVITIES OF CARICA PAPAYA FRUIT

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Abstract *Papaya, scientifically known as Carica papaya or Carica Papaya Linn is the only edible member of the Caricaceae family. Papaya is a large herbaceous plant exploited for its biological activities. Papaya's wide range of uses and activities are attributed to its abundance of enzymes, minerals, nutrients, and phyto-constituents. Its applications range from adding it to one's diet regularly to treating minor illnesses and even serious conditions like cancer. All of the papaya plant's parts; bark, flowers, fruit, latex, leaves, peel, roots, seeds, and stem have therapeutic and medical uses. The use of papaya as a food and traditional medicine is as old as mankind. Presently, to overcome antibiotic-resistant microbes, C. papaya is a natural source with far more advantages. C. papaya plant is used in commercial, industrial, medicinal, and therapeutic applications owing mainly to its anti-inflammatory, antioxidant, and anti-microbial properties. This review aims to provide a concise review of the applications of C. papaya.*

Keywords: *papaya; Carica papaya; anti-fungal; anti-microbial; anti-bacterial; antioxidant*

Introduction

Fruits are a necessary part of an individual's daily diet, not only they are good in taste and nutrition but they also confer numerous other health and nutrition advantages. *C. papaya* is one of the most beneficial fruits, regarding its nutritional value as well as its therapeutic and medical uses (Sharma *et al.*, 2020). For ages, papaya has been used as a culinary ingredient as well as for traditional medicine in many cultures across the world. In most countries, Papaya is grown as a food-crop (Nafiu *et al.*, 2019). All the parts of the papaya plant including bark, blooms, flowers, fruit, latex, leaves, peel, roots, seeds, squash, and stem have medicinal and therapeutic benefits (Ikram *et al.*, 2015). Despite being grown as a food-crop, it is used for numerous biological and commercial applications such as; (1) industrial, (2) nutritional, and (3) medicinal and therapeutic (Niklas & Marler, 2007). Industrial applications of *C. papaya* include the production of processed foods which can later be sold for commercial benefits such as jams and pickles, the use of papaya in cosmetic products such as creams and ointments for reducing acne and blemishes, and lastly for the production of alcohol. Moreover, papaya can be used as a dietary additive for animal feed or a supplement for humans. These benefits conferred by *C. papaya* are attributed to the large number of enzymes, nutrients, vitamins, minerals, and phytoconstituents that are present in it (Alara *et al.*, 2020). The papaya plant parts possess different bioactive compounds in each of its parts including alkaloids, carotenoids, flavonoids, and vitamins, all of which confer exceptional therapeutic advantages (Gayosso-García Sancho *et al.*, 2010; Fabi *et al.*, 2012; Abdullah et al., 2023; Din et al., 2023; Hamid et al., 2023). Medicinal and therapeutic uses of papaya include its use as an abortifacient, antibacterial, antifungal, anti-diabetic, anti-inflammatory, antifertility, anthelmintic, antihypertensive, anti-protozoan, antitumor, and antiviral agent. Among the most notable applications of *C. papaya* is its anti-inflammatory and anti-oxidant property which allows it to be used for a range of purposes including the treatment of fatal diseases such as cancer, as well as neurodegenerative diseases, diabetes, and skin aging (Srivastava & Singh, 2015; Anitha *et al.*, 2018; Bashir et al.,2022; Sami et al., 2023). Furthermore, *C. papaya* also exhibits immunomodulatory properties which are especially useful in the treatment of diseases that suppress the human immune system (Anjana *et al.*, 2018).

Anatomy and morphology

The papaya plant is usually a herbaceous, laticiferous, single-stemmed, semi-woody perennial, large plant with a rapid, unpredictable growth rate. It grows up to 10m (20-30 feet) in height and is not very woody in texture, lacking a proper bark (Nafiu *et al.*, 2019). The colors of papaya stems range from light green to tan-brown, which are hollow (Adiaha & Adiaha, 2017).

Despite its semi-woody nature and no proper bark, it is usually considered a tree (Jiménez*et al.,* 2007).

1. **Leaves:** The leaves crowning the papaya plant are extremely large, sometimes measuring up to more than 60 cm (2-2.5 feet), palmately lobed (5-9 lobes) with deep incisions and complete margins. They are subtended by hollow petioles which are about (30-150 cm) 1-3 feet in length, and their stems are light green to tan brown, having a diameter of approximately 20 cm (Posse *et al.,* 2009; Leal-Costa *et al.,* 2010; Aravind *et al.,* 2013). The leaves are hypo-stomatic containing stomata with either no subsidiary cells (anomocytic) or asymmetric guard cells (anisocytic). The cellular composition of the papaya leaves consists of single layers of epidermis and palisade parenchyma and four to six layers of spongy mesophyll tissue (Carneiro & Cruz, 2009).
2. **Flower:** Reproductively, the flowers of papaya plants naturally are monoecious (true hermaphrodite), dioecious (containing male and female organs on separate plants), or gynodioecious (with hermaphrodite and female organs) (Ming *et al.,* 2007; Nafiu *et al.,* 2019). However, occasionally papaya plants may also be "trioecious" meaning that the male, female, and hermaphroditic flowers are present on separate plants (Niklas & Marler, 2007; Yogiraj *et al.,* 2014). The flowers occur in small groups of three, known as cymes or solitarily. Both hermaphroditic and female flowers have waxy petals of ivory-white color attached to short peduncles on leaf axils, along the main stem. The flowers measure 0.10–0.30m in diameter and 0.15–0.45m in length (Aravind *et al.,* 2013). In terms of shape and structure, papaya flowers fall under six different categories including (1) typical female, (2) typical male, (3) hermaphrodite elongated, (4) hermaphrodite immediate and (5) hermaphrodite sterile (Alara *et al.,* 2020). The hermaphroditic flowers consist of both the female reproductive organs (ovaries) and the male reproductive organs (pollen sac), they are self-pollinating and produce the best fruits; thus, they are chosen over male or female plants for cultivation. Female flowers usually have a conical top and a rounded base. They have a conical appearance while closed, and five petals grow out from the circular base when they open. Another type of female flower has five petals with five anthers corresponding to each petal (Anitha *et al.,* 2018). Plants with smaller flowers attached to longer stalks are generally regarded as male papaya plants. They possess a long, thin corolla composed of anthers in two sets of five, where the series are different in length, one short and one long (Adiaha & Adiaha, 2017).
3. **Fruit:** Papaya fruits are large and oval, with salmon-colored (pink-orange) flesh encircling a central seed hole matching that of melons. The only portion of the fruit that can be eaten is the meat (Panzarini *et al.,* 2014). Though they can sometimes show up in little groups, the fruits are usually affixed to the main stem separately. The weight of each papaya fruit ranges from 0.2 to 9 kg (0.5 to 20 pounds), and as it ripens, its colour changes from green to yellow to red-orange (Aravind *et al.,* 2013). The melon-like fruit can be pyriform, obovoid, globose, or ovoid in shape. The fruit's typical dimensions are 0.15 to 0.50 m in length and 0.10 to 0.20 m in thickness (Crane, 2005; Anitha *et al.,* 2018).

