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Veersain

Research Scholar, Department of Fruit Science, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

Arvind Kumar

Associate Professor, Department of Fruit Science, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

Mohit Kumar

Research Scholar, Department of Fruit Science, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

P Thilagam

Associate Professor, Department of Agricultural Entomology, Tamil Nadu Agricultural University, Horticultural College and Research Institute, Jeenuur Krishnagiri, Tamil Nadu, India

Rishabh Yadav

Research Scholar Department of Agricultural Extension Education, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

Shankar Rajpoot

Research Scholar, Department of Post-Harvest Technology, Banda University of Agriculture and Technology, Banda, Uttar Pradesh, India

Shubham Yadav

Research Scholar, Department of Fruit Science, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

Suneel Kumar

Research Scholar, Department of Soil Science and Agricultural Chemistry, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

Corresponding Author:

Shubham Yadav

Research Scholar, Department of Fruit Science, Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut, Uttar Pradesh, India

A comprehensive review of papaya's multidimensional impact on health and wellness

Veersain, Arvind Kumar, Mohit Kumar, P Thilagam, Rishabh Yadav, Shankar Rajpoot, Shubham Yadav and Suneel Kumar

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Abstract

Papaya, renowned for its delectable fruit, conceals hidden treasures within its plant. The papaya's fruit, with its high vitamin C content and nutritional richness, supports overall health, while its often-overlooked seeds harbor antimicrobial and digestive benefits. Papaya leaves, steeped in traditional medicine, offer antioxidants and potential remedies for various health issues. Surprisingly, papaya skin contains enzymes with skin-rejuvenating properties. The less-studied papaya roots hint at digestive health and anti-inflammatory potential. Papaya flowers bring unique flavors to culinary delights and offer antioxidant and anti-inflammatory possibilities. Lastly, papaya enzymes, particularly papain, facilitate digestion, find use in dietary supplements, and serve as natural meat tenderizers or skincare agents. These diverse facets of the papaya plant highlight its holistic significance, transcending its famed fruit's sweetness, encouraging a deeper appreciation of this tropical treasure's multifaceted contributions to health and well-being.

Keywords: Multidimensional, anti-inflammatory, deeper

Introduction

Papaya (*Carica papaya*)

Papaya (*Carica papaya*), known as "Papita" in Hindi, holds a special place in the hearts of Indians, not only for its delightful taste but also for its myriad health benefits and versatile applications. This tropical fruit, with its unique botanical characteristics and a history intertwined with Indian culture, has become an integral part of both dietary traditions and traditional medicine practices in the country. In Indian cuisine, papaya's role is multifaceted. The ripe fruit graces breakfast tables, fruit salads, and fruit chaats, while the raw papaya is transformed into sabzis (vegetable dishes) and pickles. Papaya is developed broadly in all tropical and sub-tropical parts of the world. Papaya has been viewed as a standout among the most profitable tropical organic products that contain beta-carotene, protein, starch, vitamins, and minerals. Anjana G.V *et al.* (2018) [1]. Prepared papaya feels fragile, the skin has yellowish shading, and when opened it has a sensitive orange yellowish tissue with different minimal dim seeds embedded at the vacant core interest Yogiraj V.A., and Goyal P.K. (2014) [2]. Papaya belongs to the family Caricaceae having four genera in the world. The genus *carica* linn. is represented by four species in India, of which *Carica papaya* linn. is the most widely cultivated and best-known species. The average height is about 5 to 10 m. The leaves of the plant are spirally arranged up to the top stem. Normally, the leaves are big with oval shape with about 20–28 in. diameter. (Wadekar *et al.* 2021) [3]. Papaya leaves, fruits, latex including its extract are used widely in Medical, Pharmaceutical, Herbal, Industrial and for Research purposes. Papain, a major chemical compound extracted from Papaya fruit and stem latex is used in brewing and wine making, in textile/tanning industries and for meat tenderization (Bruneton, 1999; Bhattacharjee, 2001; Feng 2014) [4-6]. According to the World Health Organization (WHO), 80% of the population living in developing countries relies on traditional medicine for their primary health care needs (Bongo *et al.* 2017, Inkoto *et al.* 2017, Ngbolua *et al.* 2019) [7-9].

