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Potential health benefits of papaya (*Carica papaya*) in modern and traditional medicine with considering its phytochemistry and nutritional components

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Abstract. The plant-derived products contain different advantages over synthetic drugs, such as being readily available, being more affordable, with less adverse effects after long-term or short-term consumption. *Carica papaya* can be found in almost all sub-tropical and tropical regions. The aim of the study is to present and summarize knowledge about papaya in terms of its phytochemistry, nutritional value and use in traditional and modern medicine. Extensive research data from reputable sources such as PubMed, Google Scholar, Web of Science, and Scopus were scrutinized to collate related information. The application of papaya in folk medicine is made possible by the phytochemicals present in the plant, which include steroids, tannins, phenols, saponins, flavonoids, alkaloids, proanthocyanidins, cardiac glycosides, and anthraquinones. The seeds and leaves of papaya have high nutritional value, and are sometimes added to products like tea and flour to increase the nutritional value. Its seeds contain minerals that include zinc, copper, calcium, potassium, and magnesium as well as phenolic components such as carotenoids, β-carotene, β-cryptoxanthin, tocopherols, glucosinolates, and benzylisothiocyanate. *In vivo* and *in vitro* studies show that papaya has different pharmacological benefits such as antimicrobial, antiinflammatory, anticancer, wound healing, antidiarrheal, anxiolytic, larvicidal, hepatoprotective, neuroprotective, antihyperlipidemic, antidiabetic, antiulcer, antiobesity, anthelminthic, antithrombocytopenic, and contraceptive activities. Our study concluded that the extensive application of different parts of the papaya plant is needed in modern medicinal sciences as well as traditional medicine.

Keywords: *Carica papaya*, medicinal approach, papain, phytochemistry, therapeutic benefits.

INTRODUCTION

Carica papaya L. is a perennial plant, belonging to the family of *Caricaceae*, which is cultivated in almost all over subtropical and tropical regions of the world, especially in China, West of India, South America, East Equatorial Africa, and Srilanka (Shahrajabian, Sun, 2024a,b,c,d), and almost all parts of the plant can be used by humans for medicinal and food purposes (Shahrajabian, Sun, 2023a,b,c,d). It is commonly known as the papaya tree (Allan, 2001; Correa et al., 2010). It is a tropical fruit, which is well recognized for many health benefits and nutritional values (Dathe et al., 1991; Monmarson et al., 1995; Brewer, Chambers, 2022; Shaheen et al., 2023; Vitoria et al., 2004). The fruit appears in a group with delicious and is healthy, each part of the plant such as pulp, seed, peel, root, bark, and fruit possess medicinal qualities (Castillo et al., 1998; Basha et al., 2011), therefore it cannot be wrong to say that it is a complete medicinal herb (Allan, Carlson, 2007). The roots show abortifacient action, reveal antifungal and antibacterial activity, and also act as a generative toxin to cure piles (Saeed et al., 2014). Papaya fruits also

have high nutritional benefits (Cruz et al., 2017; Kumaar et al., 2022). The excellent plant fruit contains enzymes and compounds with various activities that can prevent cancer aging and help in building a healthy heart. It is both a delicious fruit, and fortified with essential vitamins and minerals, which can provide many nutritional characteristics (Barragan-Iglesias et al., 2019; Ashour et al., 2020; Soto et al., 2021). The most important component in its leaves is the macrocyclic lactone carpaine (see last row in Table 1), which can reduce heart rate, blood pressure, and movement of the intestinal strops (Sato et al., 2003).

Being a nutritional powerhouse and convenient throughout the year, papaya is commonly used as a folk nutritious herbal medicine (Llerena-Suster et al., 2011; Armendariz-Ruiz et al., 2015). It is also an important source of strong antioxidants such as vitamin E, vitamin B, vitamin A, and vitamin C; minerals include magnesium and potassium, and also contains folate and pantothenic acid, and fiber (Singh et al., 2019; Taychaworaditsakul et al., 2024). It contains a digestive enzyme papain which prevents allergies, wound causes, and injuries caused by sports effectively (Khoshkharam, Shahrajabian, 2021; Khoshkharam et al., 2021; Khoshkharam et al., 2024). Its leaf extract is rich in bioactive components such as tannins, phenolics, phytosterols, saponins, alkaloids, and flavonoids (Otsuki et al., 2010; Lim et al., 2021; Teh et al., 2022). Different parts of papaya are shown wound-healing capacities (Mahmood et al., 2005), antitumor activity (Sathyapalan et al., 2020), hematological characteristic (Patil et al. 2014), antioxidant (Nariya, Jhala, 2017), hypolipidemic (Sheneni et al., 2018), hypoglycemic (Sobia et al., 2016), gastroprotective (Indran et al., 2008), antimalarial (Teng et al., 2019), and antibacterial activity (Baskaran et al., 2012). Tree fruit is a valuable source of beta-carotene that prevents the effects of free radicals which can form based on certain types of cancer. It is communicated that this helps in reducing heart failure with diabetes. Furthermore, papaya reduces cholesterol (Matsuane et al., 2023). Seeds are the main by-product of papaya which account for 15 to 20% of the total weight, which is rich in phytochemicals such as sterols, terpenes, polyphenols, flavonoids, alkaloids, carotenoids, saponins, tannins, benzyl isothiocyanate, and sterols (Hinostroza-Quinonez et al., 2024; Roy et al., 2024). It is reported that carpaine as the main alkaloid of papaya leaves, is widely studied for its antithrombocytopenic activity (Jadhav et al., 2022). The article aims to highlight and summarize the knowledge and information of different aspects of papaya such as phytochemistry, nutrition, and its application in both modern and traditional medicine. All the topics covered focus on the integrated and aggregate data from different scientific sources which describe and illustrate different pharmaceutical benefits of papaya. Materials search for this article involved the use of search keywords such as papaya, *Carica papaya*, antimicrobial activity, traditional medicine, carpaine, and antiviral activity found in the abstract, title, full-text, and keywords in the search queries on scientific databases such as Science Direct, PubMed, Springer, MDPI, and Wiley. These keywords were used in combination or independently with other words to denote the taxonomic group, botanical description, ethnomedicinal uses, nutritional composition, pharmacological activities, phytochemical constituents, and toxicological evaluation of the plant.

