



PHYTOCHEMISTRY AND MEDICINAL USES OF *CARICA PAPAYA* (LINN.): A REVIEW

Shweta Sharma¹ and Akshita Tiwari²

^{1,2}College of Biotechnology, DUVASU, Mathura, India (281001)

Email.id: shwetasharma.sls@gmail.com

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Abstract

The plant world is the gold mine of contemporary medicine because of the abundance of bioactive compounds and secondary metabolites it contains. In fact, it is a therapeutic and preventative dietary supplement that helps the body resist disease and age more gracefully. The papaya (*Carica papaya* L.), featured above, is an associate of the Caricaceae family and is widely regarded for its useful nutritional and therapeutic benefits around the world. Papaya's nutritional and medicinal value comes from its many parts, including its leaves, roots, skin, fruit, and seeds. It thrives in warm, humid climates and is widely distributed throughout the tropics and subtropics. This review aims to synthesize, by the end of 2022, data on papaya's functional activity culled from electronic sources, including Dimensions, Scopus, Google Scholar, Web of Science and Science Direct. Papaya is a good dietary supplement because of the wealth of research detailing the plant's utilization of many medicinal chemicals. Numerous vitamins, minerals, and enzymes, including papain, glycolendopeptidase, chymopapain, and caricain, can be found in plant extracts, notably those made from the fruits and leaves. These chemicals have anticancer actions; reduce inflammation, hyperglycemia, infertility, hypertension problems, and more thanks to their intriguing nutraceutical qualities. Papaya seeds peel, and leave have medical promise, but additional study is needed to determine dosage, mechanism of action, and safety profile. Therefore, this review urges the implementation of public health awareness initiatives to encourage the consumption of papaya so that the general public can reap the fruit's full potential in preventing and treating disease.

Keywords : Nutraceuticals, *Carica papaya*, Anticancer, Antimicrobial, Phytochemicals, Traditional medical system, Bio-pharmacological potency

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Introduction

Traditional medicine practitioners have relied on medicinal plants to cure a wide variety of illnesses since antiquity. This is because people are increasingly interested in "back to nature" practices and because herbal remedies are safer than synthetic ones. *Carica Papaya* Linn is a member of the *Carica* family of flowering plants. In its natural habitat, this plant can reach a height of 10 meters (Tona *et al.*, 1998). Jelly, sweets, jam, and pickles are just some of the processed forms in which papaya fruit finds a home in people's diets (Tan *et al.*, 2020). For many years, people in tropical and subtropical regions have relied on this plant's medicinal properties (Ali *et al.*, 2011; Singh *et al.*, 2019). The peels, roots, flowers, leaves, latex, fruits, and seeds of papaya plants all have useful nutritional and therapeutic properties. For this reason, agricultural science, food science, and preventative medicine can all contribute to the development of functional food plants employing cutting-edge technologies (Zeng *et al.*, 2022).

Papaya (*Carica papaya* L.) is a crucial crop and has great value consistent with some previous studies, processed papaya seeds have several important health benefits. All parts of the papaya, from the roots of the tree to the flowers,

leaves, fruit and seeds, have excellent medicinal properties (Lienny, 2013). Plants are rich during a sort of accessory metabolites like terpenoids, tannins, alkaloids and flavonoids, which are shown to possess antimicrobial properties in vitro.

According to scientific research (Alara *et al.*, 2022) there are a number of advantageous chemicals present in papaya leaves, including glycosides, alkaloids, flavonoids, saponins, amino acids, phenolic compounds, lipids, enzymes, vitamins, carbohydrates, and minerals. According to multiple studies (Singh *et al.*, 2019a; Nakamura *et al.*, 2007; Archampong *et al.*, 2019; and Juárez-Rojop *et al.*, 2012), both papaya seeds and leaves can help treat diabetes mellitus and its consequences (including liver disease and renal disease), hyperglycemia, infertility, amoebic dysentery, and tumor growth. There are many different types of phytochemicals in papaya, and it is thought that this is what gives the plant its therapeutic properties (Tan *et al.*, 2020; Archampong *et al.*, 2019; Wang *et al.*, 2020; Olcum *et al.*, 2020; Doan *et al.*, 2020; Singh *et al.*, 2019b; Odhong *et al.*, 2014).

Toxic waste, pesticides, environmental pollutants, medications, food preservatives, industrial chemicals, and so on are all examples of xenobiotics to which we are

continually exposed in our everyday lives (Patterson *et al.*, 2010). Chemicals those are rich in free radicals can damage membranes and cause various diseases (Pham-Huy *et al.*, 2008). They accommodate and set aside bioactive compounds involved in health promotion and immune insusceptible. Congestive heart failure, liver illness, cancer, dementia, diabetes, and aging-related functional decline account for around one-third of all deaths in the United States (Singh *et al.*, 2016a; Singh *et al.*, 2016b). Those can be treated with the right nutritional supplement. Research like this suggests that the abundant vitamins, antioxidants, and other phytochemicals found in plant-based nutraceuticals can greatly reduce the prevalence of chronic disease.

Due to their beneficial effects on health, nutraceuticals are in high demand. Foods and food additives that have therapeutic effects, such as preventing or slowing the development of disease, are known as nutraceuticals. Nutraceuticals called antioxidants can be found in many of the foods we eat. Most cells have two layers of defense against oxidative stress: an enzymatic component (such as glutathione peroxidase or superoxide dismutase) and a low molecular weight non-enzymatic antioxidant component (such as vitamins A, C, E, lutein, glutathione, quercetin), carotenoids, selenium, polyphenols, etc. (Singh *et al.*, 2013).