The many benefits of papaya are owned due to high content of vitamin A, B, C, proteolytic enzymes like papain and chymopapain which have antiviral, antifungal and antibacterial properties (Tarun V. and Yash P., (2015) ^[10].

Importance of Studying Papaya's Health Benefits

In recent decades, there has been a growing interest in understanding the health-promoting properties of papaya. This interest arises from the recognition of the vital role diet plays in maintaining and enhancing health. Papaya stands out as a unique fruit with a diverse array of nutrients and bioactive compounds that have the potential to positively impact various aspects of health and wellness (Gironés-Vilaplana, A. 2015) ^[11].

As the global population grapples with a rise in diet-related health issues, including obesity, heart disease, and diabetes, exploring the potential of natural foods like papaya to mitigate these concerns is of paramount importance Gorski, MT, &Roberto, CA, (2015) ^[12] and Roy, JR, *et al*, (2023) ^[13]. Additionally, the shift towards natural and plant-based remedies has renewed interest in traditional uses of papaya for

promoting well-being (Sun-Waterhouse, D, 2011) ^[14].

Objectives of the Review

The primary objective of this comprehensive review is to provide a thorough examination of papaya's multidimensional impact on health and wellness. To achieve this, the review will delve into the fruit's nutritional composition, its effects on various aspects of health, and its historical and cultural significance in traditional medicine. By synthesizing existing research and knowledge, this review aims to shed light on the ways in which papaya can be harnessed as a valuable dietary and therapeutic resource.

Nutritional Composition of Papaya

Papaya is celebrated not only for its delicious taste but also for its impressive nutrient composition. This tropical fruit is a nutritional powerhouse, offering a wide array of vitamins, minerals, and bioactive compounds that contribute to its health-promoting properties (Bergonio 2016) ^[15]. Detailed constitution of the macronutrients and micronutrients present in papaya.

Table 1: Nutritional value of fruit

Constituent	Green Papaya	Ripe Papaya
Macronutrients		
Sodium	283.8 mg	128.4 mg
Potassium	2743 mg	1238 mg
Magnesium	635.1 mg	229.4 mg
Calcium	635.1 mg	146.8 mg
Micronutrient		
Iron	8.11 mg	12.84 mg
Copper	0.14 mg	0.18 mg
Zinc	0	0.92 mg

Vitamins, minerals, dietary fiber, and antioxidant content of papaya

Papaya fruit is a rich source of nutrients such as provitamin A, carotenoids, vitamin C, vitamin B, lycopene, dietary minerals and dietary fibre.

Table 2: Papaya fruit is a rich source

Constituent	Green Papaya	Ripe Papaya
Vitamins		
Vitamin	391.9 mg	568.8 mg
Thiamine	0.54 mg	0.28 mg
Riboflavin	26 mg	0.28 mg
Niacin	4.05 mg	2.08 mg
Carotene	0	7807 mg
Micronutrient		
Iron	12.84 mg	8.11 mg
Copper	0.18 mg	0.14 mg
Zinc	0.92 mg	0

Vitamins in Papaya

- **Vitamin C:** Papaya is one of the richest sources of vitamin C, an essential antioxidant that plays a critical role in immune support, collagen production, and overall skin health (Barbosa, N. S., and Kalaaji AN (2014) ^[16]. Ripe papaya is particularly abundant in vitamin C (Yogiraj VA, and Goyal PK (2014) ^[2].
- **Vitamin A:** The fruit is also a potent source of vitamin A, in the form of beta-carotene, which is important for maintaining healthy vision, skin, and mucous membranes. Green papaya contains notable amounts of beta-carotene, which increases as it ripens Kandasamy, P., & Shanmugapriya, C. (2015) ^[17].

- **Vitamin E:** Papaya contains vitamin E, another antioxidant that helps protect cells from oxidative damage. It contributes to the overall antioxidant capacity of the fruit (Kong, Y. R. *et al*. 2021) ^[18].
- **Vitamin K:** This vitamin plays a role in blood clotting and bone health. While both green and ripe papaya contain vitamin K, the concentration may vary (Sinbad, O. O. *et al*. 2019) ^[19].