PAPAYA DESCRIPTION AND USES

The tree is native to South and Central America, especially in subtropical and tropical areas (Otsuki et al., 2010). The plant has different names such papaya, kepaya, pawpaw, or tapaya on the basis of location (Kong et al., 2021). It is an herbaceous perennial plant, with a milky latex which can reach 12 m in height; its each fruit weighs between 1000 and 3000 g, and it has a year-round fruit production (Krishna et al., 2008). The stem is usually solitary, hollow, and straight with conspicuous leaf scars. The leaves are palmately lobed, large, spirally organized, and clustered at the crown (Chen et al., 2002; Silva et al., 2007). A papaya plant may live for up to 25 years or even longer (Zhu et al., 2006). Papaya can grow in three sexes: male, female, and hermaphrodite (flowers with both female and male reproductive organs). The shape of the fruit also changes among various varieties; some are oval to nearly round, club-shaped, elongated, pyriform, and have variable weights (Karunamoorthi et al., 2014; Saeed et al., 2014). The fleshy fruits can change from yellow to reddish, with a length of 7–30 cm and thin, green skin, smooth, which turns yellow or orange when rise (Ezike et al., 2009; Yap et al., 2020). The seeds comprise at least 7% of the fruit weight (Yanty et al., 2014). The papaya genome was estimated to be 372.0 Mb by using flow cytometry (Arumuganathan, Earle, 1991; Zou et al., 2020). Papaya plants can be propagated vegetatively using classic methods such as grafting and cutting (Allan et al., 2010; Oparaku et al., 2024), but in for large-scale production, papayas are usually propagated from seeds (Encina et al., 2023). This plant grows rapidly (within three years), although it is very susceptible to a frosty environment, that causes restraining production of fruits in tropical climates. Recently, Papaya has become the main agricultural export product to different countries, which have significantly influenced many lives in Latin America and Asia (Jahangir et al., 2023). Papaya fruit can be eaten raw in salads, pickled, dehydrated, crystallized, or processed into wine both in unripe and mature phases. The main phytochemical compounds present in its pulp are glutathione peroxidase, glutathione transferase, glutathione reductase, catalase, glucose-6-phosphate, total phenols, terpenols, alkaloids, flavonoids and saponins in the pulp; β-cryptoxanthine, β-carotene, tocopherols (α and δ), fatty acids such as palmitic, oleic, stearic, and linoleic in its seeds; benzyl isothiocyanate, tocopherol, lycopene,

pro-anthocyanin, saponins, flavonoids, and polyphenols in its leaves (Ching, Mohamed, 2001; Basu, Haldar, 2008; Bouanga-Kalou et al., 2011). It has been placed in the top five fruits together with guava, grapefruit, watermelon, and kiwi on the basis of nutritional scores (De Oliveira, Vitoria, 2011; Alara et al., 2020).

PAPAYA IN TRADITIONAL MEDICINE

Medicinal plants are used globally for medication and therapeutically for the prevention and treatment of various diseases (Sun et al., 2021; Sun et al., 2022; Sun, Shahrajabian, 2023a,b; Sun et al., 2023; Sun et al., 2024a,b). Decoctions from various parts of the plants have shown significant curative potency in traditional medicine (Nafiu, Rahman, 2015; Nguyen et al., 2016). In traditional medicinal science, papaya leaf extract is used for treatment of dengue fever and its related symptoms, as its methanolic extracts, containing flavonoids and triterpenoids with cytotoxic activity (Joseph et al., 2015). In traditional medicinal sciences, various parts of papaya are applied in the treatment of different ailments such as fever, helminth infections, diabetes, eczema, ulcers, and asthma (Nguyen et al., 2013). The plants contain papain, which is a globular cysteine-protease family including a single polypeptide chain with a sulfhydryl group and three disulfide bridges necessary for proteolytic activity (Babalola et al., 2023). Different parts of this medicinal plant have been traditional used as ethnomedicine for various disorders such as cancer, for example it is reported that consumption of tea extract made from its leaves have shown antitumor activity (Otsuki et al., 2010). In Africa, they have been used the yellow red parts of the dried leaves to treat gastric problems (Gupta et al., 1990), as well as an appropriate treatment for different diseases such as infectious diseases and cancer (Adebiyi et al., 2002; Songsermsakul et al., 2013). In Ethiopian traditional medicine, papaya has been used to relieve stress and anxiety, and treat many diseases (Kebebew, Shibeshi, 2013). In the traditional Indonesian medicinal science, the antiplasmodial activity of papaya leaves are reported which can be associated to alkaloids contents (Julianti et al., 2014).

ACTIVE SUBSTANCES OF PAPAYA

Papaya is a nutrient store having a good source of active substances including antioxidants, different vitamins, especially pantothenic acid (B5) and folate (B9), and minerals such as potassium and magnesium (Rao et al., 2013; Kaur et al., 2022). Its raw extracts include various secondary metabolites such as terpenoids, sugars, flavonoids, alkaloids, saponins, glycosides, and steroids (Drew, Miller, 1989; Chareekhot et al., 2014; Vos, Arancon, 2020). The papain which is also a digestive enzyme is extracted from papaya (Chareekhot et al., 2016; Senrayan, Venkatachalam, 2018). The papain and chymopapain enzymes and antioxidants present in papaya were found to be beneficial in reducing inflammatory problems and healing burns (Bhardwaj, 2013; Munir et al., 2022). Papaya seeds have been confirmed to be a good source of protein, lipids, dietary fiber, etc. (Marfo et al., 1986). It is reported that its seeds contain minerals such as zinc, copper, calcium, potassium, and magnesium (Amin et al., 2019), as well as phenolic components such as tocopherols, glucosinolates, benzylisothiocyanate, carotenoids, β-carotene, and β-cryptoxanthin (Afzan et al., 2012). It is reported that the seeds extract also have low concentrations of fixed oils, fats, carbohydrates, and resins (Amazu et al., 2010). The other bioactive components of seeds are methyl ester, hexadecenoic acid, octadecanoic acid, hexadecenoic acid, and oleic acid which are also considered as antidiabetic components (Agada et al., 2021).