About 50,000 persons each day are lost to infectious diseases, making them the leading cause of death worldwide (Ahmad and Beg, 2001). The resistance of various infectious agents to synthetic drugs may be a major reason for the development of alternative antibiotics. In most cases, bacteria can genetically pass on and develop resistance to antimicrobial medicines (Cohen, 1992). Such data raises red flags because of the increased vulnerability of hospitalized patients with compromised immune systems and the emergence of novel, multi-resistant bacterial strains. This can lead to the spread of germs and an increase in hospital mortality rates. Antimicrobial resistance is a growing problem, and its future application seems cloudy at best.

From the past several years plants have been a invaluable source of genuine product for medical management, and research into natural health practitioner has intensified. The use of plant substances for pharmaceutical purposes has increased worldwide. As reported by World Health Organization, herbal medicinal products are the credible source for acquisition of various medicines (Santos *et al.*, 1995). About 80% of the world's population lives in developing countries and uses traditional remedies made of chemicals derived from medicinal plants. Therefore, research into such medicinal plants is warranted so that we may better comprehend their properties, safety, and efficacy (Ellof, 1998). However, the primary benefit of using plants as medication is that it is both effective and affordable (Pretorius and Walt, 2001).

Insight into the utilization of *Carica papaya* for treating epidemic disorders and the illumination of phytochemicals is provided by the anthologies reviewed in this review. Results from different preclinical and clinical studies, as well as the papaya leaf's chemical make-up and pharmacological activities, are discussed. In this article, we give the medical evidence that backs up the healthcare system's usage of papaya as an adjuvant medicinal herb.

Methodology

Chemical or nutritional composition; GI ulcers; antiparasitic; antibiotic; antifungal agents; hypoglycemia; diabetes; liver; kidney; were some of the search terms used to scour electronic databases (Scopus, Dimensions, ScienceDirect, Google Scholar, and Web of Science). Use the terms "papaya" and "*carica papaya*" in your search for results until December 2022.

Plant characterization

The initial location of the *Carica papaya* was the tropical region stretching from Mexico to Panama (Garrette, 1995). The plants can be either male or female, or hermaphrodites. Table 1 lists several medical uses for fruit, leaf, seed, and latex. Papain, an enzyme found in papaya's immature fruit, is used in the pharmaceutical, culinary, textile, and leather industries. Fresh papaya is popular, but it's also processed into beverages, preserves, and sweets (Singh and Sudhakar, 2011). The optimal temperature range for growing papaya is between 21 and 33 degrees Celsius, above 12 and 14 degrees Fahrenheit.

Table 1: Botanical classification of papaya (Krishna *et al.*, 2008)

Domain	Flowering plant
Kingdom	Plantae
Sub-kingdom	Tracheobionta
Class	Magnoliopsida
Sub-class	Dilleniidae
Division	Magnoliophyta
Super-division	Spermatophyte
Phylum	Steptophyta
Order	Brassicales
Family	Caricaceae
Genus	Carica
Botanical name	<i>Carica papaya</i> Linn

Phytochemical Composition of *Carica papaya*

Many different substances can be found in herbs, including antioxidants, nutrients (such as carotene, flavonoids, vitamin C, etc.), B vitamins (such as pantothenic acid, etc.), metals (such as potassium, magnesium, etc.), and fiber. Alkaloids, calpains, pseudocalpains, caprosides, choline, and dehydrocalpains are only some of the compounds that can be found in papaya leaves, along with vitamins C and E. Table 2 lists some of the minerals, vitamins, volatile compounds, alkaloids, and glycosides that can be found in fruits. Milk is produced because this plant has milk cells, which exude latex (milk material) and transport it to all of the plant's tissues. The amount of latex in fruits, roots, and leaves varies, as noted by Azarkan *et al.* (2003). There are fewer latex-producing lactate cells in a mature papaya. Raw papaya fruit is the primary source of papain, a proteolytic enzyme (Drenth *et al.*, 1968). Vitamin C, vitamin A, and vitamin E, as well as the minerals K and Mg, can all be found in abundance in papaya. High in fiber and plenty of B vitamins like B5 and folic acid (Wall, 2021). Benzyl isothiocyanate, calpain, fatty acids, protein, fiber, myrosine enzymes, and carcaine are only some of the compounds found in theseeds.

Table 2: Phytochemicals and pharmacological properties of various parts of the *C. papaya*

Parts of Plant	Phytochemicals	Papain, chymopapain, cystatin, tocopherol, alkaloid carpain, dihydrocarpain I and II, carposide, vitamin C and E
1. Leaves	Phytochemicals	
	Pharmacological properties	Antibacterial, antiviral, antitumor, hypoglycemic, anti-inflammatory, anti dengue (Singh et al., 2020) antimalarial (Fatima and Shahid 2018) Anticancer, Antiproliferative, Antimetastatic (Pandey et al., 2018) gonorrhoea, fracture healing, indigestion, yellow fever, tonsillitis, ulcers, stomatitis, constipation (Priyadarshi and Ram 2018) sickle cell anemia (Upko et al., 2016)
2. seed	Phytochemicals	Benzyl isothiocyanate, carpain, myrosin enzymes, carcaine, fatty acid, protein and fibers
	Pharmacological properties	Nephroprotective Activity (Fatima and Shahid 2018) Antifertility, Anthelmintic, Anti-inflammatory, Analgesic (Anitha et al., 2018) Antimicrobial, Antioxidant Diabetes Mellitus Typhoid (Yogiraj et al., 2015) Antiparasitic Activity (Saba and Pattan 2022), Anticancer (Ejeh et al., 2022)
3. Flower	Phytochemicals	Phalobatanine, flavinoids
	Pharmacological properties	Antioxidant, Cytotoxic (Sianipar et al., 2018), Anti-Helminthic, Diarrhea, Anti-inflammatory, Anti-Sickling Activity, Anticoagulant Effect (Yogiraj et al., 2015)
4. Fruit	Phytochemicals	Ascorbic acid, fibers, sugar, protein, fiber, , riboflavin, niacin, and carotene, amino acid, citric acid and malic acid (green fruit), mineral: calcium, phosphorous, Iron, vitamin C, thiamine volatile compound: benzyl isothiocyanate, cis and trans 2,6- dimethyl-3,6 epoxy-7 octen2-ol
	Pharmacological properties	Anthelmintic, Anti Protozoan, Antibacterial, Antifungal, Antiviral, Free Radical Scavenging, Anti-Sickling, Neuroprotective, Diuretic, Hypoglycemic, Hypolipidemic, Antihypertensive, Antitumor, Antifertility, Anticancer, Stroke Prevention, Antiulcer, Blood Cholesterol Control (Anitha et al., 2018) Antioxidant Activity (Abhishek et al., 2020)