Species of papaya

C. papaya from the small angiosperm family, namely Caricaceae consisting of 6 genera and 43 species, all of which can be found listed on the Plant List (http://www.theplantlist.org), among these species the most commonly cultivated and economically important is *C. papaya* and the only species to grow fruits on its tree (Evans & Ballen, 2012; Carvalho & Renner, 2015; Basalingappa*et al.,* 2018). The species are listed in table 1.

Karyotype and sex expression

The genomic studies of C. papaya have revealed that the fruit possesses a total of 18 chromosomes (2n = 18), an experiment conducted by Hague in 2004 led to the conclusion that regardless of the sex of the plant, the general cytological condition of the plant has a total of 18 chromosomes (Haque, 2004; Somsri & Bussabakornkul, 2008' Araújo & Carvalho 2010; Rockinger *et al.,* 2016). The sex determination genomics system has revealed that *C. papaya* exists in three sex forms; male, female, and hermaphrodite. Several studies have demonstrated that the XY chromosome system specifies the sex of C. papaya, just like it does for many other organisms. Inverted repeats, transposable elements, and nucleotide modifications in the small non-recombinant region and autosomal chromosome sections between the X and Y chromosomes are also thought to have influenced the development of the X and Y chromosomes (Liu *et al.,* 2004). The expression of the male (XY) and hermaphrodite (XY_H) types is controlled by a tiny specific region and always occurs in the heterozygous form. On the other hand, all-female plants occur as XX forms (Ming *et al.,* 2007).

Cultivation, origin and global distribution

The exact origin of *C. papaya* is rather obscure and not exactly known, though it is known to be cultivated in tropical and sub-tropical regions. Various places of origin of the papaya fruit are mentioned in texts; the earliest evidence of the existence of *C. papaya* dates back to 1525, when papaya seeds were found in the Dominican Republic and Panama. It was then that the cultivation of papaya spread to central and tropical America in regions like Bahamas, Bermuda, and southern Mexico (Morton, 1987). In the 1950s, *C.*

papaya was introduced into Miami, New York Santa Marta (Colombia), and Puerto Rico. In 1959, an Italian entrepreneur known as Albert Santo brought papaya to Cuba. It is also believed that the Spanish might have carried the papaya seed to Malacca and the Philippines, which then became the cause of their spread to India and the Kingdom of Naples in 1626. Later, *C. papaya* was introduced as a plantation crop across all the tropical and subtropical regions of the world (Nakasone & Paull, 1998).

Presently, papaya is cultivated commercially and for personal use all around the world including countries such as Australia, Ceylon, India, Hawaii, Malaya, Philippines, and tropical Africa. The currently present variety of papaya is thought to be the fusion of two or more different varieties of papaya that originally belonged to central America and Mexico (Nafiu *et al.*, 2019). In Pakistan, varieties of papaya seeds are sowed to establish nursery plants in March and transplanting takes place in April. Regardless, the fruit is available all year long (Zhou *et al.,* 2000; Singh *et al.,* 2014).

Plant growth and habitat

C. papaya seeds germinated in well-drained, sandy, loam soils under appropriate environmental conditions including sufficient water, oxygen, light, and appropriate humidity levels, pH, and temperature (Adiaha & Adiaha, 2017). Appropriate conditions for the ideal growth of *C. papaya* include; low rainfall of around 32 inches (0.80 m) in summer and spring, temperature between 21 and 32 °C (70–90 °F), and a pH of 6.5-7.0 (Crane, 2005). Under tropical conditions and proper manure, the papaya tree grows very rapidly (Anitha *et al.,* 2018). Adequate rainfall required for papaya fruit growth is relatively lesser than that of most other plants, requiring rainfall only four times a month. In well-drained soils, the plant needs to be watered on alternate days, while in loamy soils watering the plant once in 3-4 days is sufficient (Sara *et al.,* 2015). *C. papaya* plants require an environment packed with nutrients and minerals; the macronutrients required include *Potassium > Nitrogen > Calcium > Phosphorus > Sulfur > Magnesium and micronutrients include Chloride > Iron > Manganese > Zinc > Boron > Copper > Molybdenum (*Jiménez *et al.,* 2007). After plantation under appropriate conditions, *C. papaya* plant takes approximately 8-10 months before ripe fruits are produced by the plant. However, in warm regions, the same plant takes from 6-9 months for proper and complete growth, while in temperate regions the growth period ranges from 9-11 months. The papaya plant is also able to survive in colder winters, however, it may not produce fruits (Crane, 2005). The emergence of the papaya plant from the seeds takes about 2–3 weeks (Fisher, 1980). Papaya plants usually grow speedily; they reach the juvenile phase, or flowering stage, 3–8 months after seed germination and are ready for harvest in 9–15 months (Paterson *et al.,* 2008).

Nutritional value and composition

Papaya plants can live for 20 years on average, but because of their large height and disease susceptibility, their commercial lifespan is just two to three years (Alara *et al.,* 2020). Once the tree blossoms, it requires around 5-8 months before the fruits on the plant are ripe and ready for harvesting (Sara *et al.,* 2015). The papaya plant grows flowers and fruits all year long (Alara e*t al.*, 2020).

Table 1. Nutritional Value of 100g of *C. papaya* Fruit

Components	amount
Carbohydrates	9.81
Fat	1.80
Dietary fiber	0.14
Phosphorus	0.61
Sugars	5.90
Minerals	
Calcium	24
Iron	0.10
Magnesium	10
Proteins	5
Potassium	257
Biomolecules	3 mg
Vitamins	
Vitamin A	328
Vitamin B_1 (Thiamine)	0.04 mg
Vitamin B_6	0.05 mg
Vitamin B_3 (Niacin)	0.338
Vitamin B_2 (Riboflavin)	0.10
Vitamin B_9 (Folate)	38
Others	
Energy	163KJ

C. papaya is a fruit that is high in vitamins, minerals, enzymes, and non-vitamin substances. High in calcium, iron, potassium (including folate), niacin, thiamine, vitamins A, C (ascorbic acid), and riboflavin, it has a low-calorie count and a high nutritional value. Alkaloids, sugars, flavonoids, glycosides, saponins, steroids, terpenoids, and tannins are also present in extracts of unripe C. papaya (Aravind *et al.*, 2013; Vij & Prashar, 2014).