Importance of various parts of papaya Seeds

Papaya seeds are often discarded without realizing their potential health benefits. The seeds are medically important in the treatment of sickle cell diseases and poisoning related disorder (Imaga NA, (2013) ^[20], Okpuzor J, *et al*. (2021) ^[21]. Some traditional medicinal practices use papaya seeds as a natural remedy for expelling intestinal parasites, although this use should be approached with caution and under medical guidance Srivastava AK, & Singh VK (2016) ^[22], Briones-Labarca V, (2015) ^[23],Yogiraj VA (2014) ^[2]. Papaya seeds are a concentrated source of nutrients like healthy fats, protein, and dietary fiber, which can complement the overall nutritional intake when used in moderation (Shaheen S, *et al*. (2022) ^[24].

Leaves

Papaya leaves are an often-underappreciated part of the papaya plant, yet they have garnered attention for their potential health benefits. In various traditional medicinal systems, papaya leaves have been used for their potential therapeutic properties. They are believed to have anti-inflammatory, antioxidant, and other medicinal qualities

(Yogiraj V.A., and Goyal P.K. (2014) ^[2]. Papaya leaves are rich in antioxidants, including flavonoids, polyphenols, and vitamin C. These compounds help combat oxidative stress and reduce the risk of chronic diseases. (Akbari B, *et al.* (2022) ^[25]. There is some anecdotal and preliminary scientific evidence suggesting that papaya leaf extracts may help increase platelet count, which can be particularly relevant for individuals dealing with certain illnesses like dengue fever. (Shelke, M. 2021) ^[26].

Skin

Papaya skin, often discarded as waste, actually has several surprising uses and potential benefits. The enzymes in papaya skin may also have skin-brightening effects. Regular use can help reduce the appearance of dark spots, hyperpigmentation, and uneven skin tone (Nduyu PW. (2020) ^[27]. The antioxidants in papaya skin can help fight free radicals and reduce the signs of premature aging, such as fine lines and wrinkles. (Aversa R, (2016) ^[28].

Roots

Papaya roots are a less commonly discussed part of the papaya plant, but they too offer potential health benefits that deserve attention. In some cultures, papaya roots have been used in traditional medicine for their potential therapeutic properties. They are believed to have anti-inflammatory and digestive benefits. (Karunamoorthi, K. *et al.* (2014) ^[29]. Similar to other parts of the papaya plant, papaya roots contain enzymes like papain, which can aid in digestion. They may help alleviate digestive discomfort and improve overall gut health (Yogiraj V.A., and Goyal P.K. (2014) ^[2].

Flowers

Papaya flowers are a unique and often overlooked part of the papaya plant, yet they offer both culinary delights and potential medicinal applications. Papaya flowers are rich in vitamins, minerals, and dietary fiber. They provide essential nutrients, contributing to overall nutrition when included in the diet. (Pinnamaneni, R. (2017) ^[30]. In traditional medicine, papaya flowers have been used for their potential medicinal properties. They are believed to have anti-inflammatory, antioxidant, and digestive benefits.

Phytochemical Content of Papaya

The exploration of papaya's bioactive components, including carotenoids, flavonoids, and phenolic compounds, has emerged as a pivotal area of scientific inquiry. Within the realm of flavonoids, numerous investigations have diligently delved into the specific composition harbored within *C. papaya* leaves, employing sophisticated methodologies such as ultra-performance liquid chromatography-time of flight electrospray ionization-mass spectrometry. Noteworthy contributions have surfaced from researchers like Afzan *et al.* (2012) ^[31], who astutely identified four distinct flavonoids within the *C. papaya* leaf extract: quercetin 3-(2G-rhamnosylrutinoside), kaempferol 3-(2G-rhamnosylrutinoside), quercetin 3-rutinoside, and kaempferol 3-rutinoside. Paralleling this, Nguyen *et al.* have ventured to tentatively pinpoint compounds including kaempferol b-D-glucopyranoside, luteolin b-D-glucopyranoside, myricetin 3-rhamnoside, quercetin, and rutin. In a comprehensive endeavor, (Tan *et al.* (2012) ^[32]) have unveiled a diverse assembly of compounds encompassing apigenin, kaempferol, quercetin, myricetin, isorhamnetin, catechin, hesperitin, and naringenin. Noteworthy advancements in High-Performance