Bio-pharmacological potency of *C. Papaya*

Because of its excellent nutritional and therapeutic value, papaya has become increasingly important commercially as a tropical fruit. According to numerous scientific studies, it is an effective treatment for a wide range of medical issues, such as hypertension, digestive issues, constipation, warts, sinus infections, and infections of all kinds, diabetes, inflammation, cancer, and even malaria. Papaya is an excellent source of nourishment, and it may be preserved indefinitely with careful portioning and use. Papain, an enzyme found in the liver, is highly successful in treating the underlying causes of allergies, injuries, and sports injuries. There are several pharmacological effects associated with this plant, including those that fight cancer, bacteria, dengue fever, reduce fever, kill insects, ward off mosquitoes, and heal wounds. The following are examples of some of these:

Antioxidant efficacy

Bioactive compounds in *C. papaya* operate as antioxidants and/or free-radical scavengers, blocking the harmful effects of reactive oxygen species in molecules. Exogenous antioxidant consumption from animal or vegetable sources can benefit the body by efficiently scavenging free radicals, as revealed by Singh and Singh (2018). The antioxidant activity of papaya leaf methanolic extract was determined by its capacity to scavenge free radicals (DPPH), as reported by Singh *et al.*, 2020. Hexane extract of papaya seeds had the highest DPPH elimination capacity, while aqueous extract had the lowest (Shen *et al.*, 2018). According to Sadak (2012), combining papaya extract with acrylamide effectively restored the enzyme's activity across all tissues. This is because papaya includes phytochemicals that function as antioxidants, such as vitamins C, beta-carotene, lycopene, and vitamin E, and so

decreases the body's reliance on these enzymes to fight oxidative stress.

Anticancerous effect

As a result of an unchecked cell cycle, an abnormal increase in tissue mass occurs, giving rise to tumors (Maka *et al.*, 2018). Tumors, whether benign or malignant, result from uncontrolled cell development. Many human diseases have had a reduced incidence thanks to the use of plants and plant derivatives since ancient times. According to Tripathi and Tripathi (2003), nearly 80% of the world's population relies only on plants for primary medical care. Due to its high caloric content and year-round availability, papaya is frequently utilized as an herbal remedy for humans. Phytochemicals found in certain papaya portions have been shown to eliminate cancer-causing toxins from the colon by binding to them. Phytochemical extracts have been proven to have anti-cancer properties in human and animal studies (Singh *et al.*, 2016). In particular, *C. papaya* leaf extract has shown anticancer efficacy against breast cancer (Otsuki *et al.*, 2010; Mahendran *et al.*, 2021). Multiple studies have demonstrated that *C. papaya* extract is effective in treating a wide range of malignancies, including those of the breast, liver, blood, pancreas, skin, and prostate (Parray *et al.*, 2018; Sumana *et al.*, 2019).

Ethanol in papaya leaf extract boosts cancer cell apoptosis and improves the cancer cell proliferation index in a cervical cancer animal model. This may also increase the expression of the P-53 gene and nuclear factor kappa (Peristiowati *et al.*, 2019). Papaya seed extracts, both aqueous and methanolic, may inhibit the proliferation of human breast cancer cells (Ejeh *et al.*, 2022). The papain enzyme found in this plant has been shown to inhibit cancer growth. Papain protects tumor cells from damage and degrades fibrin into amino acids. Isothiocyanates found in papaya have been shown to inhibit the growth of certain

cancers (Wadekar *et al.*, 2021). These include breast cancer, prostate cancer, pancreatic cancer, lung cancer, leukemia, and colon cancer. Evidence from this research suggests that papaya may be useful as part of a treatment strategy for combating cancer by inhibiting the growth of tumors.

When multiple human cancer cell lines were treated with extracts of papaya leaves, seeds, and peel, the results revealed a reduction in the formation of tumors, the induction of apoptosis, as well as an inhibition of cell proliferation and metastasis. The anti-tumor activity of seed, leaf, and bark extracts can be attributed to the presence of bioactive phytochemicals. Some examples of these include benzyl isothiocyanate (BITC), phenols, carotenes, glucosinolates, flavonoids, tocopherol, and lycopene.

Antidiabetic activities

Type 1 diabetes occurs when the pancreas does not create enough insulin (Roglic, 2016), while type 2 diabetes occurs when the body does not efficiently use the insulin it produces, leading to low blood sugar levels and the accumulation of glucose in the blood. Increasing numbers of people are developing diabetes nowadays because of things like being overweight, eating poorly, not exercising, getting older, and not getting enough food. There were 285 million people with diabetes in 2010, and that figure is expected to rise to 439 million by 2030 (Shaw *et al.*, 2010). Type 2 diabetes has shown a remarkable increase in prevalence and is now affecting youngsters for the first time in decades (WHO, 2004). Complications from any form of diabetes include the need for amputations, damage to nerves, kidney failure, blindness, and heart attacks. R. Hillson (2019) reports on new research into the use of several herbs for the treatment and management of diabetes and its symptoms. Papaya leaf extract was shown to have antihyperglycemic and hypolipidemic properties in diabetogenic Wistar rats (Juárez-Rojop *et al.*, 2014; Sasidharan *et al.*, 2011). Additionally, the lipid profile was enhanced and both basal and postprandial blood glucose levels were reduced when the fermented papaya fruit was administered (Aruoma *et al.*, 2014). Regenerating pancreatic beta cells and elevating insulin secretion are two of the mechanisms via which flavonoids, quercetin, steroids, quinones, and kaempferol are believed to have considerable hypoglycemic characteristics (Juárez-Rojop *et al.*, 2014).