Phytochemistry and phytoconstituents

The chemical composition varies depending on the agricultural environment, cultivar, exposure to sunlight, location, level of ripeness, and post-harvest handling (Wall, 2006; Gayosso-Garcıa Sancho *et al.*, 2011; Ikram *et al.,* 2015). The fruit portion of *C. papaya* comprises an endosperm, sarcotesta, seed coat, an outer pericarp, and an inner pericarp (Table 2). Each of these regions contains different types of molecules and has a different chemical composition. The endosperm mainly has oils and some protein content, while the pericarps are rich in proteins. The sarcostesta contains high amounts of ascorbic acid (Adesuyi & Ipinmoroti, 2010; Syed *et al.,* 2011; Saran & Choudhary, 2013).

Table 2. Phytochemicals of *C. papaya*

Stage of Fruit	Phytochemicals
Unripe Fruit	**Enzymes:** papain, glutamine cyclotransferase, lysozymes, peptidase A and B, chymopapain. **Others:**molic acid
Ripe Fruit	**Acids:** amino acids, caroxene, citric acids
	Alkaloids: 4-hydroxyl -phenyl-2-ethyl-B-D glucoside, 2-phenylethl-β-D-glucoside, benzyl-β-d glucoside, carpaine, malonated benzyl-β-D glucosides, pseudocarpaine, isomeric
	Carotenoids:α-carotene, γ-carotene, cryptoxanthin, violaxanthin, zeaxanthin, lutein and lycopene, β-carotene.
	Flavonoids: kaempferol, myricetin, quercetin
	Monoterpenoids: 4-terpineol, linalool, linalool oxidase
	Volatile Compounds: cis and trans 2, 6-dimethyl-3,6 expoxy-7 octen-2-ol. Linalool, benzylisothiocynate

As mentioned earlier, the chemical composition changes with the stages of ripening of the fruit, and the biochemical and physiological properties of the fruit change with the growth and ripening stages. As a result of these changes, the fruit loses its rigidness and softens, which indicates ripening and makes the fruit suitable for commercial and edible uses (Pereira *et al.,* 2009). *C. papaya* fruit contains carbohydrates, fat, fiber, minerals, vitamins, citric acid, malic acid, and a variety of commercially important compounds The unripe fruit is especially rich in a variety of phytochemicals and volatile compounds, such as alkaloids, carbohydrates, flavonoids, glycosides, saponins, steroids, and terpenoids, as well as a variety of health-promoting bioactive compounds and phytochemicals, including β-cryptoxanthin and carotenoids (β-carotene and lycopene), Additionally, papaya also contains several enzymes that confer several health benefits (Corral-Aguayo *et al.,* 2008; Gayosso-García Sancho *et al.,* 2010; Fabi *et al.,* 2012; Aravind *et al.,* 2013; Vij & Prashar, 2014; Fabi & Do Prado, 2019).

Carotenoids

The color of the papaya fruit significantly changes with its ripening and maturation; starts with a light-green color and changes until it reaches an amber, orange to red colorReduced synthesis of chlorophyll and increased production of esterified carotenoids (which embraces β-carotene, β-cryptoxanthin, and lycopene) are the biological causes of this colour shift. Carotenoids rapidly integrate into the membranes and build up more densely in the chromoplasts during ripening, giving the fruit its orange-red colour (Andersson *et al.,* 2009; Yahia & Ornelas-Paz, 2010). The coloration of the fruit is dependent upon the varieties of carotenoids (Ikram *et al.,* 2015; Gayosso-García Sancho *et al.,* 2017). β-carotene, and lycopene are the main carotenoids found in C. papaya fruit; lycopene alone accounts for 65% of the carotenoid content of papayas (Marelli de Souza *et al.,* 2008; Güilcin, 2012).

Known for their extraordinary antioxidant qualities, carotenoids are lipophilic substances composed of eight isoprenoid units. They are essential to human health and nutrition because they efficiently capture singlet oxygen molecules and neutralize radicals like peroxyl (Al-Duais *et al.,* 2009). Carotenoids are unique because of their vast network of double-conjugated bonds, which alternate between single and double carbon-to-carbon bonds. A polyenic chain, a resonance structure, stabilises these connections. Because of this polyenic chain, also known as the chromophore, carotenoids can operate as photoreceptors, absorbing light and offering scavenging and antioxidant qualities against reactive oxygen species (ROS) (Yahia & Ornelas-Paz, 2010). Structurally, carotenoids are divided into two major groups; (1) carotenes, those which are linked hydrocarbons, and (2) xanthophylls, those that contain at least one or more oxygen molecules. These carotenoids possess double bonds which allow them to act as photoprotectors that in turn protect the lipid membrane against peroxidation by quenching reactive oxygen species (ROS) (Tanaka *et al.,* 2008; Rivera-Pastrana *et al.,* 2010). The antioxidant capacities of carotenoids are dependent upon and vary with the structure of the carotenoids. Numerous investigations have shown that distinct carotenoids have a range of abilities, which are listed in the order: Zeaxanthin > lutein > β-cryptoxanthin > α-carotene > β-carotene > lycopene (Gayosso-García Sancho *et al.,* 2013).

Β-carotene

Because of its antioxidant qualities, β-carotene is essential for photoprotection. But occasionally, its purported prooxidant effects can outweigh this protective function (Nimal et al., 2022). Certain carotenoids behave similarly to provitamin A; they are known to lower the chances of coronary heart disease and cancer (Yahia & Ornelas-Paz, 2010).

lycopene

as lycopene's presence in plasma and serum has been inversely linked to the risk of cancer, it has gained a lot of attention recently (Nimal et al., 2022). Additionally, it is also known to quench singlet oxygen and scavenge other free radicals (Mein *et al.*, 2008). Additionally, lycopene is a useful substance in lowering the risk of obesity, osteoporosis, cardiovascular disease, and cognitive decline. Additionally, because bell peppers contain vitamin C and β-carotene, they may help prevent cataracts (Stahl and Sies, 2003).