The presence of tannins and alkaloids in the ethanolic extract of the leaves is reported, while quinones and steroids were found in the plant extract, which includes *n*-hexane, chloroform, and ethanol extracts (Pinto et al., 2015). The ethanol extracts of papaya pulp using precipitation and coloring assays which confirm the presence of saponins, alkaloids, tannins, phenolic compounds, flavonoids, terpenoids, and phlobatannins (Juarez-Rojop et al., 2014). The presence of reducing sugars, alkaloids, tannins, saponins, and terpenoids in the unripe fruit extract of papaya was also reported (Chavez-Quintal et al., 2011; Sai et al., 2019). Moreover, the identified flavonoids include kaempferol, quercetin, myricetin 3-rhamnoside, and quercetin 3-rutinoside (Gogna et al., 2015; Nugroho et al., 2016).

Various parts of papaya plants are ascribed with various medicinal activities (Nouman et al., 2022). On the basis of phytochemical analysis, its ripe fruit contains vitamins C and A, its bark contains latex, which is important in the production of leather tanning, canned meat, and digestive medicine, and the roots have been reported to have antimicrobial activity against microorganisms such as gonorrhea (Udoh, Udoh, 2005; Udoh et al., 2005). It contains high contents of minerals and phenolic components, which are responsible for its high antioxidant activity (Iskandar, Mustarichie, 2018), and the phytochemical screening of leaves and fruits prove the presence of terpenes, tannins, phenols, saponins, cardiac glycosides, flavonoids, and alkaloids (Iskandar, Mustarichie, 2018). The ethanolic leaf extract of papaya showed the highest levels of total phenols and flavonoids (Khadam et al., 2019). Moreover, the ethanol extract of its leaves contains steroids and quinones (Sarjono et al., 2019). Papain can be found in all parts of the papaya plant with numerous application and enzymatic properties (Gastelum-Martinez et al., 2019). Papaya leaves also contain ascorbic acid, glucosinolates, cyanogenic glucosides, flavonoids, cystatin, α-tocopherol, papain, and chymopapain (Gastelum-Martinez et al., 2019). Rutin and narirutin have immunomodulation activity (Bin Hyun et al., 2021), papain and chymopapain have antima-

Table 1. Different bioactive phytochemicals of different parts of papaya plant.

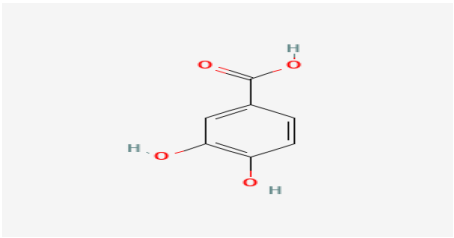
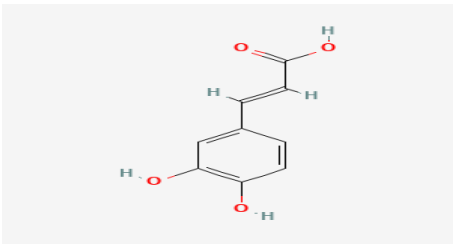
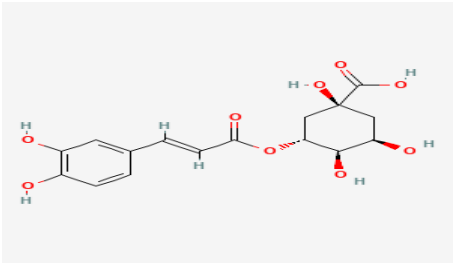
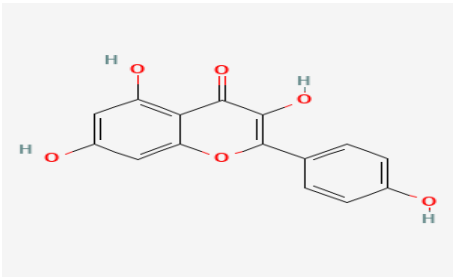
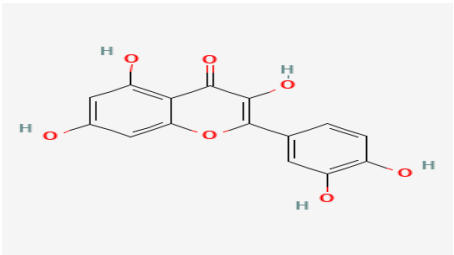
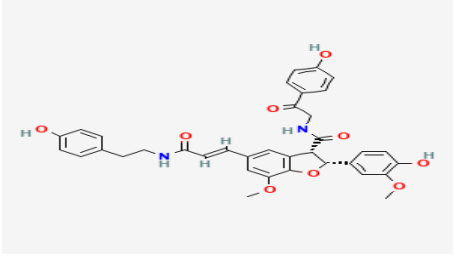
Chemical compounds	Molecular formula	Chemical structure
1	*2*	*3*
Protocatechuic acid	$C_7H_6O_4$	
Caffeic acid	$C_9H_8O_4$	
Chlorogenic acid	$C_{16}H_{18}O_9$	
Kaempferol	$C_{15}H_{10}O_6$	
Quercetin	$C_{15}H_{10}O_7$	
Tribulusamide B	$C_{33}H_{34}N_2O_9$	