Papaya seeds, leaves, and peel have shown promise as an anti-diabetic treatment in a small number of studies. To learn more about the hypoglycemic and antidiabetic properties of papaya seeds, leaves, and peel, more research is required to identify the bioactive phytochemicals.

Hepatoprotective efficacy

In the tropics, papaya is commonly used as an all-natural treatment for stomach upset. Patients suffering from post-meal heartburn, constipation, and irritable bowel syndrome (IBS) have benefited from eating papaya, according to clinical studies. The oxidative stress in the liver was found to be greatly reduced by eating papaya seeds (Sadeque *et al.*, 2012 and Raj Kapoor *et al.*, 2002). Green papaya leaves are used to brew the tea. Benefits digestion and reduces the risk of developing or aggravating conditions like high blood pressure, atherosclerosis, and heart disease. Green papaya leaves are used to brew the tea. Benefits digestion and reduces the risk of developing chronic

conditions like heart disease, high blood pressure, and diabetes (Montok, 2005). Hepatoprotective benefits of dried papaya extracts against CCl₄-induced hepatotoxicity in rats were observed in both the aqueous and ethanolic forms. Papaya extracts, both aqueous and ethanolic, were found to have hepatoprotective properties against CCl₄-induced hepatotoxicity in rats (Sadeque *et al.*, 2012), in contrast to vitamin E. Alkaline phosphatase levels were shown to be significantly altered by C. papaya, but vitamin E was found to have no effect on CCl₄-induced hepatotoxicity.

Gastroprotective efficacy

Millions of individuals throughout the world suffer from gastrointestinal illnesses, and ulcers are one of them. When stomach acid or pepsin is secreted in excess amounts, it can erode the lining of the stomach or duodenum, causing a gastrointestinal ulcer (GIU). The lifetime chance of developing a gastrointestinal ulcer is 5–10% (Nilugal *et al.*, 2018), making this a worldwide health issue. Several in vivo investigations have shown that papaya extract, namely papaya seed extract (PSE), in stomach ulcers (Oloyede *et al.*, 2015), has gastroprotective benefits. Papaya leaf extract (PLE) significantly decreased acute gastrointestinal ulceration and oxidative stress in rats exposed to alcohol, according to research published in 2008 by Indran *et al.* In another study, 32 male mice with ethanol-induced stomach ulcers were given PSE (Okewumi and Oyeyemi, 2012). They hypothesized that PSE prevented alcohol-induced mucosal damage. Ezike *et al.* (2009) used indomethacin- and ethanol-induced ulcer models in mice to demonstrate that both aqueous (AE) and methanol (ME) extracts from entire immature papaya fruit have anti-ulcer properties.

Kalpains, found in papaya leaves, are substances that kill germs that typically interfere with digestive function. A double-blind, placebo-controlled study of the papaya product Caricol® demonstrated that it aids in the maintenance of gastrointestinal physiology (Muss *et al.*, 2013). Constipation, heartburn, and IBS symptoms are just a few of the functional issues it helps with. Green papaya leaf tea aids digestion and is beneficial for conditions including chronic indigestion, excess weight, obesity, atherosclerosis, hypertension, and heart failure." (Mantok, 2005) "The preceding summary suggests that the papaya plant may help treat and prevent gastroduodenal ulcers in experimental animal models.

Antibacterial activity

The seeds of the *Carica papaya* tree possess an edible quality and exhibit a pungent and acidic flavor profile. The results of this study suggest that the seeds of *Carica papaya* possess antibacterial characteristics, rendering them effective in the treatment of ailments caused by *Escherichia coli*, *Staphylococcus*, and *Salmonella*. Chandra *et al.* (2011) identified that *C. papaya* extracts, specifically in aqueous, n-hexane, and ethanol, were efficacious against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus*. The aqueous extract exhibited the highest efficacy against *Bacillus subtilis*, *Staphylococcus aureus*, and *Escherichia coli*, whereas the ethanol and n-hexane extracts demonstrated the highest efficacy against *Staphylococcus aureus*. The elimination of intestinal parasites is feasible, and the antibacterial characteristics of *C. papaya* seeds have been demonstrated in research conducted by Arvind *et al.* (2013). Mangalanayaki and Nirosha (2013)

discovered through the utilization of the diffusion method that *C. papaya* leaf exhibited antibacterial properties against *Streptococcus pneumoniae*, *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. According to Tewari *et al.* (2014), the antibacterial properties of methanolic *C. papaya* leaf extract were observed against *Candida albicans*, *Escherichia coli*, and *Staphylococcus aureus*. According to Emeruwa A.C. (1982), there exists a hypothesis suggesting that the inhibition of bacterial growth by *C. papaya* is attributed to the modification of their cellular morphology, resulting in the formation of irregular cell walls.

Antifungal activity

The skin, nails, reproductive system, digestive system, cardiovascular system, and neurological system are only some of the many human bodily systems that fungi can negatively impact (He *et al.*, 2017). For immunocompromised patients, fungal infections like candida can be life-threatening (Morace *et al.*, 2014). Some antifungal medicines have proven to be hazardous and result in substantial adverse effects on patients (Laniado-Laborn and Cabrales-Vargas, 2009), yet the use of broad-spectrum antifungal drugs has increased (Sheikh *et al.*, 2018). Scientists have taken notice, and they're investigating the natural remedy's efficacy against fungal infections (Rahmani and Aldebasi, 2016).