PhenolicsPhenolic compounds are aromatic, containing at least one or more aromatic rings with a hydroxyl group that enables them to act against ROS and mitigate oxidative stress. They are produced as a result of secondary metabolism in plants (Wojdyło *et al.,* 2009). The phenolic compound content has been studied in several varieties and stages of papayas and it has been found that the most ripened papaya contains the lowest of phenolic compounds (Mahattanatawee *et al.*, 2006; Corral-Aguayo *et al.*, 2008). Compounds of phenolic may or may not act as antioxidants, depending on their structure. It is assumed that the antioxidant capabilities of phenolic compounds depend upon the number of hydroxyl groups present in their structure (Wang *et al.*, 2008). Moreover, phenols are also crucial in determining the color and taste of C. papaya fruit. (Al-Duais, 2009; Gorinstein*etal.*,2009.Fruits and vegetables contain va rying levels of phenolic compounds, which are essen tial in protecting against oxidative stress caused by R OS and free radicals. Phenolic compounds confer health benefits in more than one way; they are capable of preventing oxidative damage caused by ROS and oxygen free radicals which in turn prevent several disorders (Valko *et al.,* 2007). Various studies have also demonstrated that the consumption of foods rich in phenolic acids is inversely proportional to the incidence of various diseases (Gayosso-García Sancho*et al.*, 2017).

Saponified papaya extracts mostly contain hydroxycinnamic acid sugar derivatives as phenolic compounds, but non-saponified extracts only contain trace levels of acylated versions of these compounds. Phenolic acids found in C. papaya include caffeic acids, ferulic acids, and p-coumaric acids (Rivera-Pastrana *et al.*, 2010; Gayosso-García Sancho *et al.*, 2011). Phenolic compounds protect the plant from damage caused by UV-radiations and possess anticarcinogenic, antimutagenic, and antiradical properties (Hounsome *et al.*, 2008; Cantin *et al.*, 2009). Many studies have proved the anticarcinogenic mechanisms carried out by phenolic compounds by stimulating the production and cytoprotective effect of various enzymes (Gayosso-García Sancho *et al.*, 2017).

Caffeic acid

Caffeic acid, a key component of several fruits, vegetables, and coffee usually occur in and esterified form, in combination with quinic acid known as chlorogenic acidStrong antioxidants with notable anti-inflammatory qualities are caffeic acid and its derivatives, including octyl caffeate and caffeic acid phenethyl ester (CAPE) (Da Cunha *et al.*, 2004). Herein, among natural compounds we focused on caffeic acid (CA), the major representative of hydroxycinnamic acids and phenolic acid, produced through the secondary metabolism of several vegetables, including olives, coffee beans, fruits, potatoes, carrots and propolis. It is usually found as various simple derivatives such as glycosides, amides, esters and sugar esters (Reddy *et al.*, 2010; Alam *et al.,* 2022). Several studies have been performed to investigate the total antioxidant capacity (TAC) of caffeic acid, its TAC is dependent upon its structure, the number of hydroxyl groups and its concentration in the fruit (Jaikang & Chaiyasut, 2010; Gayosso-García Sancho *et al.*., 2013)

Ferulic acids

Ferulic acids are found in conjugation with glycoproteins and insoluble carbohydrate biopolymers anchored to the cell membranes. Among the benefits of ferulic acids are their anti-inflammatory and anti-oxidant effects. By inhibiting choline acetyltransferase's enzymatic activity by electron donation from the 3-methoxy and 4-hydroxyl groups on the benzene ring, the anti-inflammatory action is accomplished (Itagaki *et al.,* 2009).

P-coumaric acid

P-coumaric acid, another phenolic compound forms as an intermediate during phenylpropanoid synthesis; it has conferred several benefits such as antioxidant activity, the ability to reduce cholesterol levels and prevent atherosclerosis. It has also been shown that a regular oral intake of 370mg p-coumaric acid for 30 days significantly reduced cholesterol levels by preventing the oxidation of low-density lipids (LDL), without interfering with the levels of high-density lipids (HDL). The mechanism of action of p-coumaric acid depends upon its ability to remove ROS and exert antioxidant effects (Rodriguez *et al.,* 2022).

vitamin C

Vitamin C also known as ascorbic acid has been known for ages for its exceptional antioxidant properties and its role in mitigating oxidative stress. It is found in several fruits, vegetables, and other foods and demonstrates high sensitivity towards environmental conditions and factors (Comunian *et al.,* 2020). By nature, vitamin C is a hydrosoluble antioxidant capable of trapping hydroxyl and superoxide radicals. Furthermore, it plays a part in the production of collagen (Odriozola-Serrano *et al.*, 2008). An intake of 200-250mg of vitamin C or ascorbic acid can significantly reduce oxidative stress and damage (Tariq, 2007). In *C. papaya* fruit, vitamin C is found in both the skin and the pulp; it occurs either as L-ascorbic acid or as isoascorbic acid. The vitamin C content increases with the stage of ripeness of the fruit (Gayosso-García Sancho *et al.*, 2011).

Cultural and traditional uses

C. papaya is a common edible fruit used by several cultures (Table 3) and nations for a variety of purposes (Nayak *et al.*, 2007; Anuar *et al.*, 2008). In most Asian countries, *C. papaya* is used in the production of processed foods such as cocktails, canned and sugar-coated in syrups, ice-creams, jams, and soft drinks (Ezike *et al.*, 2009). In other countries, papaya is also used to make pickles, salads, sweetmeat and is commonly eaten with rice (Table 4) (Ikram *et al.*, 2015).

Table 3. Traditional uses of *C. papaya* fruit in various countries.