Table 1 continuation

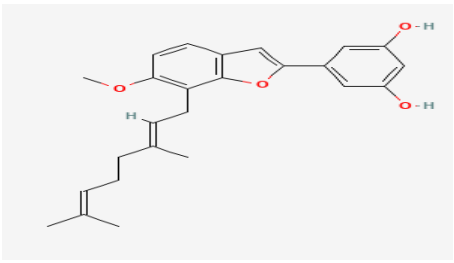
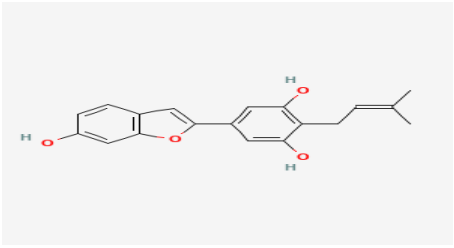
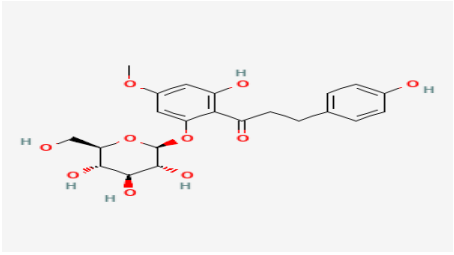
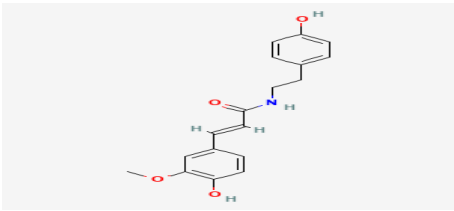
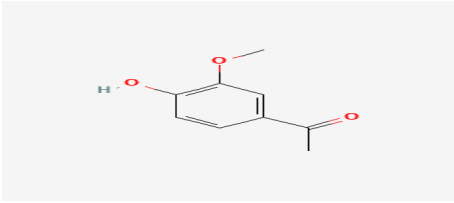
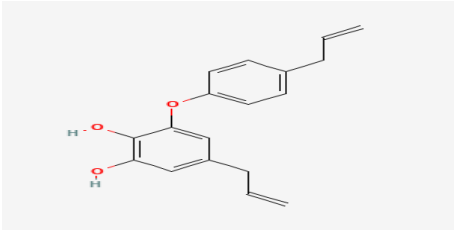
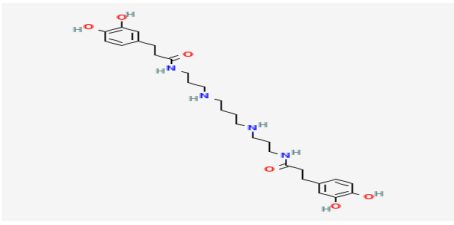
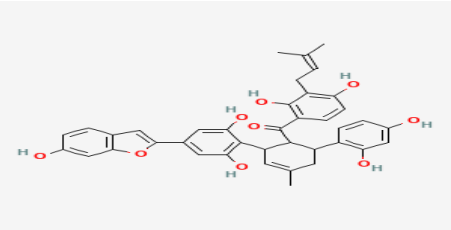
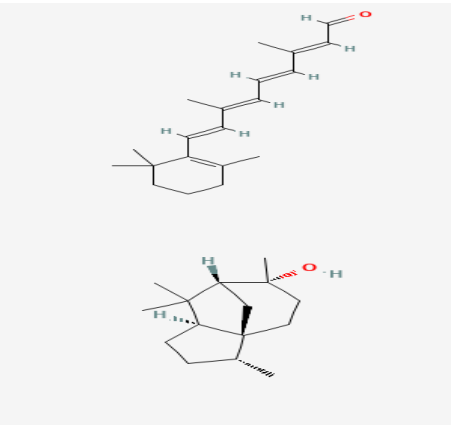
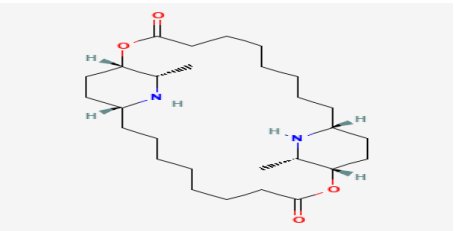
1	*2*	*3*
Mulberrofuran B	$C_{25}H_{28}O_4$	
Moracin C	$C_{19}H_{18}O_4$	
Asebotin	$C_{22}H_{26}O_{10}$	
Moupinamide	$C_{18}H_{19}NO_4$	
Apocynin	$C_9H_{10}O_3$	
Obovatol	$C_{18}H_{18}O_3$	
Kukoamine A	$C_{28}H_{42}N_4O_6$	

Table 1 continuation

1	*2*	*3*
Chalcomoracin	$C_{39}H_{36}O_9$	
Retinal	$C_{20}H_{28}O$	
Cedrol	$C_{15}H_{26}O$	
Carpaine	$C_{28}H_{50}N_2O_4$	

Source: PubChem.

larial activity as they can cause immunity against insect attack (Shirole et al., 2021), quercetin has antiviral activity through binds viral proteases, ceases viral replication, and inhibits and destroy viral activity (Bere et al., 2021), flavonoids can cause cell-cycle arrest in cancer cells, inhibit reactive oxygen species, and cause cell-cycle arrest in cancer cells (Airaodion, 2019; Singh et al., 2021), polyphenol have hypoglycemic activity, and they can retard and lower glucose absorption (Airaodion et al., 2019), quercetin and lycopene have shown antiangiogenic activity as they can reduce size, length, and junction of blood vessels, and inhibit the formation of abnormal new blood vessels (Tayal et al., 2019), ascorbic acid and tocopherol have antioxidant activity (Luiz et al., 2020), and alkaloids can inhibit bacterial growth, prevent bacterial colonies formation and destroy bacteria (Abdel-Halim et al., 2020). Vinha et al. (2024) reported that papaya seeds contain a high ash content, which showing a potential application as mineral source, and different fatty acids with oleic acid as the most abundant in the seeds, and α-linolenic acid as the most abundant in the peels with high antioxidant activity. Other researchers have shown that all papaya by-products are abundant in oils, proteins, flavonoids, fibers, saponins, tannins, anthraquinones, alkaloids, and benzyl isothiocyanate (Dotto, Abihudi, 2021; Li et al., 2021). Identified bioactive components in different parts of papaya are shown in Table 1. The most important health benefits of papaya are presented in Figure 1.