Candida albicans, *Aspergillus flavus*, *Penicillium citrinium*, *Coletotrichum gloosporioides*, and *Fusarium* spp. are all killed by aqueous and alcoholic extracts of papaya seeds, leaves, peels, and roots (He *et al.*, 2017; Chávez-Quintal *et al.*, 2011). Leaf extracts can be used for a variety of purposes. For *Fusarium* spp., the MIC₅₀ for PLE was 0.625 mg/mL, but for *C. gloeosporioides*, it was greater than 10 mg/ml (Chávez-Quintal, 2011). The antifungal effects of PSE, the breakdown of mitochondrial membrane potential (MMP), and the reduced activity of mitochondrial respiratory chain enzymes may all be attributable to the formation of oxygen radicals (Zhang and Chen *et al.*, 2017).

Anti-dengue effect

Between 50 and 100 million people are diagnosed with dengue fever every year. Dengue virus (DENV) 1-4 is what causes dengue fever, and the mosquito *Aedes aegypti* is its primary vector. Herbal therapy is another option for treating Cyclospora-caused dengue fever. Extracts from papaya leaves dramatically raised low platelet counts associated with dengue fever. Important components found in papaya leaves maintain membranes, shield blood cells from stress-induced damage, and stop platelet lysis in dengue patients, according to research by Ranasinghe *et al.* in 2012. Patients infected with the dengue virus may benefit from treatment with papaya leaf juice, according to research published in 2012 by Ranasinghe *et al.* An *in vitro* hemolysis test suggested that papaya leaf extract might be able to stabilize membranes.

Other Benefits of Papaya

- As an acne remedy
- Stimulates appetite,
- Relieves menstrual cramps,
- Relieves nausea
- As laxative

- Fight against Dandruff etc.

Conclusion

In terms of nutrition, medicine, and nutraceuticals, the *Carica papaya* is among the most vital fruits. Many cancer-related diseases and disorders can benefit from using papaya as a dietary supplement. Anticancer agents, gastroprotectants, antioxidants, antifungal agents, antiparasitic agents, hypoglycemic activity, antibacterial activity, contraceptive activity, and hepatoprotective activity are just some of the bioactive compounds found in *C. papaya* that have been the focus of numerous studies around the world. There is preliminary evidence that papaya dietary supplements can help with everything from common colds to deadly diseases. More research is needed to verify the primary mechanism of action of the papaya leaves' therapeutic phytochemicals. Papaya leaf extract has been shown in multiple tests to reduce blood sugar and slow the spread of cancer cells. It was also determined that there were various holes in the existing literature on bioagents derived from papaya (seed, peel, and leaf). It is important to use recently established models to verify its safety profile as a dietary supplement and to illustrate its alleged biological mechanism.

There is a dearth of information about the bioactive compounds and metabolites in papaya, including their identification, characterization, and pharmacokinetics. More research is required to determine how papaya biologics and their metabolites affect pharmacodynamics. The potential of *C. papaya* seeds, peels, and leaves as functional foods is discussed in this review, which focuses on these bioactives' different nutraceutical effects.

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References

- Agada, R., Usman, W.A., Shehu, S. and Thagariki, D. (2020). *In vitro* and *in vivo* inhibitory effects of *Carica papaya* seed on α -amylase and α -glucosidase enzymes Heliyon, 6 (3).
- Ahmad, I. and Beg, A. (2001). Antimicrobial and phytochemicals studies on 45 indian medicinal plants against multidrug resistant human pathogens Ethnopharm. 74(87): 113-23.
- Alara, O.R., Abdurahman, N.H. and Alara, J.A. (2022). *Carica papaya*: comprehensive overview of the nutritional values, phytochemicals and pharmacological activities, *Advances in Traditional Medicine*, 22: 17–47.
- Ali, A., Devarajan, S., Waly, M., Essa, M.M. and Rahman, M. (2011). Nutritional and medicinal value of papaya (*Carica papaya* L.),” in *Natural Products and Bioactive Compounds in Disease Prevention*. Nova Science Publishers, pp. 34-42.
- Anitha, B., Raghu, N., Gopenath, T.S., Karthikeyan, M., Gnanasekaran, A., Chandrashekrappa, G.K. and Basalingappa, K.M. (2018). Medicinal Uses of *Carica papaya*. *J Nat Ayu Med.*, 2(6): 000144.
- Aravind, G., Bhowmik, D., Duraivel, S. and Harish, G. (2013). Traditional and Medicinal Uses of *Carica papaya*. *J Med Plants Stud*, 1:7-15.