Liquid Chromatography (HPLC), as harnessed by Andarwulan *et al.* (2012) ^[33], have enabled the discernment of quercetin, kaempferol, and apigenin. Amid these endeavors, a resounding theme has emerged—the prevalence of antioxidant-rich flavonoids within *C. papaya* leaves, with an accentuated significance placed on the role of kaempferol 3-(2G-rhamnosylrutinoside) as a prominent contributor. These revelations collectively deepen our comprehension of the intricate flavonoid composition within *C. papaya* leaves. Moreover, they gain added resonance through tangible physical and chemical substantiation, as demonstrated by Nugroho *et al.* (2017) ^[34]. Such evidence takes on heightened relevance when juxtaposed with antecedent research that similarly identified these flavonoids within *C. papaya* leaves, employing techniques centered on liquid chromatography electrospray ionization-mass spectrometry detection (Afzan, 2012 ^[31]; Andarwulan *et al.*, 2012 ^[33]; Nguyen *et al.*, (2016) ^[35].

Medicinal Properties of Papaya

Exploration of Traditional and Folk Medicinal Uses of Papaya across Cultures:

The well-established significance of medicinal plants and their applications in promoting human health is undeniable. Among the vast array of the world's medicinal plants, India accounts for around 15%, exemplifying its rich botanical heritage. Despite modern advancements, an estimated 70-80% of the global population continues to rely on traditional medicine practices. Throughout different cultures, an array of herbal plants is integrated into daily life as remedies to combat a wide spectrum of illnesses. A concerning rise in antibiotic resistance in recent years has given rise to therapeutic challenges, as emphasized by Prabhu A.K. *et al.* in 2017 ^[36]. Within Southeast Asia, the traditional use of papaya leaves to address dengue fever has persisted. While the scientific validation for this application remains limited, the practice echoes the cultural reverence that papaya holds within the region's healing traditions. Furthermore, as noted by Pinnamaneni R. in 2018 ^[37], there is compelling evidence indicating that *Carica papaya* leaves possess properties that alleviate symptoms of conditions such as asthma, worm infestations, and dysentery

Digestive Health and Enzymes

Exploration of Papain and Other Enzymes in Papaya

Facilitating Digestion: Papaya stands as a bounteous reservoir of diverse enzymes, contributing significantly to its nutritional profile. The presence of papain, a vegetable pepsin prominently found in substantial quantities within unripe fruit, serves as an exceptional aid in digestion. This enzyme effectively aids in the breakdown of dietary proteins across various pH ranges encompassing acidic, alkaline, and neutral mediums, a characteristic highlighted by Yogiraj V.A., and Goyal P.K. (2014) ^[2]. Notably, in its raw state, *Carica papaya* displays notable antidiarrheal potential against gut pathogens. A noteworthy revelation is the discerned antidiarrheal efficacy of ripe *Carica papaya* extract, particularly in its effectiveness against *Plesiomonas shigelloides*, as highlighted by Prabhu A.K. *et al.* in 2017 ^[36].

Understanding the Mechanisms Underlying Papain's Contribution to Digestive Health:

Navigating the challenge of treating diarrheal diseases amidst the rise of antimicrobial-resistant pathogens has compelled a shift towards embracing traditional medicine and natural compounds in the era of

antibiotic resistance. Nature has long served as a wellspring of medicinal plants, and while numerous modern drugs trace their origins to these conventional sources, attention is increasingly turning toward plant-derived solutions. Presently, these botanical products are capturing attention in the realm of research, propelled by their virtues of cost-effectiveness, widespread accessibility, and minimal or negligible side effects. An array of plant-based therapeutic agents can be harnessed from various parts of plants, encompassing fruits, peels, seeds, leaves, flowers, roots, and barks, as elucidated by Lydia E *et al.* in [38].