DIFFERENT ACTIVITIES OF PAPAYA COMPOUNDS

Antiviral activity

It is reported that papaya leaves extract could be used against chikungunya virus and dengue virus type 2, and its leaves in lyophilized form, the leaves are based silver nanoparticles and supercritical fluid extract were used for screening the antiviral activity (Patil et al., 2022). Papaya seeds flour has a high fiber and protein content with high antiviral activity (Lira et al., 2023).

Figure 1. The most important health benefits of papaya.

Antimicrobial activity

Sharma et al. (2020) showed the antimicrobial activity of dried and fresh leaves of papaya against fungi and bacteria. It is also reported that the leaves extract of papaya contains cytotoxic activity and antibacterial activity against sepsis infection (Usmani et al., 2023). Bere et al. (2021) revealed that methanolic silver synthesized nanoparticles from papaya leaf suppressed the activity of dengue virus type 2. The antimicrobial activity of papaya against *Staphylococcus aureus*, *Enterococcus faecalis*, *S. epidermididis*, *S. saprophyticus*, and *Candida albicans* are also reported (Jimenez-Coello et al., 2013; Mbosso Teinkela et al., 2016).

The papain component available in the leaves is accountable for the antimicrobial activity, especially against *Staphylococcus aureus* and *Escherichia coli* (Gayathri et al., 2023).

The plant is a famous medicinal plant used to treat many diseases in Western and Asian countries (Zou et al., 2023). Papaya is considered one of the main nutritious fruits, being rich in flavonoids, vitamins, carotenoids, and other phytonutrients that act as antioxidants in our body (Oboh et al., 2013). In one study, the reduced fasting blood glucose levels by chloroform extract from papaya in streptozotocin-induced diabetic rats is reported (Miranda-Osorio et al., 2016), and in other study, the antidiabetic effects of aqueous extract of papaya evaluated (0.75, 1.5, and 3 g/100 mL) (Juarez-Rojop et al., 2012). The effects of 600 mg/kg of ethanolic extract against streptozotocin-induced diabetes in mice is identified (Roy et al., 2022a,b). Papaya restored the adipocytokines and the gene expression, restoring the changed effects in the fatty tissue of streptozotocin-induced type 2 diabetic rats (Roy et al., 2023).

Antimalarial activity

The dichloromethane extract from the leaves revealed high antimalarial activity (Teng et al., 2018), and its methanolic leaf extract showed high antimalarial characteristics (Momoh et al., 2020).

Larvicidal activity

Different parts of papaya have shown larvicidal activities (Cabral et al., 2019). In one experiment, the hexane extract from its seeds exhibited significant larvicidal effects against *Strongyloides venezuelensis* via a series of *in vitro* tests (Cabral et al., 2019). Methanol, chloroform, and aqueous extract of papaya has been used in treatment against larvae of *Culex quinquefasciatus* and *Aedes aegypti* (Chandrasekaran et al., 2018), and the ethanolic extract of papaya inhibited the embryonic development of eggs and decreased larval survival (Wabo Pone et al., 2011).

Antidiabetic activity

Treatment with papaya can regulate the levels of glycolytic and gluconeogenic enzymes and the levels of Akt and insulin receptor substrate-1 (IRS-1) in skeletal muscle

Table 2. Examples of benefits of various parts of papaya.

Benefits	Key-points	References
1	*2*	*3*
Health benefits		
Antiviral activity	Its fruits could effectively treat post-Covid clinical signs via pro-energy mechanisms, redox balancing, and immune-modulating processes.	Kharaeva et al., 2022
	Its leaves have positive effects against Covid-19 at both cellular and molecular levels.	Hariyono et al., 2021
	It has *n*-hexane, and it showed high antiviral activity which is important against Covid-19.	Adel et al., 2022
	Carica papaya leaves aqueous extract exhibited potential activity against Dengue fever.	Ahmad et al., 2011
Antibacterial activity	Its ethanolic extract revealed high antibacterial activity.	Siddique et al., 2018
	The antibacterial activity of its extracts against *Micrococcus luteus* is reported.	Baskaran et al., 2012
	The fruit extract-based Fe_2O_3 NPs were characterized and synthesized, and it showed antibacterial effects against Gram-negative bacteria.	Malaikozhundan et al., 2022
Antimicrobial activity	Its leaf contains saponins, glycosides, terpenoids, phytosterols, flavonoids, and alkaloids with antimicrobial activity against *Aspergillus niger*, *Aspergillus fumigatus*, *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Streptococcus mutans*.	Devanesan et al., 2021 Joshi et al., 2023
	The plant extracts showed antimicrobial activity against *Trichophyton rubrum*, *Candida albicans*, *Salmonella typhimurium*, *Escherichia coli*, *Klebsiella pneumonia*, *Staphylococcus aureus*, and *Enterococcus faecalis*.	Teinkela et al., 2016
Anticancer activity	Its various parts such as roots, seeds, latex, and fruits have anticancer activities.	Haber et al., 2023 Heung et al., 2023
	The flavonoid-enriched benzene fraction of its seed aqueous extract showed high anticancer activity.	Pathak et al., 2014
	The alkaloid extract of its fruits can decrease alpha-fetoprotein levels, and prevent the establishment of hepatocellular carcinoma.	Kyei-Barffour et al., 2021
Antidiabetic activity	The antidiabetic impacts of papaya are because of the presence of tannin, saponin, alkaloids, and flavonoids.	Sasidharan et al., 2011 Somanah et al., 2012 Raffaelli et al., 2015 Agada et al., 2020
	It reinstates the glycemic impact in the diabetic skeletal muscle by increasing the expression of glucose transporter-4 (GLUT4) and the insulin receptor (IR).	Roy et al., 2022a
	p-coumaric acid, caffeic acid, kaempferol, and quercetin have shown high antidiabetic activity, and it was able to restore the changed levels in the hepatic tissues of type-2 diabetic male rats.	Roy et al., 2023
	Its chemical components such as oleic acid, n-hexadecanoic acid, methyl ester, hexadecenoic acid, and 11-octadecenoic acid have been found effective because of their antidiabetic and antioxidant activities.	Agada et al., 2021
Antiinflammatory activity	Different parts of the plant have antiinflammatory and immunomodulatory activities.	Pandey et al., 2014 Pandey et al., 2016 Singh et al., 2020
	It can be used as a natural source against inflammation related diseases and irresistible microbial infections.	Amazu et al., 2010 Kousar et al., 2023
	The papaya polysaccharide fractions containing mannose components, galacturonic acid, and xylose have shown high antiinflammatory activity.	Owoyele et al., 2008 Od-Ek et al., 2020 Lin et al., 2023
Antioxidant activity	There is a correlation between total flavonoid contents and flavonoid and polyphenol concentrations ethanol extracts of plants which were both correlated to the antioxidant characteristic.	Vuong et al., 2013 Bhatt, Patel, 2015 Im et al., 2016
	Its flavonoid and phenolic content of fruits and seeds have shown high antioxidant activity.	Annegowda et al., 2014 Zunjar et al., 2015
	Its leaves contain high antioxidant components, which can decrease lipid peroxidation level.	Wang et al., 2015