- Archampong, T.N., Asmah, R.H., Richards, C.J., Martin, V.J., Bayliss, C.D., Botão, E., David, L., Beleza, S. and Carrilho, C. (2019). Gastro-duodenal disease in Africa: literature review and clinical data from accra, *Ghana World J. Gastroenterol.*, 25(26): 3344-3358.
- Aruoma, O.I., Somanah, J., Bourdon, E., Rondeau, P. and Bahorun, T. (2014). Diabetes as a risk factor to cancer: functional role of fermented papaya preparation as phytonutraceutical adjunct in the treatment of diabetes and cancer. *Mutat. Res.*, 768 (C).
- Azarkan, A.M., Moussaoui, E., Wuytswinkel, D. van, Dehon, G., Looze, Y. (2003). Fractionation and purification Analyt Technol of the enzyme stored in the latex of *Carica papaya*. *J Chromatogr B Biomed Appl*, 790: 229-238.
- Azevedo, L. and Campagnol, P. (2014). Papaya seed flour (*Carica papaya*) affects the technological and sensory quality of hamburgers, *Int. Food Res. J.*, 21(6): 2141.
- Bushra, I., Fozia Abdul, W., Ali, R., Ullah, H., Iqbal, H., Almas, M. and Ahmad, A. (2012). Antimicrobial activity of *Malvaneglecta* and *Nasturtium microphyllum*. *Int J Res Ayurveda Pharm*, 3: 808-810.
- Chandra, G., Bhattacharjee, I., Chatterjee, S.K. and Ghosh, A. (2011). Antibacterial activities of some plant extracts used in Indian traditional folk medicine. *Asian Pac J Trop Biomed*, S165-S169.
- Chávez-Quintal, P., González-Flores, T., Rodríguez-Buenfil, I., Gallegos-Tintoré, S. (2011). Antifungal activity in ethanolic extracts of *Carica papaya* L. cv. Maradol leaves and seeds. *Indian J. Microbiol.*, 51(1): 54-60.
- Cohen, M.L. (1992). Epidemiology of drug resistance: implications for a postantimicrobial era. *Science*, 257: 1050-1055.
- Doan, M.T.N., Huynh, M.C., Pham, A.N.V., Chau, N.D.Q., Le, P.T.K. (2020). Extracting seed oil and phenolic compounds from papaya seeds by ultrasound-assisted extraction method and their properties, *Chem. Eng. Trans.* 78: 493-498.
- Drenth, J., Jansonius, J.N., Koekoek, R., Wolthers, H.M. (1968). Structure of papain. *Nature*, 218: 929-932.
- Ejeh, E., Dan, V.M., Dikwa, K.B. and Mshelia, A.S. (2022). Assessment of the effects of ripe *Carica papaya* seeds extracts on MCF-7 Breast cancer cell lines. *ISOR J Biotech Biochem*, 8(1): 12-1.
- Ellof, J.N. (1998). Which extractant should be used for the screening and isolation of antimicrobial components from plants? *J. Ethnopharmacol.* 60: 1-6.
- Emeruwa A.C. (1982). Antibacterial substance from *Carica papaya* fruit extract. *J. Nat. Prod.*, 45(2): 123-127.
- Ezike, A.C., Akah, P.A., Okoli, C.O., Ezeuchenne, N.A., Ezeugwu, S. (2009). *Carica papaya* (Paw-Paw) unripe fruit may be beneficial in ulcer. *J. Med. Food*, 12(6): 1268-1273.
- Fatima, U. and Shahid, S. (2018). Pharmacological Activities of *Carica papaya* Linn. *J Basic Appl Sci*, 14: 210-216.
- Garrett, A. (1995). The pollination biology of papaw (*Carica papaya* L.) in Central Queensland. PhD Thesis, Central Queensland University, Rockhampton, 125 pp.
- He, X., Ma, Y., Yi, G., Wu, J., Zhou, L., Guo, H. (2017). Chemical composition and antifungal activity of *Carica papaya* linn. Seed essential oil against *Candida* spp. *Lett. Appl. Microbiol.*, 64 (5) (2017), pp. 350-354.
- Hillson R. Herbs and Diabetes, 36, John Wiley & Sons (2019), pp. 159-160.
- Indran M., Mahmood A.A. , Kuppusamy U.R.(2008). Protective effect of *Carica papaya* L leaf extract against alcohol induced acute gastric damage and blood oxidative stress in rats. *West Indian Med. J.*, 57(4): 323-326.
- Juárez-Rojop, I.E., Díaz-Zagoya, J.C., Ble-Castillo, J.L., Miranda-Osorio, P.H., Castell-Rodríguez, A.E., TovillaZárate, C.A., Rodríguez-Hernández, A., AguilarMariscal, H., Ramón-Frías, T., Bermúdez-Ocaña, D.Y. (2012). Hypoglycemic effect of *Carica papaya* leaves in streptozotocin-induced diabetic rats. *BMC Complementary and Alternative Medicine*; 12: 236.
- Krishna, K.L., Paridhavi, M. and Patel, J.A. (2008). Review on nutritional, medicinal and pharmacological properties of papaya (*Carica papaya* Linn.). *Natural Product Radiance* 7(4): 364-373.
- Laniado-Laborín, R. and Cabrales-Vargas, M.N. (2009). Amphotericin B: side effects and toxicity. *Rev. Iberoam. Micol*, 26(4): 223-227.
- Mahendra, C.G. and Nikhil, D.A. (2016). Nutritional, medicinal and pharmacological properties of papaya (*Carica papaya* linn.): a review *J. Innov. Pharm. Biol. Sci.*, 3(1): 162-169.
- Mahendran, V.S., Sophiya, K., Sruthimalvika, S., Suganthi, B. and Sujitha, E. (2021). *Carica papaya*: Anticancer activity in MCF-7 Breast cancer cell lines. *Int J Pharm Sci Res*, 12(1): 176-182.
- Maka, K.K., Tana, J.J., Marappana, P., Balijepallib, M.K., Choudhury, H., Ramamurthy, S., Pichika, M.R. (2018). Galangin's potential as a functional food ingredient. *J. Funct. Foods*, 46: 490-503.
- Mantok, C. (2005). Multiple Usage of Green Papaya in Healing at Tao Garden. Tao Garden Health spa & Resort. Thailand.
- Morace, G., Perdoni, F. and Borghi, E. (2014). Antifungal drug resistance in *candida* species. *J. Glob. Antimicrob. Resist.* 2(4): 254-259.
- Mulyono, L.M. (2013). Antibacterial activity of papaya (*Carica papaya* L.) seed ethanol extract against *Escherichia coli* and *Staphylococcus aureus*, *Jurnal Ilmiah Mahasiswa Universitas Surabaya*, 2(2): 1-9.
- Muss C, Mosgoeller W, Endler T. (2013). Papaya preparation (Caricol) in digestive disorders. *Neuro Endocrinol Lett.*, 34: 38-46.
- Nakamura, Y., Yoshimoto, M., Murata, Y., Shimoishi, Y., Asai, Y., Park, E.Y., Sato, K., Nakamura, Y. (2007). Papaya seed represents a rich source of biologically active isothiocyanate. *J. Agric. Food Chem.*, 55(11): 4407-4413.
- Nilugal, K., Fattedpur, S., Veerapandian, V., Asmani, F., Bacayo, M., Abdulah, I., Yusuf, E. (2018). Evaluation of anti-ulcer effect of papaya juice in combination with cumin seed in ethanol induced peptic ulcers in experimental rats. Proceedings of the Bromo Conference, Symposium on Natural Products and Biodiversity, p. 94.
- Oche, O., Rosemary, A., John, O., Chidi, E., Rebecca, S.M. and Vincent, U.A. (2017). Chemical constituents and nutrient composition of *Carica papaya* and *Vernonia amygdalina* leaf extracts. *J. Complement. Altern. Med. Res.*, 1-8.
- Odhong, C., Wahome, R.G., Vaarst, M.S., Nalubwama, W., Kiggundu, M., Halb, N., Githigia, S. (2014). *In vitro*