Exploring Antioxidant and Anti-Inflammatory Attributes

- Investigating Papaya's Antioxidant Characteristics and Its Ability to Confront Oxidative Stress. In a clinical investigation, the assessment of histological severity in cases of inflammatory bowel disease served as a pivotal gauge for the efficacy of papain in addressing chronic inflammatory and associated ailments, signifying its safety and effectiveness, as outlined by Carlos ES in 2008 [39]. Moreover, the anti-inflammatory potency of papaya seeds has also been substantiated, as reported by Amazu LU *et al.* in 2010 [40]. When delving into the anti-inflammatory prowess of papaya leaves extract, including comparisons with a reference drug, the carrageenan method revealed a modest impact. At the dosage of 100 mg/kg, the extract displayed its highest efficacy at 3 hours post-carrageenan injection, registering a 2.7% effect, whereas the 200 mg/kg extract mirrored a reservoir of antioxidant nutrients, counting carotenes, vitamin C, and flavonoids, each heralding cardiovascular well-being and providing a shield against colon cancer. The presence of phenolic compounds within papaya, including caffeic acid and its derivatives, ushers in anti-inflammatory capabilities while augmenting the antioxidant capacity – a direct ally in tackling reactive oxygen species (ROS) removal. This intricate interplay was underscored by Rahman, A. in 2013 [41].

Anti-Cancer Potential

Delving into Papaya's Potential Anticancer Attributes. Historically, pharmaceutical formulations harnessing diverse proteolytic enzymes, such as papain, have been adjuncts in malignant disease treatment, despite a lack of insight into their mode of operation. Empirical evidence suggests that the effects following oral administration of polyenzymes preparations stem from the triggering of cytokine production by human peripheral blood mononuclear cells. These revelations unfolded through the experiments by Desser L *et al.* in 1993 [42].

The prowess of papaya in countering cancer also transpired within *in vitro* studies, unveiling its efficacy against numerous cancer cell lines, thus underscoring its potent anticancer activity. Central to this activity is the papain enzyme, adept at dismantling the fibrin cancer cell wall and proteins into amino acid forms. Further fortifying papaya's anticancer profile is lycopene, a fervent oxygen and free radical scavenger. Additionally, isothiocyanate emerges as a formidable adversary against cancer, spanning breast, lung, colon, pancreas, prostate, and leukemia malignancies. With the power to hinder both the initiation and progression of cancer cells, these enzymes stand as a pivotal revelation, elucidated by Fauziya S in 2013 [43].

The conscious decision to regularly incorporate lycopene-rich fruits, among which papaya stands strong, alongside the

consumption of green tea, presents a substantial reduction in the risk of prostate cancer development. This notion is buttressed by research findings published in the Asia Pacific Journal of Clinical Nutrition, underscoring the significance of such dietary choices in cancer prevention (Jian, L. *et al.*, 2007; Dosil-Día *et al.*, 2008) [44, 45].

Anti-sickling activity

Papaya (*Carica papaya*) has been studied for its potential anti-sickling activity, particularly in the context of sickle cell disease (SCD). SCD is a genetic disorder characterized by the presence of abnormal hemoglobin known as hemoglobin S (HbS), which can cause red blood cells to become misshapen and fragile, leading to various complications, including pain crises and organ damage. Okpuzor, J. 2021 [46], Nader, E. 2020 [47]. Research has shown that papaya leaf extract contains certain bioactive compounds, such as flavonoids and phenolic acids, that exhibit anti-sickling properties. (Farooq, M. U 2020) [48]. Papaya leaf extract has been reported to improve red blood cell indices, such as mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), which are important indicators of red blood cell health. (Ekokotu, P. A. 2018) [49].