Table 2 continuation

1	*2*	*3*
Antiplasmodial activity	The main alkaloids present in its leaves have revealed high antiplasmodial (antimalarian) activity.	Haldar et al., 2020
Antihelminthic activity	Its dried seeds have been applied for antihelminthic purposes.	Okeniyi et al., 2007
	The flavonoids fraction of papaya is a combination of different flavonoids such as luteolin, kaempferol, quercetin, and quercetin dimer. The butanolic extract of Carica papaya young leaves inhibited H_2O_2 induced hemolysis and lipid peroxidation.	Kumar et al., 2023
Antithrombocytopenic and immunomodulatory activity	Its leaves contain coumaric acid, quercetin, kaempferol, ferulic acid, cinnamic acid, vanillic acid, malic acid, sinapic acid, linoleic acid, carpaine, isochlorogenic acid, and beta sitosterol which can mediate the release of platelets providing means for prevention and treatment of dengue.	Anjum et al., 2017 Srikanth et al., 2019
Antihyperlipidemic activity	Its water fraction and extract revealed protection activity by boosting the high-density lipoprotein (HDL) cholesterol level.	Iyer et al., 2011
	The papaya leaves extract meaningfully reduced the LDL cholesterol, and total cholesterol levels at all doses administered, and the inverse relationship with the cholesterol levels and papaya leaves showed the effectiveness of its leaves extract in the treatment of hypercholesterolemia and cardiovascular diseases.	Ademuyiwa et al., 2023
Oral diseases	It used to treat oral diseases, and synthesis of nanoparticles has now become a turning point in the dentistry field.	Jiang et al., 2024 Subha et al., 2024
	Its leaf extract has noticeable application in dental treatments, as the functional groups of its bioactive components have been found effective in reduction of silver ions, and inhibitory effects against tooth decay causing bacteria.	Subha et al., 2024
Skin health and wound healing	Its fruit extract is appropriate for the treatment of burn injuries.	Nayak et al., 2007 Gurung, Skalko-Basnet, 2009 Nayak et al., 2012 Balaji et al., 2016
	The antioxidant enzyme activity in its extracts can inhibit wound inflammation by regulating the expression of proinflammatory parameters and increase wound healing rate.	Nafiu, Rahman, 2015 Jarisarapurin et al., 2019
	Papaya seed extract has many potential bioactive molecules with positive effects for parasitic and bacterial skin infections.	Gnanamangai et al., 2022
	Papaya is a natural drug with both antiinflammatory and antibacterial activity, and papaya loaded poly (vinyl) alcohol (PVA)/Gelatin nanofibrous scaffold can be considered as an important candidate for wound healing.	Ahlawat et al., 2019
	Papaya loaded PVA/Gelatin nanofibers were validated by physico-chemical characterizations and used for wound dressing application.	Ahlawat et al., 2019
Other benefits		
Antifungal activity	Its plant extract can decrease rot in papaya fruit caused by *Cladosporium herbarum*.	Bello et al., 2022
	Hot and cold water leaf extract of papaya is effective in decreasing the growth of powdery mildew fungi on pepper plants.	Amadioha, 1998
Antimalarial (antimosquitoes) activity	Its leaves extract and the ethanol leaf extract have wonderful potential to be used as the appropriate approaches for the control of vector mosquitoes.	Kovendan et al., 2012
Biocidal-green inhibitor	Its peel extract has shown biocorrosion inhibition of mild steel in the crude oil-water environment.	Agarry et al., 2019
Insecticidal activity	Its chemical components such as alkaloid carpaine, rutin, kaempferol, quercetin, and the flavanol-glycosides quercetin can be used against the leaf-cutter ant (*Acromyrmex octospinosus*).	Lobo-Echeverri et al., 2020
Larvicidal activity	Its leaf extract has larvicidal activity against *Anopheles culicifacies*.	Olawuyi et al., 2014 Dwivedi et al., 2023
	Its latex was found useful for control of *Rhipicephalus microplus*.	Filgueiras et al., 2021
	Its extract at different concentrations can be used for the inhibition of egg hatch and mortality of larva of root-knot nematode, *Meloidogyne incognita*.	Bello et al., 2014

of type 2 diabetic animals, and papaya restored the normoglycemic impacts in diabetic skeletal muscle by increasing the expression of IRS-1 and Akt (Roy et al., 2022a,b).

Antioxidant activity

Antioxidants are important in increasing resistance against high production of free radicals in the body due to their capability to donate electrons which can neutralize radical formation. Three methods can be used to determine the total antioxidant activities of papaya such as radical scavenging assay and the ferric reducing antioxidant power (FRAP), the 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), and the 2,2′-dipehnyl-1-picrylhydrazul (DPPH) radical scavenging assay (Zhang et al., 2022).

