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# Exploring the Anti-Diabetic and Anti-Cancer Properties of Carica Papaya L.

\*Santoshi Shah

Assistant Professor, School of Pharmaceutical sciences, The ICFAI University, Dehradun, Uttarakhand, India

\*Corresponding Author's email: <a href="mailto:santoshishah@iudehradun.edu.in">santoshishah@iudehradun.edu.in</a>

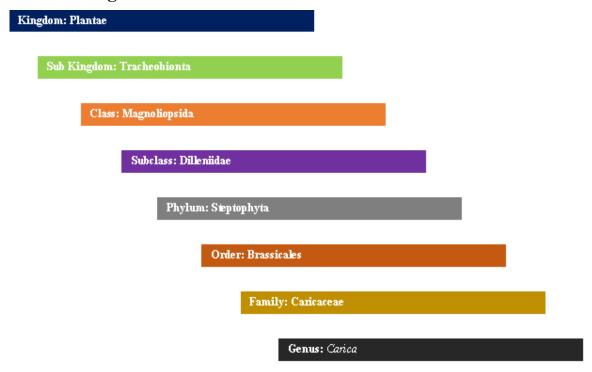
papaya is a powerhouse of nutrients and is available throughout the year. It is a rich source of three powerful antioxidant vitamin C, vitamin A and vitamin E. The minerals, magnesium and potassium, vitamin B pantothenic acid and folate and fiber. In addition to all this, it contains a digestive enzyme-papain that effectively treats causes of trauma, allergies and sports injuries. All the nutrients of papaya as a whole improve cardiovascular system, protect against heart diseases, heart attacks, strokes and prevent colon cancer. The fruit is an excellent source of beta carotene that prevents damage caused by free radicals that may cause some forms of cancer. It is reported that it helped in the prevention of diabetic heart disease. Papaya lowers high cholesterol levels as it is a good source of fiber. Papaya, Carica papaya L., is one of the major fruit crops cultivated in tropical and sub-tropical zones. Worldwide over 6.8 million tonnes of fruit were produced in 2004 on about 3,89,990 ha (FAO 2004). Of this volume, 47% was produced in Central and South America (mainly in Brazil), 30% in Asia and 20% in Africa. The papaya industry in Brazil is one of the world's largest that continues to show rapid growth. In contrast to being identified as the papita in Hindi, and erandakarkati in Sanskrit, papaya in English, the Carica papaya Linn. plant is a species of the Caricaceae family. The plant was imported through tropical America to India mostly in 16th century. A terminal cluster of massive, long-stalked leaves and a weak, frail, and frequently unbranched stem, which exudes large amounts of white latex, seem to be traits of the plant. These leaves seem to exhibit a fast growth rate and can grow as high as 20 m. Flowers fragrant, male flowers in lax many-flowered, densly pubescent cymes at the tips of the pendulous, fistular rachis; females flowers large, solitary or in few flowered racemes, different types of enzymes. Papain, vegetable pepsin present in good amount in unripe fruit is an excellent aid to digestion, which helps to digest the protein in food at acid, alkaline or neutral medium. Thus it can be prescribed for dyspeptic patients, who cannot digest the wheat protein gliandin, can tolerate it, if it is treated with crude papain. Papaya has the property of tenderizing meat. The fermented papaya fruit is a promising neutraceutical as an antioxidant. It improves the antioxidant defence in elderly patients even without any overt antioxidant deficiency state at the dose of 9 g/day orally (Marotta et al.,2006). The seed contains phenolic compounds, such as benzylisothiocyanate, glucosinolates, tocopherols (and), cryptoxanthin, carotene and carotenoids, while the seed oil principally presents oleic fatty acid, followed by palmitic, linoleic and stearic acids. The leaves have a high content of food fibers and polyphenolic compounds, such as flavonoids, saponins, pro-anthocyanins, tocopherol and benzyl isothiocyanate

#### Parts and medicinal uses of C. papaya

C. papaya is a pack of enzymes. Different parts contain different enzymes: unripe fruit (papain, chymopapain), fruits (B carotene, carotenoids, crytoxanthin, monoterpenoids, linalool), roots (carposides), seeds (papaya oil, glucosinolates, benzyl isothyocynate), leaves

(Zn, Mn, Fe, K, minerals), shoots (flavanoids, kaemferol, myricetin, minerals, Ca, Mg, Fe) and leaves (vitamin C and E, alkaloids, carpaine).