Country	Uses of Papaya	References
Africa		
Gambia	Tropical pastes for treating burns	Ikram *et al.*,2015
Nigeria	Used in the management of diabetes mellitus.	Abo *et al.*, 2008
Asia		
India	Consumed in the form of spinach to treat asthma, beriberi, colic, malaria, stomach disorders, urinary tract infections (UTIs), skin burns, another skin disease, to remove snake bite poisons, and to combat obesity.	Krishna *et al.*, 2008; Yogiraj et al., 2015; Nariya & Jhala, 2017
Indonesia	As a birth control, To prevent menstrual bleeding and uterine contractions post-delivery.	Kapoor, 2009; Hainida *et al.*, 2015
Japan	Used to prevent and treat degenerative diseases (aging, cirrhosis, diabetes, and thalassemia.	Aruoma *et al.*, 2010
Malaysia	To treat corns, epithelioma, warts, skin diseases, and ulcers of the mouth, tongue, and throat. Other uses include the removal of acne and blemishes.	Kapoor & Saraf, 2011; Lim, 2012; Alara *et al.*, 2020
Pakistan	Mainly leaves are used for treating conditions such as dengue fever.	Ahmad *et al.*, 2011; Siddique *et al.*, 2014
Philippines	To treat corn, epithelioma, warts, skin diseases.	Kapoor & Saraf, 2011; Lim, 2012;

Table 4. Common Uses of *C. papaya*

Uses of *C. papaya*	References
Unripe Papaya	
Abortifacent, antibacterial activity, diuretic, laxative, mouth ulcers pimples, prophylactic, skin inflammation, mouth ulcer	Vij & Prashar, 2014; Anjana *et al.*, 2018; Nafiu *et al.*, 2019
Ripe Papaya	
Amenorrhoea, anthelmintic, antihepatotoxic, antibacterial, anti-sickling, antioxidant, anti-inflammatory, bleeding piles, carminative diuretic, chronic diarrhea, clogging farts, constipation, digestive dysentery, dyspepsia, enhances hunger, expectorant, relieves obesity, ring worms, round worms, sedative, skin disease psoriasis, tonic, UTIs, wounds of the urinary tract	Krishna *et al.*, 2008; Mojisola *et al.*, 2008, Ocloo *et al.*, 2012; Aravind *et al.*, 2013; Nafiu & Rahman, 2015

Medicinal and therapeutic properties

Anthelmintic activity

Helminthiasis is a disease where an organ in the body becomes infested with worms like pinworms, roundworms, or tapeworms. These worms usually inhibit the gastrointestinal tract (GIT) or the liver in some cases and cause adverse effects on human host health by depriving them of blood, food, and by the secretion of toxins. *C. papaya* effectively acts against parasites and parasitic worms (Dwivedi *et al.*, 2011; Shrivastava & Singh, 2015). In recent years, latex, seeds, and other parts of papaya have been used for the removal of parasitic worms from the GIT. Most research related to the anthelmintic effect of *C. papaya* has been carried out on the Indian earthworm (*Pheretima posthuman)* since it is easily available and closely resembles other parasitic worms. The use od papaya extract alongside honey is also very effective as an anthelmintic treatment (Ortega, 2011; Kanthal, 2012).

Anti-diabetic property

The use of *C. papaya* has been a traditional use for ages. More recently, scientific reports of animal models have also supported the antidiabetic effects of *C. papaya;* it lowers blood sugar levels (hyperglycemia), proposing regenerative capacity

(Gbolade, 2009; Sasidharan *et al.*, 2011; Juárez-Rojop *et al.,* 2012; Maniyar & Bhixavatimath, 2012). Further studies on diabetic animal models have also shown that papaya extracts can restore basal insulin levels, this ability is attributed to beta cell regeneration. Additionally, it has also been shown that C. papaya may also affect anti-glucosidase activity (Loh & Hadira, 2011; Oboh *et al.,* 2014). Studies on humans have also assessed C. papaya's antidiabetic potential, and it has been determined that this potential stems from its hypoglycemic effect (Somanah *et al.*, 2012).

Anti-diarrheal activity

Chloroform extracts from raw *C. papaya* fruits combined with acetone extract from ripe *C. papaya* fruits are proven to be effective anti-diarrheal agents as they possess antimicrobial activity against gut pathogens, *Plesiomonas shigelloides* in particular (Prabhu *et al.,* 2017). Other parts of *C. papaya* used for the treatment of diarrhea include aqueous leaf and root extracts (Akindele *et al.,* 2011; Zanna *et al.,* 2017).

Anti-hypertensive property

Only a small number of scientific investigations have demonstrated C. papaya's antihypertensive ability; evidence indicates that intravenous (IV) injection of C. papaya reduces mean arterial pressure in renal and deoxycorticosterone acetate-induced hypertension in animal models (Santana et al., 2019). Other studies have also suggested that the antihypertensive effect of papaya is exerted via adrenoceptor antagonism (Brasil *et al.,* 2014).

Anti-fertility activity

C. papaya causes infertility in both males and females, however, the effect on females is far more severe and if consumed by pregnant females, it may lead to abortion. Experiments have been carried out on pregnant rodents with each part of the plant and it has been shown that the unripe fruit interferes with the estrous cycles in pregnant rodents and removes the instigated fetus (Memudu & Oluwole, 2022). When consumed by males, it causes infertility, and in pregnant females, *C. papaya* acts as pessary to increase blood flow in the pelvic region to induce abortion (*Krishna et al.*, 2008; Yogiraj *et al.,* 2015 Hainida *et al.,* 2015). However, ripe papaya fruit does not pose any significant dangers during pregnancy, the unripe contains latex which causes uterine contractions (Budama-Kilinc*et al.,* 2018).

Anti-inflammatory property

Inflammation, which is associated with pain, redness, and swelling brought on by the release of prostaglandin mediators, is one of the body's most natural defense mechanisms against infections (Chen *et al.*, 2017). The pathophysiology of inflammation is initiated by tissue injury, followed by antigen-presenting cells (APCs) and macrophage activation. Vascular events, or repercussions in the microvasculature, usually happen minutes after tissue damage or microbial infection, especially when other inflammatory stimuli are present. The ROS are produced to eliminate invaders, consequently, ROS also causes the activation of nuclear factor kappa-B (NF-*k*B) which induces the inducible enzyme iNOS and thus the production of NO. Excessive ROS-upregulated prostaglandin (PGE2) promotes the expression of cyclooxygenase-2 (COX-2) and worsens inflammation (Morgan & Liu,2011; Hussain *et al.,* 2016; Kanda *et al.,* 2017). Other studies have suggested that ROS enhances the inflammation reaction by causing an increase in the expression of genes that code for inflammatory proteins such as activator protein 1 (AP-1), NF-*k*B, and peroxisome proliferator activator receptor gamma (PPAR-γ). Other inflammatory chemokines and cytokines also increase ROS production via several signaling molecules and pathways such as mitogen-activated protein kinase (MAPK), NADPH oxidase 2 (NOX), polymorphonuclear neutrophils (PMN), protein kinase C (PKC), and c-Jun-N-terminal kinase (JNK) pathways (Chatterjee, 2016). Several research studies have shown that *C. papaya* extracts contain phytochemicals such as benzyl isothiocyanate (BiTC), β-carotene, lycopene, and vitamin C that exert protective effects by attenuating ROS production and by causing a reduction in the release of pro-inflammatory cytokines secretion of interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1) and TNF-α. Additionally, these phytochemicals also upregulate enzyme activity and reduce oxidative stress (Somanah *et al.,* 2017). Moreover, polyphenols present in *C. papaya* also play a role in the scavenging of free radicals and upregulation of antioxidant enzymes (Od-ek *et al.,* 2020).