On the basis of phytochemical analysis, there are high amounts of phenols and flavonoids in the flowers of papaya with antioxidant activity (Halder et al., 2022: Insanu et al., 2022). Its leaf is rich in kaempferol glucoside and quercetin derivatives, and its butanolic extract revealed significant antioxidant activities, and it is proved that chemical components which contain quercetin has more antioxidant activity than compounds with kaempferol and its glucoside derivatives (Kumar et al., 2022). Unripe *Carica papaya* fruit extract showed anticancer and antioxidant activities, and it showed cytotoxic impact against various cancer cells (Anadozie et al., 2022). Oloyede et al. (2015) showed that its extract significantly increased the percentage of ulcer inhibition and gastric pH, and the extract significantly reduced gastric acid output, gastric acidity, ulcer index, gastric pepsin secretion, and gastric secretion volume relative to group B, and this also reveals the aqueous extract of its seeds have antioxidant and antiulcerogenic effects. After evaluation of antioxidant effectiveness of unripe papaya extracts against EA.hy926 cells treated with Methylglyoxal, it is reported that pretreatment of the cell lines with unripe papaya inhibited Akt phosphorylation and decreased the expression of NF-kB-activated iNOS and COX-2 (Jarisarapurin et al., 2021). The pigment lycopene reacts with free radicals and oxygen (Sharma et al., 2020)

Anticancer activity

he papaya fiber is able of binding to toxins in the colon that can lead to cancer and hold these out from the normal healthy cells of the colon (Sani et al., 2022). These nutrients are capable of colon cells with synergistic protection against free-radical damage to their DNA (Nandini et al., 2021). Researches have shown that papaya leaf aqueous extracts suppress the growth of cancer cells, and the development of key signaling molecules named Th1-type cytokines, helps in stimulating the immune system (Alara et al., 2021). Its combination with moringa leaves can be used to slow tumor tissue growth and delay the production of cancer tissues (Arif et al., 2020; El-Sayed et al., 2020), and the medium polar fraction of leaf juice can prohibit metastatic PC-3 cells from adhering and migrating (Pandey et al., 2017). Maran et al. (2022) reported that quercetin molecule identified to be more stable with COX2, and COX2-quercetin complex shown to have more structural stability, and less flexibility, and on the basis of toxicity analysis, the quercetin can be considered as a main promising chemopreventive agent. The inhibitory effect of this fruit extract on the progression of both stable hematopoietic cell lines and tumor cell lines have now been confirmed by different scientific studies (Giron-Ramirez et al., 2021; Gaur et al., 2023). The enzyme papain inhibits cancer through the breakdown of fibrin in tumor cells (Sharma et al., 2020). Also, the alkaloidal extract of papaya has shown the notable protective activity against carbon tetrachloride-induced hepatocellular carcinoma (Kyei-Barffour et al., 2021).

Analgesic activity

The plant has been used experimentally as food or treatment for urinary tract disorders, kidney stones, hypertension, diarrhea, menstrual abdominal pain, analgesics, dysentery, and fever (Rivera et al., 2013). The analgesic effect of extracts of papaya leaves (n-hexane, ethyl acetate, and ethanol) was tested in the mouse model of pain caused by acetic acid (Siegmund method), and the results revealed that the ethanol extract is demonstrated the best analgesic activity compared to aspirin. The researchers reported that ethanol extract from CP leaves, which is an effective plant for the production of medicines for visceral pain (Ashour et al., 2018; Ojiako et al., 2019).

Hepatroprotective activity

The prophylactic and curative/restorative impacts of papaya water extract against CCl_4-induced hepatotoxicity in male rats is reported (Ojo et al., 2017; Shaban et al., 2023). The ethanolic and aqueous extracts of papaya against carbon tetrachloride (CCl_4) induced toxicity (Rajkapoor et al., 2002). It is revealed that the hepatoprotective effect of 100 and 300 mg/kg of extract obtained from unripe fruits and leaves of papaya, and its application can increase the levels of antioxidant enzymes and liver biomarkers (Awodele et al., 2016).

Antiinflammatory activity

The antiinflammatory activity of methanolic seed and pulp extracts of papaya is reported (Amin et al., 2019). The ability of papaya extract was assessed, and it is reported that papaya extract together with either zinc or selenium

can suppress inflammation (Nafiu, Rahman, 2015). The antiinflammatory activity of papaya showed that its reduction of carrageenan-induced paw oedema (Owoyele et al., 2008; Sun et al., 2025a,b,c). Application of papaya leaf extract noticeably showed that it can inhibit cytokines production and decreased the expression of cyclooxygenase-2 mRNA, and proteins in mice with autoimmune prostatitis (Jin et al., 2021). In another experiment, the antiinflammatory effects of papain isolated from papaya against obese mice is reported (Kang et al., 2021).

In the aqueous extract of papaya, novel bioactive components including benzyl glucosinolate were reported and showed antigrowth activities on several tumor cell lines (Oghenerukevwe et al., 2023). The antioxidant activities of papaya fruit extracts were tested in a cellular analysis. It was understood that appropriate evidence of the antioxidant activities of papaya fruit was given using cellular models of oxidative stress, discussed in a few reports already (Elsamadony et al., 2015; Agada et al., 2020). The results of the study suggested that papaya leaf is the main source of chemotherapeutic agents (anticancer compounds) and enocurage more scientific research to verify the conventional application of papaya leaf in the treatment of cancer (Zubairi et al., 2023). Its leaves can significantly suppress UVB-induced activation of activator protein-1 (AP-1) and mitogen-activated protein kinases (MAPKs) by scavenging reactive oxygen species (ROS), and its leaves prevented degradation of type I procollagen by significantly modulating transforming growth factor-β1 (TGF-β1) and negatively regulating MMPs (Seo et al., 2020). Different benefits of various parts of papaya are shown in Table 2.