#### **Botanical categorization**



#### Cancer

Cancer, a broad category of disorders characterized by aberrant body cell proliferation, can affect any organ in the human body. A malignant tumor is another commonly used phrase for cancer since cancer cells have a tendency to multiply quickly from the original organs to other people. An estimated 10.5 million people die from cancer each year, making it one of the leading causes of mortality in the world today. Given that there have been anecdotal reports of cancer patients of all kinds experiencing positive outcomes, such as following the use of papaya plant components, it is important to note (Otsuki *et al.*, 2020). Due to the expense, side effects, and continued growth in both new occurrences of cancer and cancer-related mortality, research into the effectiveness of natural remedies for cancer therapy and management is gaining more and more traction.

#### **Diabetes Mellitus**

Traditional plant therapies for diabetes have gained popularity in recent decades. This study sought to determine whether a fluid extract prepared from C. papaya leaves would cause hypoglycemia in diabetic rats. Many studies have shown that the various components of the C. papaya plant have antihyperglycemic effects on both humans and animals (Sasidharan et al., 2011). Diabetes mellitus is a long-standing ailment, and medicative herb formulations have remained a plentiful supply source of medically beneficial phytocompounds and a workable option in treating a variety of illnesses afflicting humans. Some plants have bioactive chemicals that have reportedly been utilised to cure and prevent diabetes all over the world. In the mechanism of healing diabetes, flavonoids are thought to play a significant role in increasing the activity of antioxidant enzymes and are able to regenerate damaged βpancreatic cells so that insulin deficiency can be overcome. The flavonoids contained in plants are thought to also improve the sensitivity of insulin receptors. Flavonoids can inhibit β cell damage on the pancreatic Langerhans island which produces insulin and stimulates the release of insulin in pancreatic  $\beta$  cells to be secreted into the blood, in addition flavonoids can also restore insulin receptor sensitivity to cells. The inhibitory mechanism of flavonoids for the  $\alpha$ -glucosidase enzyme is through hydroxylation bonds and substitution on the  $\beta$  ring. The principle of this inhibition is to produce a delay in carbohydrate hydrolysis and glucose

absorption and to inhibit sucrose metabolism into glucose (Rorong and Pontoh, 2013). Food fiber is a part of plants that can be consumed and consists of carbohydrates which have resistance to digestion and absorption in the small intestine.

Table 1: Main phytochemical compounds present in C. papaya L. (papaya): ripe fruit pulp, seeds and leaves (Basu *et al.*, 2008)

Phytochemical Composition		
Pulp	Seeds	Leaves
<ul> <li>Glutathione         peroxidase</li> <li>Glutathione         transferase</li> <li>Glutathione reductase</li> <li>Alkaloids</li> <li>Flavonoids</li> <li>Saponins</li> </ul>	<ul> <li>Phenolic compounds</li> <li>Carotenoids</li> <li>Tocopherols</li> <li>Fatty acids oleic, palmitic</li> <li>B-carotene</li> </ul>	<ul> <li>Flavonoids</li> <li>Saponins</li> <li>Polyphenols</li> <li>Lycopene</li> <li>Benzyl isothiocyanate</li> </ul>

#### Papaya leaf extract's anti-cancer properties

Cancer, a broad class of diseases characterized by uncontrollable cellular proliferation in the body, can damage any organ. Another term for cancer that is widely used is a malignant tumour, because cancerous cells have the ability to quickly spread from their initial organ to others. A current major cause of mortality, malignancy is thought to account for 8.97million deaths annually worldwide (Pertiwi *et al.*, 2019). While females are more prone to acquire colorectal, breast, thyroid, lung, and cervical cancers, men are more likely to suffer liver, lung, stomach, prostate, and colorectal cancers. Papaya leaf extract may lessen metastatic cancer by functioning as an anti-cancerous agent by reducing the extracellular matrix content, which also attracts PC-3 cells for adherence and migration (Soib *et al.*, 2020). As a result, the extraction suggests the ability to stop DNA synthesis and stop the reproduction of cancer cells.