Anti-malarial activity

Petroleum ether extract of raw *C. papaya* fruit demonstrates antimalarial activity (Krishna *et al.,* 2008; Vij & Prashar, 2015). Papaya plant has traditionally been used as an antimalarial agent in a lot of cultures and even currently, in several cultures such as Africa, India, and South America, malarial patients are suggested to consume papaya herbs as an allopathic medication in combination with antimalarial drugs. It is assumed that C. papaya extracts enhance the efficacy of antimalarial drugs while being safe and cost-friendly (Onaku *et al.,* 2011; Kovendan *et al.,* 2012).

Anti-microbial activity

The antimicrobial effects of *C. papaya* have been long known and exploited. Over time, most pathogenic strains of bacteria and fungi have developed resistance against several treatments and antibiotics. Additionally, antibiotics and synthetic treatments have side effects thus, natural remedies from medicinal plants can be considered as a safer alternate option (Tambekal *et al*., 2012; Lohidas *et al.,* 2015). Several published studies have shown tremendous evidence supporting the chemo-preventive activity of different parts of *C. papaya*. However, seeds, latex, leaves, and roots have greater antimicrobial potentials than the fruit on its own (Abdullah *et al.,* 2011; Alabi *et al.,* 2012; Baskaran *et al.,* 2012; Ghosh *et al.,* 2017; Callixte *et al.,* 2020). *C. papaya* plant exhibits antifungal activity but the fruit in particular does not demonstrate any antifungal activities, rather the antifungal activity is attributed to the latex (Vij & Prashar, 2015). The use of plants as medicines is a common practice in many cultures and nations. Plants have been used as a primary remedy against several diseases owing to their exceptional pharmaceutical properties. Presently, even with the advent of modern and synthetic medications, the use of plants as medicine is common in Asia, Africa, and Latin America. Not only the *C. papaya* fruit but also other parts of the plant are proven to be beneficial in several health conditions. Additionally, plants such as *C. papaya* can also be used for the pharmaceutical production of drugs. Extracts from papaya fruits have shown evidence by acting as antimicrobial agents against fever, gastroenteritis, otitis media, typhoid, and urethritis. *Pseudomonas aeruginosa*, *Shigella flexneri*, *Staphylococcus aureus*, *Escherichia col*i, and *Bacillus cereus* have all been shown to exhibit bactericidal action (Oloyede, 2005; Doughari *et al.,* 2007; Krishna *et al.,* 2008; Sasirekha *et al.,*2018).

Anti-neoplastic property

Unripe fruit extract of C. papaya contains hydroethanol, which when concentrated exerts anti-neoplastic activity. This was proven by a study conducted on animal models. (Sasidharan *et al.,* 2011; Ranasinghe *et al.,* 2012; Praveena *et al.,* 2017).

Antioxidant properties

Oxidative stress, a persistent issue, is described as an imbalance between antioxidants, pro-oxidants, ROS, and free radicals. It is characterized by either an excess of pro-oxidants or a lack of the body's inherent antioxidant defense system (Kong et al., 2021). Free radicals are continuously produced within cells and play important roles in aging and the etiology of several degenerative diseases because of their ability to disrupt and change the structure and function of biomolecules, including proteins, lipids, carbohydrates, and nucleic acids. ROS are produced via both endogenous and exogenous sources (Genestra, 2007). Oxidative damage caused by free radicals and ROS leads to inflammation which in turn is linked to several health conditions and diseases including Alzheimer's disease (AD), asthma, atherosclerosis, cancers, cataracts, cardiovascular diseases (CVDs), rheumatoid arthritis and skin conditions such as wrinkling (Silva *et al.,* 2010; Park *et al.,* 2016). Molecular oxygen and nutrients are constantly processed throughout the body by enzymes involved in complex metabolic activities, these processes are necessary for yielding oxidants that have a positive impact on the body. However, oxidants must be produced at a basal level and cause no harm to human health or nutrition. Under normal conditions, the human body's endogenous antioxidant defense system contains antioxidant enzymes including catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), all of which scavenge free radicals and inhibit the generation of oxidative stress (Kong *et al.,* 2021). Diet, environment, and exposure to sunlight are common sources of free radicals (Sies, 2015; Pizzino *et al.,* 2017).

The production of excess oxidants and free radicals such as ROS, reactive nitrogen species (RNS), hydroxyl, and peroxides occur under several health conditions and diseases that alter tissue metabolism including chronic wound healing, diabetes mellitus, inflammation-associated diseases, and microbial infections. Conditions such as the above mentioned alter the mechanism of tissue metabolism suppress the endogenous antioxidant defense system and lead to oxidative damage/stress. When endogenous defense systems fail, exogenous antioxidants find relevance (Nafiu *et al.,*2019). Antioxidants, as the name suggests are compounds that inhibit oxidation, prevent the formation of and scavenge free radicals. Several compounds, nutritional components, and phytochemicals present in the fruit *C. papaya* are proven to have antioxidant activities (Chakrabirty *et al.,* 2015; Somanah *et al.,* 2017). Phytoconstituents of *C. papaya* with antioxidant roles include carotenoids, flavonoids, flavonols and polyphenols, and traditional antioxidants vitamins such as vitamins C and E. Additionally, adding selenium to this antioxidant regime exerts a far greater synergistic effect (Maisarah *et al.,* 2013; Nafiu *et al.,* 2019). Several clinical and epidemiological studies have shown that *C. papaya* extracts have significantly reduced oxidative stress in several health conditions, these conditions are discussed below.

Alzheimer's disease (AD)

The relationship between oxidative stress and the onset and development of AD is well-established and well-acknowledged. Aggregation of β-amyloid peptides and the formation of neurofibrillary tangles in the brain are the most typical characteristics of AD (Gella & Durany, 2009). The accumulation of β-amyloid in the brain leads to the generation of ROS which causes lipid and protein peroxidation and results in neurotoxicity in the brain. AD generally results in the impairment of defense mechanisms against oxidative stress characterized by low glutathione levels. Moreover, it is also discovered that ROS in the brain inhibits α-secretase activity, and promotes the activity of β-secretase and γ-secretase by generating neurotoxic β-amyloid 40 and 42. Another proposed mechanism of AD pathophysiology suggests that β-amyloid impedes and interferes with mitochondrial function in the neuronal cells. Studies have also proven that β-amyloid causes impairment of the antioxidative stress mechanism by interfering with the expression of uncoupling proteins (UCPs) which mainly function in reducing the ROS generated (Zhao & Zhao, 2013). FPP is one of the most commonly used papaya products which acts as a source of exogenous antioxidants and free radical scavengers (Zhang *et al.,* 2006).