- anthelmintic effects of crude aqueous extracts of *Tephrosia vogelii*, *tephrosia villosa* and *Carica papaya* leaves and seeds, *Afr. J. Biotechnol.* 13(52): 4667–4672.
- Okewumi, T.A. and Oyeyemi, A.W. (2012). Gastro-protective activity of aqueous *Carica papaya* seed extract on ethanol induced gastric ulcer in male rats. *Afr. J. Biotechnol.*, 11(34): 8612-8615.
- Olcum, M., Tastan, B., Ercan, I., Eltutan, I.B. and Genc, S. (2020). Inhibitory effects of phytochemicals on NLRP3 inflammasome activation: a review, *Phytomedicine*. 75: 153-238.
- Oloyede, H.O.B., Adaja, M.C., Ajiboye, T.O., Salawu, M.O. (2015). Anti-ulcerogenic activity of aqueous extract of *Carica papaya* seed on indomethacin-induced peptic ulcer in male albino rats. *J. Integr. Med.*, 13(2): 105-114.
- Otsuki, N., Dang, N.H., Kumagai, E., Kondo, A., Iwata, S. and Morimoto, C. (2010). Aqueous extract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effects. *J Ethnopharmacol*, 127: 760-767.
- Pandey, P., Walpole, C., Shaw, P.N., Cabot, P.J., Hewavitharana, A.K. and Batra, J. (2018). Bio-Guided Fractionation of Papaya leaf juice for Delineating the Components Responsible for Selective Anti-proliferative Effects on Prostate Cancer cells. *Front Pharmacol*, 9: 1319.
- Parray, Z.A., Parray, S.A., Khan, J.A., Zohaib, S., Nikhat, S. (2018). Anticancer activities of papaya (*Carica papaya*): A review. *Cell Ortho Med Pharma Assoc*, 8(4):201-205.
- Patterson, A.D., Gonzalez, F.J. and Idle, J.R. (2010). Xenobiotic metabolism: a view through the metabolometer. *Chem Res Toxicol.*, 23(5): 851- 860.
- Peristiowati, Y., Puspitasari, Y., Indasah (2019). Effects of Papaya leaf Extract on Cellular Proliferation and Apoptosis in Cervical cancer Mice model. *Phytothérapie*, 17: 265-275.
- Pham-Huy, L.A., He, H., Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. *Int J Biomed Sci*, 4(2):89-96.
- Pretorius, C. and Walt, E. (2001). Purification and identification of active compound of *Carpobrotus edulis* L. *J. Ethnopharm.*, 76: 87–91.
- Priyadarshi, A. and Ram, B. (2018). A Review on pharmacognosy, phytochemistry and pharmacological activity of *Carica papaya* leaf. *Int J Pharm Sci Res*, 9(10): 4071-4078.
- Rahmani, A.H. and Aldebasi, Y.H. (2016). Potential role of *Carica papaya* and their active constituents in the prevention and treatment of diseases. *Int. J. Pharm. Pharm. Sci.*, 8(1): 11-15.
- Raj Kapoor, B., Jayakar, B. and Kavimani, S. (2002). Effect of *Carica papaya* on hepatotoxicity. *Biol Pharm Bull.*, 25: 1645-1646.
- Ranasinghe, P., Abeyesekera, W.P., Permakumara, G.A., Perera, Y.S., Gurugama, P., Guanatilake, S.B. (2012). *In vitro* erythrocyte membrane stabilization properties of *Carica papaya* L. leaf extract. *Pharmacogn Res*, 4(4): 196-202.
- Roglic, G. (2016). WHO global report on diabetes: a summary. *Int. J. Non Commun. Dis.*, 1: 3-8.
- Saba, S. and Pattan, N. (2022). The Potential Health Benefits of Papaya Seeds. *Int J Res Appl Sci Eng Tech*, 10(1): 44-50.
- Sadeque, M.Z., Begum, Z.A., Umar, B.U., Ferdous, A.H., Sultana, S., Uddin, M.K. (2012). Comparative efficacy of dried fruits of *Carica papaya* Linn. And Vitamin E on preventing hepatotoxicity in rats. *Faridpur Med Coll J*; 7: 29-32.
- Santos, P.R.V., Oliveira, A.C.X., Tomassini, T.C.B. (1995). Controle microbiológico de produtos fitoterápicos. *Rev. Farm. Bioquím.* 31: 35-38.
- Sasidharan, S., Sumathi, V., Jegathambigai, N.R. and Latha, L.Y. (2011). Antihyperglycaemic effects of ethanol extracts of *Carica papaya* and *Pandanus amaryfollius* leaf in streptozotocin-induced diabetic mice. *Nat Prod Res*, 25(20): 1982-1987.
- Shaw, J.E., Sicree, R.A. and Zimmet, P.Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res. Clin. Pract.* 87(1): 4-14.
- Sheikh, N., Jahagirdar, V., Kothadia, S. and Nagoba, B. (2018). Antifungal drug resistance in candida species, pp. 254-258.
- Shen, W., Han, J., Yan, P. *et al.* (2018). Soluble expression of biologically active methionine sulfoxide reductase B1 (PaMsrb1) from *Carica papaya* in *Escherichia coli* and isolation of its protein targets, *Protein Expression and Purification*, 146: 17–22.
- Sianipar, M.P., Suwarso, E., Roshidah, R. (2018). Antioxidant and Anticancer Activities of Hexane fraction from *Carica papaya* L. Male Flower. *Asian J Pharm Clin Res*, 11(3): 81-83.
- Singh, P., Kakkar, P., Singh, R.L. (2016). Protective Effect of *Trigonella foenum-graecum* and *Foeniculum vulgare* Mature Leaf Against tBHP induced Toxicity in Primary Rat Hepatocytes. *J Exp Food Chem.*, 2: 111.
- Singh, P., Singh, R.L. (2018). Quantification of Phytochemicals Imparting Antioxidant Activities in Commonly Used Vegetables. *Int J Appl Sci Biotech*, 6(2):107-112.
- Singh, P., Singh, R.L. and Kakkar, P. (2016). Antioxidant, DNA Damage Protective and hepatoprotective Activities of *Amorphophallus campanulatus*. *Int J Pharm Pharm Sci*, 8(3): 330-338.
- Singh, P.G., Madhu, S.B., Shailasresekhar, G.T.S., Basalingappa, K.M. and Sushma, B.V. (2020). *In vitro* antioxidant, anti-inflammatory and anti-microbial activity of *Carica papaya* seeds, *Global Journal of Medical Research*, 20: 19–38.
- Singh, S., Sharma, B., Kanwar, S.S., Kumar, A. (2016). Lead phytochemicals for anticancer drug development. *Front. Plant Sci.*, 7: 1667.
- Singh, S.P. and Sudhakar Rao, D.V. (2011). Papaya (*Carica papaya* L.). Postharvest Biology and Technology of Tropical and Subtropical Fruits, (pp.86-126e).
- Singh, S.P., Kumar, S., Mathan, S.V., Tomar, M.S., Singh, R., Verma, P.K., Kumar, A., Kumar, S., Singh, R.P. and Acharya, A. (2020). Therapeutic application of *Carica papaya* leaf extract in the management of human diseases. *DARU J Pharm Sci*, 28(2): 735-744.
- Singh, S.P., Kumar, S., Tomar, M.S., Singh, R.K., Verma, P.K., Kumar, A., Kumar, S., Acharya, A. (2019). Aqueous extract of *Carica papaya* leaf elicits the production of TNF- α and modulates the expression of