Table 2: In vivo research on the anti-cancer effects of Carica papaya leaf extract

Treatment	Effect on malignant cells	
The C. papaya leaf isolate in aqueous solution (1.25–27 mg/mL).	On tumor cell lines (including the ovarian tumor cell line Dov-13, the colon tumor cell line DLD-1, the stomach tumor cell line AGS, the pancreatic tumor cell line Capan-1. limiting the incorporation of 3H-thymidine to minimize DNA synthesis (Soib <i>et al.</i> , 2020).	
C. papaya leaf extract in water (0.625–20 mg/mL)	Malignant and hemopoietic cell lines' proliferative responses are inhibited. immunological modulatory gene expression is increased	
Extract of C. papaya leaves in water (659.63 µg/mL)	Papaya leaf extract demonstrated antiproliferative and apoptotic triggered action suppresses cellular expansion in breast cancer in individuals.  MCF-7 cell line death was seen in extracts from papaya leaves (22.54%) (Singh <i>et al.</i> , 2017)	

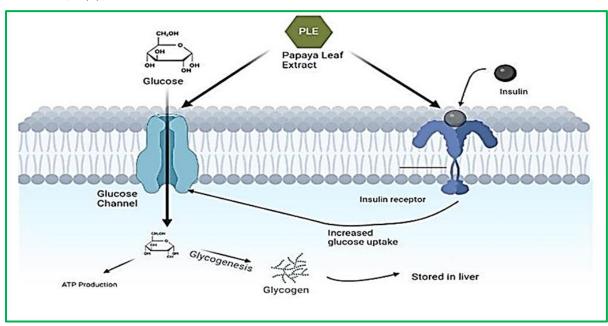
#### Conclusion

Several species of the Caricaceae family, which includes the *Carica papaya*, have been utilized as remedies for a variety of illnesses. Today, the entire tropical region is home to the perennial plant C. papaya. Said to have started in Mexico's southern area. Numerous scientific research have been conducted to evaluate the biological activities of various sections. The many parts of the papaya plant have been used medicinally since ancient times. Papaya leaves have anti-inflammatory, anti-cancer, anti-diabetic, and many other disease-preventive properties. They also have a lot of potential for treating viral infections and

increasing immunity. To identify the primary mechanisms of action of the phytonutrients included in papaya leaf extract as therapeutic agents, more investigation is needed. Papaya leaf extract lowers blood sugar levels and stops the growth of cancer cells, according to numerous studies.

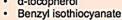
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#### **Phytochemicals**

- Caffeic acid
- d α-tocopherol
- MyricetinQuercetin
- Kaempferol
- Papain





Carica Papaya

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#### **Possible Antioxidative MOAs**

- · Free radical scavenging action
- ↓ Lipid peroxidation
- ↓ Overall ROS production

## Inflammation and Chronic conditions

### (Diabetes, Alzheimer's Disease, Periodontal disease)

- J MAPK/ERK, JNK
- NF-kB, iNOS, IL-4, IL-5, eotaxin, TNFq
- ↓ Leucocyte counts, inflammatory cell infiltration
- Ion-reducing capacity, 

  Fenton reaction
- † Antioxidative enzymes (GSH, GPx, SOD and CAT)
- † eNOS, mass of β cells, ↓ postprandial BGL
- ↓ Mitochondrial dysfunction, cell apoptosis

#### Cancer

- Chelation of ROS generating agents
- ↓ IL-6, IL-8 (↓ glioma cell metastasis)
- ↓ ROS thus ↑ tumour suppressor genes
- † ROS thus † cancer cells autophagy and apoptosis

#### Skin

- (Aging, Wound Healing)
- Act as exfoliant
- Type I collagen
- ↓ Myeloperoxidase, proteinases
- ↓ AP-1, MAPK, Nrf2
- · ↑ SOD, CAT, GSH

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