Cancer

There is currently no proven cure for the long-standing illness known as cancer. Some cancers are incurable, but others can be managed or cured to a certain degree. Both the development and possible eradication of malignancy are influenced by reactive oxygen species (ROS), which originate from mitochondrial metabolic activities. The two main processes that cause the progression of tumors and cancers are angiogenesis and metastasis, increased oxidative stress caused by ROD diminishes the body's anti-oxidant defense mechanisms against angiogenesis and metastasis thereby promoting the growth of cancer cells (Nourazarian *et al.,* 2014). In basal and tolerable concentrations of ROS, cancers in the body result from alterations and mutations in the genomic DNA, which in turn interfere with the normal physiological signaling pathways; pathways such as the cycling D, JNK, ERK, and MAP-K are all thought to have roles in the progression of cancer (Saha *et al.,* 2017). Normal cells have a lower tolerance for ROS and eventually undergo cellular damage or death in high concentrations of ROS. Unlike normal cells, cancer cells have a higher resistance and tolerance towards ROS; however, after a certain limit, ROS reduces the growth and progression of cancer cells (Sosa *et al.,* 2013). Additionally, it is also proposed that ROS causes the induction of carcinogenesis by interfering with the activities of tumor-suppressor genes (Saliasi *et al.,* 2018). Certain studies have shown that FPP was able to impede DNA fragmentation, otherwise caused by free H_2O_2 and free radicals (Aruoma *et al.,* 2006). The anti-cancer activity of FPP is owed to its ability to trigger cellular signaling mechanisms that cause apoptosis (Garcia-Solis *et al.,* 2009). As already known, C. papaya is enriched with flavonoids which confer chemo-preventive and chemotherapeutic properties; the underlying preventive mechanisms include; (1) activation of tumor-suppressor genes, (2) deactivation of oncogene products, (3) decreasing oxidative stress by free radical scavenging and by preventing lipoxygenase action via chelating agents, 4) elevation of anti-oxidant enzyme levels such as and (5) preventing DNA from any structural damage that may be caused by free radicals or genotoxins (Waly *et al.,* 2014; Murakami *et al.,* 2014; Pathak *et al.,* 2016; Somanah *et al.,* 2016).

Diabetes

With advancements in the age and duration of diabetes, there is a gradual tendency for the level of blood sugar to rise along with a subsequent increase in the HbA1c as well as in the fasting insulin level (Skyler *et al.,* 2017). It is evident from numerous researches that oxidative stress plays a role in the progression of diabetes Reactive oxygen species (ROS) generation is increased in diabetes, according to a wealth of experimental and clinical data, oxidative stress is closely associated with the progression of diabetes (Leisegang, 2022). There is an overwhelmingly high amount of evidence that uncontrolled hyperglycemia is correlated to the promotion of ROS and weakening of antioxidant defense systems; the defense systems are weakened by glucose oxidation, induction of lipid peroxidation of low-density lipoprotein (LDL), and glycation of proteins. Advanced glycation end products (AGEs), which are produced when glucose and proteins interact non-enzymatically, increase the creation of reactive nitrogen species (RNS), such as nitric oxide (NO). This oxidative stress and resultant free radicals hinder the functionality of β-cells in the islets of Langerhans, potentially leading to diabetes (King *et al.,* 2004; Rolo *et al.,* 2006). Antioxidants are therefore essential for the treatment of diabetes. Studies have demonstrated that the antioxidants in fermented papaya preparation (FPP) aid prevent atherosclerotic plaque, reduced lipid peroxidation, and raise superoxide dismutase (SOD) levels, among other diabetes problems (Raffaelli *et al.,* 2015).

Periodontal disease

Periodontal disease is a condition characterized by the infection and inflammation of the gums, which is very likely to be related to oxidative damage and stress (Highfield, 2009). Periodontal inflammation is triggered and augmented by the production of unnecessary ROS and leukocytes. Epidemiological trials on humans have shown that the application of standardized fermented papaya gel (SFPG) significantly improves gum health, bleeding, and inflammation by decreasing the levels of inflammatory cytokines, nitrate (NO_3^-), and nitrite level (NO_2^-) (Saliasi *et al.,* 2018). SFPG also inhibits the activity of bacterial catalase and thereby reduces infection (Kharaeva *et al.,* 2016).

Skin aging

The degradation of the extracellular matrix (ECM) is the main process that leads to the aging of the skin; it makes the skin drier, thinner, unevenly pigmented, and wrinkled. For ages the skin damage has been attributed to ROS; ROS is also known to cause premature aging of the skin as a result of oxidative stress and inflammation. ROS are also generated as a result of exposure to ultraviolet (UV) radiations, which activate signaling molecules and pathways such as AP-1, extracellular signal-regulated kinase (ERK), Jun N-terminal kinase (JNK), MAP-K, nuclear factor kappa B (NF-κB). These factors and pathways are responsible for the induction of matrix metalloproteinase (MMP) 1, 3, 9 expression and collagen production in keratinocytes and fibroblasts which eventually lead to ECM damage and thus, aging (Rinnerthaler *et al.,* 2015). Another phenomenon induced by ROS is melanogenesis mediated by an increase in melanogenic factors such as tyrosinase-related protein 1 (TYRP-1) and tyrosinase that eventually cause pigmentation of the skin. Furthermore, UV also increases the amount of cholesterol hydroperoxides, oxidized lipids, and triglyceride hydroperoxides which cause infections like acne vulgaris *Propionibacterium acnes*, which eventually leads to further generation of ROS (Masaki, 2010). *C. papaya* is used for its anti-aging properties due to its anti-inflammatory and anti-oxidant properties. Extracts of unripe *C. papaya* have been shown to prevent H_2O_2-induced endothelial cell death; these extracts alter the defense mechanisms by attenuating NF-κB and upregulating CAT and SOD activities. ROS leads to the depletion of the natural anti-oxidants and promotes aging while using papaya extracts maintains redox homeostasis and thus prevents aging (Jarisarpurin *et al.,* 2019; Sanchez *et al.,* 2019).