Sickle cell patients often experience painful vaso-occlusive crises due to the abnormal shape and behavior of their red blood cells. Some studies have suggested that papaya leaf extract may help reduce the frequency and severity of pain crises, improving the quality of life for individuals with SCD Oniyangi, O., & Cohall, D. H. (2020) [50]. Papaya leaf extract contains antioxidants that can help reduce oxidative stress in the body. Oxidative stress is a contributing factor to the complications associated with SCD. By mitigating oxidative damage, papaya leaf extract may provide further benefits to individuals with the condition. Ibrahim, A., & Muhammad, S. A. (2023) [51].

Skin Health and Wound Healing

Scrutinizing Papaya's Role in Skin Care and Wound Healing. The intriguing parallels observed between latex coagulation in papaya and the mammalian coagulation process have prompted the hypothesis that shared factors might exist within both systems. This suggests the tantalizing possibility that certain plant metabolites implicated in plant healing could potentially play a role in mammalian clot formation during the healing process Whitten, M. M., and Coates, C. J. (2017) [52]. The notable proliferative impact achieved by papain, exceeding control values by 15%, indicates the specificity of this effect for select proteolytic enzymes Singer AJ and Clark RA (1999) [53]. Furthermore, a study showcased the efficacy of papain from *C. papaya* latex in shielding rats against histamine-induced ulcers, achieved through the inhibition of acid secretion Mahajan, K. C. *et al.* 2023 [54].

Pharmacological Applications

Surveying the Exploration of Papaya's Pharmacological Attributes. The diverse pharmacological repertoire of *Carica papaya* (papaya) can be attributed to the array of phytochemicals such as phenolics, flavonoids, and alkaloids that permeate its distinct components. [Pharmacological activities associated with papaya encompass antioxidant, antibacterial, anticancer, anti-inflammatory, antiulcer, antidiabetic, and hepatoprotective effects. Noteworthy therapeutic potential is evident in the realms of conditions like pyrexia, diabetes, syphilis, wound healing, and even dengue fever, as illuminated by Ateeq Rahman in 2013. Papaya's

holistic contribution extends to insecticidal and repellent capabilities exhibited by its fruit, leaves, bark, root, and seeds. The application spectrum of papaya even embraces nanoparticle synthesis, unraveling a plethora of potential utilities, as underscored by Sharma, A *et al.* in 2020.

Conclusion

In the domain of health and well-being, the vibrant papaya emerges as a polymodal gem, its potential transcending manifold dimensions. Beyond its gustatory delight, papaya's nutritional opulence beckons attention. Its profusion of pivotal nutrients, including carotenoids, vitamin C, and flavonoids, positions it as a potent contender in bolstering immune functionality and mitigating oxidative stress.

Delving more profoundly, papaya's enzymatic prowess, notably through the presence of papain, proffers digestive benefits that traverse pH gradients. From ameliorating gastrointestinal maladies to optimizing hydrolysis, papaya assumes the mantle of a natural digestive adjunct. These attributes cascade into skin health and wound healing, where intriguing parallels between papaya's coagulative pathways and mammalian thrombogenesis offer enticing possibilities for regenerative applications.

Venturing further, papaya's efficacy finds manifestation within the realm of cardiovascular vigor. Phenolic compounds and antioxidants synergize, augmenting cardiovascular robustness while concomitantly suppressing inflammatory cascades. Meanwhile, its potential in abating carcinogenesis is compelling, underscored by papain's prowess in lysing cancer cell membranes, coupled with the presence of lycopene and isothiocyanate, which collectively amplify its therapeutic spectrum.

Papaya's pharmacological versatility radiates through its phytochemical diversity. Its repertoire spans antioxidative, antibacterial, anti-inflammatory, and antiulcerative attributes, among others, engendering a confluence of health paradigms. Moreover, its entrenchment in insecticidal applications and contributions to nanoparticle synthesis attests to its multi-dimensional implications.

In synthesis, papaya transcends its tropical allure, emerging as a stalwart in holistic well-being. Its impact resonates across cultural topographies, embodying a repository of benefits that bridge traditional sagacity and contemporary research. With each stratum plumbed, papaya's salience in fostering health gains sharper resolution, solidifying its stature as a nutritional and medicinal trove with the potential to amplify and enrich human existence.

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