- cell surface receptors in tumor-associated macrophages, *Biosci. Biotechnol. Res. Commun.* 12(4): 115–1122.
- Singh, S.P., Mathan, S.V., Dheeraj, A., Tailor, D., Singh, R.P. and Acharya, A. (2019). Anticancer Effects and Associated Molecular Changes of *Carica papaya* against Prostate Cancer, In American Association for Cancer Research Annual Meeting, DOI, American Association for Cancer Research.
- Soib, H.H., Ismail, H.F., Husin, F., Abu Bakar, M.H., Yaakob, H. and Sarmidi, M.R. (2020). Bioassay-guided different extraction techniques of *Carica papaya* (Linn.) Leaves on *in vitro* wound-healing activities, *Molecules*, 25(3): 517.
- Sumana, S., Kumar, G.T. (2019). Breaking the Barrier of cancer through papaya extract and their formulation. *Anticancer Agents Med Chem*, 19(13): 1577-1587.
- Tan, C.X., Tan, S.T., Tan, S.S. (2020). An overview of papaya seed oil extraction methods, *Int. J. Food Sci. Technol*, 55(4): 1506–1514.
- Tona, L., Kambu, K., Ngimbi, N., Cimanga, K., Vlietinck, A.J. (1998). Antiamoebic and phytochemical screening of some congolese medicinal plants, *J. Ethnopharmacol*, 61(1): 57–65.
- Upko, G.E., Owalabi, M.A., Image, N.O.A., Oribayo, O.O., Ejiroghene, A.J. (2016). Effect of *Carica papaya* aqueous leaf extract on pharmacokinetic profile of ciprofloxacin in rabbits. *Trop J Pharm Res*, 16(1): 127-134.
- Wadekar, A.B., Nimbawar, M.G., Panchale, W.A., Gudalwar, B.R., Lanwar, J.V., Bakal, R.L. (2021). Morphology, Phytochemistry and Pharmacological aspects of *Carica papaya* : a review. *GSC Biol Pharm Sci*, 14(03): 234-248.
- Wall, M.M. (2021). Ascorbic acid, vitamin A, and mineral composition of banana (*Musa* sp.) and papaya (*Carica papaya*) cultivars grown in Hawaii. *J food Compos Anal*, 19(5): 434-445.
- Wang, X., Contreras, M.D.M., Xu, D., Xing, C., Wang, L. and Yang, D. (2020). Different distribution of free and bound phenolic compounds affects the oxidative stability of tea seed oil: a novel perspective on lipid antioxidation, *LWT-Food Science and Technology*, 129 109389.
- WHO. (2004). Diabetes Action Now Booklet. Geneva, Switzerland: World Health Organization. 49(2).
- Yogiraj, V., Goyal, P.K., Chauhan, C.S., Goyal, A., Vyas, B. (2015). *Carica papaya* Linn.:An overview. *Int J Herb Med*, 2(5): 01-08.
- Zeng, Y., Ali, M.K., Du, J. *et al.* (2022). Resistant starch in rice: its biosynthesis and mechanism of action against diabetesrelated diseases, *Food Reviews International*, pp. 1–24.
- Zhang, T. and Chen, W. (2017). The *Candida albicans* inhibitory activity of the extract from papaya (*Carica papaya* L.) seed relates to mitochondria dysfunction. *Int. J. Mol. Sci.*, 18 (9).