Wound healing

Wound-healing is a complex and well-coordinated biological process that has several stages; inflammation, homeostasis, proliferation, and modeling (Guo & Dipietro, 2010; Janis & Harrison, 2016). The process and rate of wound-healing can significantly be affected and altered by oxidative stress; oxidative stress and redox signaling play crucial roles in normal healing of wounds by facilitating (1) angiogenesis, (2) development and maturation of ECM, (3) granulation, (4) hemostasis, (5) inflammation, (6) tissue formation and (7) wound closure (Sen & Roy, 2010; Gonzalez *et al.,* 2016; Cano Sanchez *et al.,* 2018). Though lower concentrations of ROS prevent infection, higher concentrations of ROS can be cytotoxic and impair skin lipids, reduce their fluidity, and damage cellular membranes, DNA, and tissues thereby promoting inflammation (Suntar *et al.,* 2012; Gonzalez *et al.,* 2016; Lephart, 2016; Cano Sanchez *et al.,* 2018; Robinson *et al.,* 2022). In vivo research with FPP has shown that FFP inhibits hydroxyl radicals, superoxide and reduces the general content of ROS (Nafiu & Rahman, 2015). *C. papaya* extracts and topical applications enhance and speed up the process of wound-healing by reducing inflammation, producing antioxidant enzymes, and causing arginine metabolism (Leitao *et al.,* 2022). Oral administration of FPP has also been proven to enhance wound closure in diabetic wounds (Collard & Roy, 2010).

Anti-sickling activity

Sickle cell disease (SCD) is a fatal genetic hematological disorder characterized by the presence of abnormally shaped red blood cells (RBCs) (Dash *et al.,* 2013). The search for natural anti-sickling agents and plants has been a long struggle. The anti-sickling potential of *C. papaya* has been long recognized, it was first recognized in 1987 (Thomas & Ajani, 1987). After the discovery of the anti-sickling potential of papaya, FPP was used in sickle cell and thalassemic patients showing an improvement in the RBC sensitivity towards hemolysis (Amer *et al.,* 2008; Fibach & Rachmilwitz, 2010; Nurain *et al.,* 2016).

Hepatoprotective effect

Aqueous and ethanol extracts of *C. papaya* confer and possess exceptional hepatoprotective activity, especially against carbon tetrachloride (CCl_4) induced hepatoxicity. It is also concluded that C. papaya extracts along with vitamin E further enhance the hepatoprotective effect. Nevertheless, the exact underlying mechanisms and principles by which the hepatoprotective effects are conferred are yet to be elucidated (Adeneye *et al.,* 2009; Sadeque *et al.,* 2012; You *et al.,* 2017).

Immunomodulatory properties

Immune system strengthening is crucial for avoiding infections in diseases like HIV and immunosuppressed states (Yogiraj *et al.,* 2015; Pandey *et al.,* 2016). Recent research has shown that *C. papaya* extracts increase leukocyte, lymphocyte, monocyte, and platelet count in bone marrow cells in rat animal models (Jayasinghe *et al.,* 2017). Additionally, high doses of *C. papaya* extract also significantly decrease the levels of pro-inflammatory cytokines. The most commonly exploited parts of C. papaya used for their immunomodulatory effects are the leaf and the seed (Anjana *et al.,* 2018). Papaya extracts dramatically increased the cytotoxic activity and immunomodulatory effects of human peripheral blood mononuclear cells (PBMC) against cancer cells, according to a different study. Additionally, the study indicated that *C. papaya* extracts might be employed in vaccination therapy as an immunoadjuvant (Otsuki *et al.,* 2010).

Other uses

Alcohol production

Among the current challenges faced by the world's biofuel industries is the production of a low-cost, environment-friendly method of ethanol production. Traditional petroleum-based methods of ethanol via fermentation are highly toxic to the environment. One of the alternate approaches is the production of ethanol and other alcohols by using agro-waste. C. papaya fruit extracts are proven to be a good alternate source of ethanol production as they have a high content of energy, nutrients, and phytochemicals (Saeed *et al.,* 2014).

Animal feed

Seeds of *C. papaya* are added to animal feed to enhance animal health, nutrition, and production. There are several advantages of doing so; (1) animals feed more and gain more nutrients, (2) enzymes and phytochemicals are added to their diet which protect the animal against microorganisms of the GIT, (3) increased rate of ovulation, (4) increase production of milk and (5) bloating intestinal parasitic load is reduced (Farrag *et al.*, 2014; Hainida *et al.*, 2015). When added to a broiler diet, C. *papaya* containing diets are cost-friendly and reduce the amount of fecal ammonia produced (Bolu *et al.,* 2009).

Cosmetics

Other than its application as a food, papaya can be used in cosmetics and topical creams. One of the earliest uses of *C. papaya* was to reduce acne and pimples and diminish blemishes and scars on the skin. In cosmetics, papaya is used as either peeled or mashed forms (Hainida et al., 2015; Lim, 2012). The peels of papaya contain vitamin A, which has antioxidant properties and therefore is even more suitable for its use in cosmetics (Aravind *et al.,* 2013).

Culinary

C. papaya is known for its culinary uses and its use as a fruit to be eaten regularly. In various countries, papaya is consumed on its own or it is cooked, fermented, or processed to make commercially available food products. Papaya is eaten raw in some countries as one of the daily nutrients, and is made into deserts, jams, pickles salads, and sweet dishes (Aruoma *et al.*, 2014). Other parts of the plant such as leaves are cooked as soup and used as a medicinal herb. In some other regions such as India, papaya seeds are used to replace black pepper seeds (Krishna *et al.,* 2008; Hainida *et al.,* 2015).

Conclusion

The health benefits of *C. papaya* are far too many to be counted; it contains enzymes, minerals, nutrients, and vitamins which not only are necessary for the normal diet of an individual but also provide numerous health and nutritional benefits. The fruit on the plant grows throughout the year and all of its parts can be used for their potential bioactivities. Enzymes present in *C. papaya* such as chymopapain and papain aid the digestion process and ease dyspepsia. Vitamins A, C, and E present in papaya confer antioxidant activities and prevent human health from several diseases such as aging of the skin, cancer, and high levels of cholesterol. Additionally, phytochemicals including alkaloids, carotenoids, flavonoids, and phenols also contribute to the many advantages conferred by *C. papaya.* Therefore, it can be concluded, that the papaya plant is a safe and natural option to improve human health and nutrition.

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All authors contributed equally.

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