Anticancer Potential of Carica papaya Extracts in Colorectal Cancer: A Comprehensive Review of Mechanisms and Bioactive Compounds

Manthan Chhagan Nimane[1], Soanli Tambe[2], Rajeshree Muke[3], Pooja Pagare[4], Rupali Tasgaonkar[5]
[1,3,4]*Student, Yadavrao Tasgaonkar Institute of Pharmacy, Bhivpuri road Karjat., India.*
[2]*Assistant Professor, Yadavrao Tasgaonkar Institute of Pharmacy, Bhivpuri road Karjat, India.*
[5]*Pricipal and Professor, Yadavrao Tasgaonkar Institute of Pharmacy, Bhivpuri Road Karjat, India.*

***Abstract*—Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality worldwide, with increasing incidence in developing countries including India. Despite advancements in surgery, chemotherapy, radiotherapy, and targeted therapies,**
treatment-associated toxicity, drug resistance, and high recurrence rates remain major challenges. These limitations have stimulated interest in plant-derived bioactive compounds as safer and complementary therapeutic agents. Carica papaya Linn., a widely consumed tropical plant, has gained significant attention due to its diverse pharmacological properties, including antioxidant, anti-inflammatory, immunomodulatory, and anticancer activities. Various parts of the plant such as leaves, seeds, fruits, and peels contain biologically active compounds like flavonoids, phenolic acids, alkaloids, isothiocyanates, carotenoids, and vitamins.

This review comprehensively summarizes current scientific evidence on the anticancer potential of Carica papaya extracts in colorectal cancer. It highlights the phytochemical composition, molecular mechanisms involved in CRC inhibition, including apoptosis induction, cell cycle arrest, modulation of oxidative stress, and immune regulation. Additionally, limitations of current studies and future research perspectives are discussed to support the development of papaya-based therapeutics for colorectal cancer management.

I. INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths globally. According to recent epidemiological data, lifestyle changes, dietary habits, obesity, smoking, alcohol consumption, and genetic predisposition contribute significantly to CRC development. Conventional treatment strategies such as chemotherapy and radiotherapy, although effective, are often associated with severe side effects including immunosuppression, gastrointestinal toxicity, and development of chemoresistance.

Natural products have historically played a vital role in drug discovery, particularly in oncology. More than 60% of currently used anticancer drugs are derived from natural sources or their derivatives. Among medicinal plants, Carica papaya Linn. (family: Caricaceae) has been extensively studied for its therapeutic potential. Traditionally used in folk medicine for treating digestive disorders, infections, inflammation, and thrombocytopenia, papaya has recently emerged as a promising source of anticancer agents.

The anticancer potential of Carica papaya has been demonstrated against various cancer types, including breast, prostate, liver, pancreatic, lung, and colorectal cancers. This review focuses specifically on colorectal cancer, summarizing experimental evidence and elucidating the underlying molecular mechanisms responsible for its anticancer effects.

II. BOTANICAL DEPICTION AND CONVENTIONAL EMPLOYMENTS OF CARICA PAPAYA

Carica papaya is a quickly developing, herbaceous plant that starts from Central America and is

presently developed in numerous tropical and subtropical areas.

The plant has a empty stem, wide lobed takes off, and pear-shaped natural products that contain numerous dark seeds. About each portion of the plant has been utilized in conventional medicine.

In conventional hones, the takes off of the papaya plant have been utilized to treat dengue fever, jungle fever, and issues with digestion.

The seeds are recognized for their capacity to battle microbes and parasites, whereas the natural product is eaten for its nutritious and antioxidant qualities. The wide run of conventional employments recommends that the plant contains different dynamic compounds that may offer assistance in avoiding cancer.

III. PHYTOCHEMICAL COMPOSITION OF CARICA PAPAYA

The anticancer activity of Carica papaya is attributed to its rich phytochemical profile. Major bioactive compounds identified from different parts of the plant include:

Flavonoids (quercetin, kaempferol)

Phenolic acids (caffeic acid, ferulic acid, gallic acid) Alkaloids (carpaine)
Isothiocyanates (benzyl isothiocyanate) Carotenoids (β-carotene, lycopene) Vitamins (vitamin C, vitamin E) Enzymes (papain, chymopapain)
Among these, benzyl isothiocyanate and flavonoids have shown strong anticancer effects by modulating multiple signaling pathways involved in cancer progression. Antioxidant compounds such as phenolics and carotenoids also play a crucial role in neutralizing reactive oxygen species (ROS), thereby preventing DNA damage and tumor initiation.

IV. COLORECTAL CANCER: PATHOGENESIS AND MOLECULAR TARGETS

Colorectal cancer develops through a multistep process involving genetic and epigenetic alterations. Key molecular events include mutations in APC, KRAS, TP53, and dysregulation of signaling pathways such as Wnt/β-catenin, PI3K/Akt, MAPK, and NF-κB. Chronic inflammation and oxidative stress further contribute to tumor initiation and progression.
Targeting these pathways using plant-derived compounds offers a promising approach for CRC prevention and therapy. Carica papaya extracts have been reported to interact with several of these molecular targets, leading to inhibition of tumor growth and metastasis.