OTHER BENEFITS

It is reported that the embryogenie calli cultured of *Carica papaya* L. in a liquid phase maturation medium can induce to noticeably higher frequency of somatic regeneration and embryogenesis than parallel treatments on agar-solidified medium (Castillo et al., 1998; Julaeha et al., 2015). The ethanol extract of papaya seeds caused reversible antifertility impacts in male rats which were dependent on the mode and duration of drug administration (Lohiya et al., 1992). Bataller et al. (2012) reported that papaya can be used as an alternative to Amistar fungicide for the control of shelf life, fungal pathogens growth, soluble solids content and seed germination percentage. In another experiment, it is shown that the proteolytic preparations derived from the latex of papaya could be applied for a cleaner technology in tanneries, either for sulphide- and lime-free dehairing or for the valorization and treatment of protein waste (Errasti et al., 2020). The dried papaya skin was found to give similar food conversion effectiveness, food consumption, survivability and meat yields to a control diet, and it can be useful in the diet of broiler

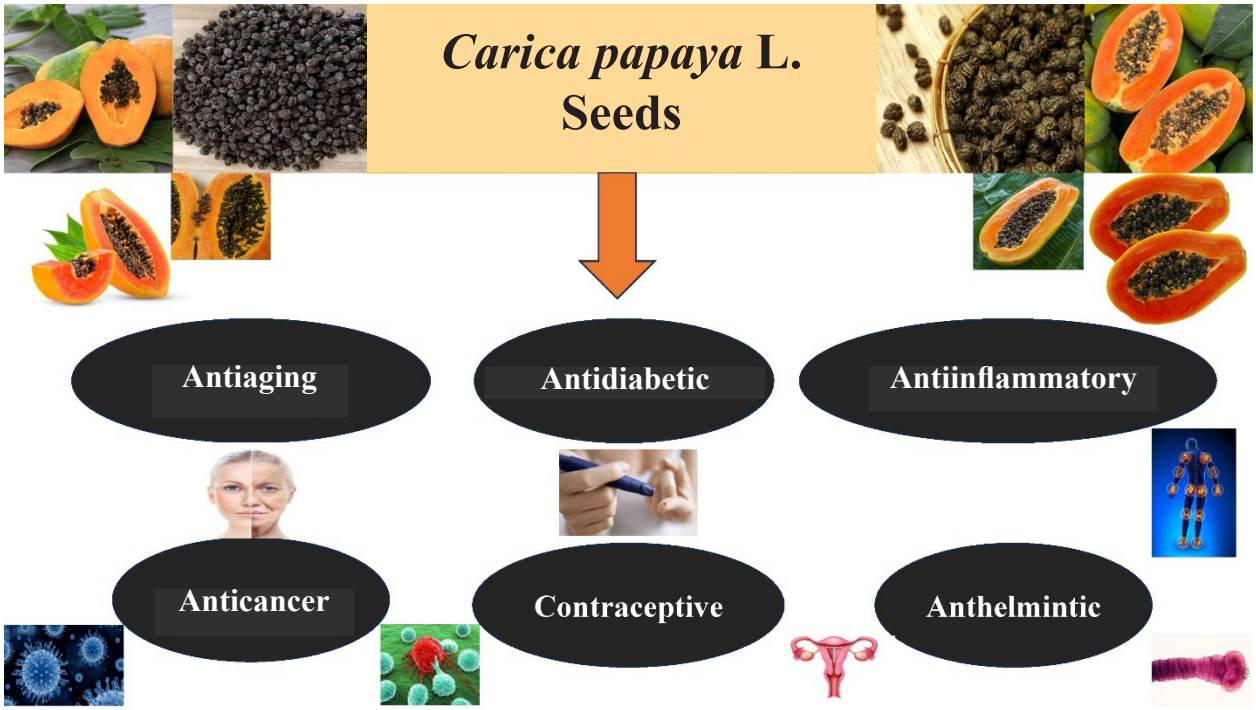


Figure 2. The most important health benefits of papaya seeds.

chickens (Kamaruzzaman et al., 2005). To maintain the nutritious and antioxidant characteristics of food throughout food processing, the food industry has largely considered new products (Shahrajabian et al., 2023). Fermented papaya is a product of yeast fermentation of the papaya fruit with seeds, and it is used in the Philippines and Japan as a dietary supplement to support immunity and digestion, especially in the elderly (Goriainov et al., 2023). Tropical fruits like pineapple, papaya, and mango, together with antioxidant-rich beverages like green and black teas grown in Reunion Island were chosen as substrates for lactic acid fermentation using autochthonous lactic acid bacteria (Chai et al., 2020; Chen et al., 2020; Ruas et al., 2022). A tau class glutathione *S*-transferase (GST) from papaya can catalyze the degradation of the fungicides thiabendazole and chlorothalonil (Wang et al., 2024). Hamid et al. (2022) reported that the papaya leaf extract is suggested as a feed additive to increase red hybrid tilapia fry growth. It is also reported that papaya seed can be used as a source of dietary antioxidants. Sodium bicarbonate and acetic acid treatment can increase papaya seed palatability, and they improved rheological properties of cornmeal porridges (Avila et al., 2020). Its stem can be considered as a feedstock for green catalyst, i.a. in biodiesel production (Gohain et al., 2020). Figure 2 shows the most important health benefits of its seeds.

CONCLUSION

Papaya is an important medicinal and economic plant with various pharmacological and nutritional benefits. Different parts of the plant such as seeds, fruits, roots, stem and leaves are used to treat different diseases in traditional medicinal sciences. This article reveals that papaya has anti-inflammatory, anticancer, antimicrobial, larvicidal, wound healing, antidiabetic, hepatoprotective, antihyperlipidemic, antiulcerogenic, anthelminthic and antithrombocytopenic activities. It also contains high amount of vitamin C and vitamin A, and various bioactive components with pharmacological activities. Different carotenoids such as cryptoxanthin, β carotene, zeaxanthin, and violaxanthin are found in fruits, various enzymes such as chymopapain A and B, papain are found in unripe fruit. Calcium, magnesium, potassium, zinc, copper, and iron can be found in leaves and shoots. Flavonoids such as kaempferol, myricetin, and quercetin are found in shoots, alkaloids such as carposide, choline, pseudocarpine, carpiane, and carpinine – in leaves and seeds. Moreover, vitamins such as ascorbic acid, niacin, riboflavin, and thiamine can be identified in booth leaves and shoots. Fruits contain high amounts of fructose, sucrose, and glucose. There are not enough researches and studies on pharmacological activities of different bioactive components isolated from papaya and there is still more researches and studies are needed to evaluate pharmacological benefits, and bioactive compounds of papaya.

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