V. ANTICANCER ACTIVITY OF CARICA PAPAYA EXTRACTS IN COLORECTAL CANCER

5.1. In Vitro Studies

Several in vitro studies have demonstrated the cytotoxic effects of Carica papaya extracts on colorectal cancer cell lines such as Caco-2, HT-29, and HCT-116. Methanolic and aqueous extracts of papaya seeds and leaves have shown dose-dependent inhibition of cancer cell proliferation while exhibiting minimal toxicity toward normal cells.
A notable study reported that papaya black seed extract significantly reduced cell viability in Caco-2 cells by inducing apoptosis and cell cycle arrest. The extract enhanced caspase-3 activity and upregulated pro-apoptotic proteins such as Bax while downregulating anti-apoptotic Bcl-2 proteins.

5.2. In Vivo Evidence

Although limited, animal studies have provided supportive evidence for the anticancer potential of papaya extracts. Administration of papaya leaf extract in experimental tumor models resulted in reduced tumor volume, decreased oxidative stress markers, and improved immune response. These findings suggest that papaya extracts may exert systemic anticancer effects beyond direct cytotoxicity.

VI. MOLECULAR MECHANISMS OF ANTICANCER ACTION

6.1. Induction of Apoptosis: -

Apoptosis is a programmed cell death mechanism often dysregulated in cancer cells. Carica papaya extracts have been shown to activate intrinsic apoptotic pathways by increasing mitochondrial

membrane permeability and activating caspase cascades. The modulation of p53 and Bax/Bcl-2 ratio plays a key role in apoptosis induction in colorectal cancer cells.

6.2. Cell Cycle Arrest: -
Papaya extracts can inhibit uncontrolled cell division by arresting the cell cycle at G0/G1 or G2/M phases. This effect is mediated through the regulation of cyclins and cyclin-dependent kinases, ultimately preventing cancer cell proliferation.

6.3. Antioxidant and Anti-Inflammatory Effects: -
Oxidative stress and chronic inflammation are major contributors to CRC development. The antioxidant compounds present in papaya extracts scavenge free radicals and reduce lipid
peroxidation. Additionally, papaya phytochemicals inhibit pro-inflammatory mediators such as COX-2, TNF-α, and NF-κB, thereby suppressing inflammation-driven tumor progression.

6.4. Immunomodulatory Activity: -
Papaya leaf extracts have demonstrated immunomodulatory effects by enhancing cytokine production and activating immune cells. Improved immune surveillance may contribute to the suppression of tumor growth and metastasis in colorectal cancer.

VII. ADVANTAGES OF CARICA PAPAYA AS A POTENTIAL ANTICANCER AGENT

Natural origin with wide dietary acceptance Multiple bioactive compounds acting synergistically
Lower toxicity compared to conventional chemotherapy Potential use as adjuvant therapy
Cost-effective and easily available in tropical countries

VIII. LIMITATIONS AND CHALLENGES

Despite promising results, several limitations exist:

Lack of large-scale in vivo and clinical studies
Variability in extract composition due to extraction methods Absence of standardized dosage and formulations
Limited understanding of pharmacokinetics and bioavailability Addressing these challenges is essential before clinical application.

IX. FUTURE PERSPECTIVES

Future research should focus on isolating and characterizing individual bioactive compounds from Carica papaya and evaluating their synergistic effects. Advanced drug delivery systems such as nanoparticles may enhance bioavailability and therapeutic efficacy. Well-designed clinical trials are required to validate the safety and effectiveness of papaya-based formulations in colorectal cancer patients.

X. CONCLUSION

Carica papaya is a promising natural source of anticancer compounds for managing colorectal cancer.
Its extracts show strong anticancer effects through various mechanisms such as promoting cell death, stopping the cell cycle, providing antioxidant protection, reducing inflammation, and enhancing immune function. Although most of the current evidence comes from preclinical studies, the results strongly suggest that compounds from papaya should be further studied as possible complementary or alternative treatments for colorectal cancer. With thorough scientific research, Carica papaya could play a role in creating safer and more effective cancer treatments.

REFERENCES

[1] Mahrous, S., & Noseer, E. A. (2023). Anticancer potential of Carica papaya Linn black seed extract against human colon cancer cell line: An in vitro study. BMC Complementary Medicine and Therapies, 23, 271.
[2] Kong, Y. R., et al. (2021). Beneficial role of Carica papaya extracts and phytochemicals on oxidative stress and related diseases: A mini review. Biology (Basel), 10(4), 287.
[3] Patel, S., et al. (2024). Anticancer activity of phytochemicals of the papaya plant: A narrative review. Journal of Cancer Prevention, 29(1), 45–60.

[4] Otsuki, N., Dang, N. H., Kumagai, E., Kondo, A., Iwata, S., & Morimoto, C. (2010). Aqueous extract of Carica papaya leaves exhibits anti-tumor activity and immunomodulatory effects. Journal of Ethnopharmacology, 127(3), 760–767.

[5] Les, F., et al. (2021). Phytochemical composition and biological activities of Carica papaya extracts. *Pl