



Papaya Leaves and Its Anticancer Activity

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ABSTRACT

Cancer has become a significant global phenomenon and health challenges, with conventional curatives similar to chemotherapy and radiation nearing their efficacy limits. This has produced growing interest in indispensable treatments, including those deduced from natural sources. Carica papaya, particularly its leaves, has surfaced as a promising seeker due to its rich array of bioactive phytochemicals. These composites have demonstrated anti-inflammatory, antimicrobial, and free revolutionary-scavenging parcels, conceivably contributing to their anticancer goods. This review synthesizes findings from preclinical examinations into the anticancer parcels of papaya splint excerpt(PLE). Studies indicate that PLE can inhibit cancer cell growth and induce apoptosis through colorful mechanisms, affecting multiple cancer cells, including those from the prostate, bone, lung, and liver. While preclinical data is promising, comprehensive clinical confirmation is essential to confirm the efficacy and safety of PLE in mortal cancer remedies. Bridging this gap in translational exploration is critical for considering PLE as a feasible adjuvant or volition to established cancer treatment protocols.

Keywords: Papaya leaves, Cancer treatment , Anticancer agent, Carica papaya, Phytochemicals .

INTRODUCTION:-

Papaya Leaves in Cancer Treatment

Papaya leaves have been gaining attention for their implicit part in cancer treatment. Rich in natural composites like flavonoids, Acetogenins, and antioxidants, these leaves are believed to help the body fight cancer by reducing inflammation, boosting impunity, and decelerating cancer cell growth. Some studies suggest that papaya splint excerpts may spark apoptosis(natural cell death) in cancer cells while leaving healthy cells unharmed. They may also help cancer cases witnessing chemotherapy by supporting platelet products and reducing side goods like fatigue and oxidative stress. While exploration is still ongoing, numerous people see papaya leaves as a promising natural supplement alongside conventional cancer treatments(1).

Despite significant strides in cancer exploration over the past many decades, the fight against cancer continues to be a monumental challenge. Cancer encompasses a growing list of conditions that affect cells going mischief and disregarding the body's nonsupervisory checkpoints. Experimenters are constantly exploring new treatment styles and operation strategies due to the absence of a one-size-fits-all cure and the complaint's adding frequency.

While cancer cases are on the rise, the effectiveness of conventional treatments like chemotherapy has reached a table. Also, these traditional treatments are frequently associated with a plethora of side goods, including toxins, weakened vulnerable systems, swelling, blood clots, and hair loss. This has led to a growing interest in indispensable curatives that have shown a pledge to halt the growth of cancer cells and reduce the threat of developing cancer. Studies have stressed that a diet rich in fruits and vegetables is linked to a lower threat of colorful cancers, including those affecting the bone, colon, lungs, pancreas, bladder, larynx, stomach, mouth, and Oesophagus(2).

Enter chemotherapeutic prevention, a volition to chemotherapy that uses natural or synthetic agents to help, suppress, or reverse the early stages of cancer development or to stop precancerous cells from getting nasty esophagus. Agents work in two ways: protecting against DNA damage that can lead to cancer or precluding the division of cells with damaged DNA. Using these agents as a volition to traditional cancer treatments is a logical approach to managing cancer. Salutary factors similar to capsaicin(set up in chili peppers), cucurbitacin B(from cucumbers), flavonoids, catechins(in tea), lycopene(in tomatoes), benzyl isothiocyanate and



phenethyl isothiocyanate(in cruciferous vegetables), resveratrol(in grapes and red wine), and Piperlongumine(from long pepper) have shown implicit in precluding cancer. (2)

The Carica papaya factory, generally known as the papaya factory, is famed for its multitudinous medicinal benefits. This presto-growing factory is generally set up in tropical and tropical regions worldwide. In colorful societies, especially among Indian and Indigenous Australian lines, the dinghy, leaves, and seeds of the papaya factory have been employed as natural remedies for digestive issues and indeed as precautionary measures against cancer. (3)

The factory is rich in colorful phytochemical composites that have demonstrated cancer-fighting parcels. These include substances similar as cucurbitacin B(set up in cucumbers), catechins(set up in tea), lycopene(set up in tomatoes), as well as benzyl isothiocyanate, phenethyl isothiocyanate, resveratrol(set up in grapes and red wine), Oesophagus. Alkaloids, glycosides, tannins, and flavonoids. These factors work together to boost the vulnerable system inhibition growth of cancer cells and indeed induce the natural death of these cells. (3)

Botanical Characteristics of Papaya Leaves

- **Shape:** Papaya leaves are large, lobed, and palmately emulsion, suggesting an open hand with fritters spread out.
- **Size** These leaves can grow up to 60 centimeters in length, furnishing a broad face area.
- **Texture** The face of papaya leaves is rough and slightly hairy, with prominent modes creating an intricate pattern.
- **Colour** They're generally vibrant green, indicating their health and vitality.
- **arrangement:** Papaya leaves are arranged in a helical pattern around the stem, optimizing sun prisoner.
- **Petiole:** The splint stalk(petiole) is long and sturdy, supporting the weight of the large splint blade and easing nutrient transport.
- **Stomata:** Papaya leaves have stomata(bitsy pores) on their face, allowing gas exchange necessary for photosynthesis and respiration. (4)



Fig; 1 Papaya leaves

Phytochemical composition of papaya

Papaya is a hustler of bioactive composites, including alkaloids, flavonoids, tannins, saponins, glycosides, marvels, and vitamins. These phytochemicals are responsible for the different mending parcels of the factory, from anti-inflammatory and antimicrobial goods to antioxidant and anti-cancer conditioning.



1. Alkaloids are composites that contain nitrogen that has significant pharmacological goods. Alkaloids similar to carpain were linked in the papaya. carpaine is known for its anti-inflammatory and antimicrobial parcels, making it precious in the treatment of colorful infections and seditious conditions. (4)

2. Flavonoid flavonoids are a group of polyphenolic composites that show strong antioxidant exertion. They help neutralize free revolutionaries and cover cells from oxidative damage. Papaya leaves are rich in flavonoids that contribute to their anti-inflammatory, antimicrobial, and anti-cancer goods. Quercetin and Kaempferol are two important flavonoids set up in the papaya leaves. (3)

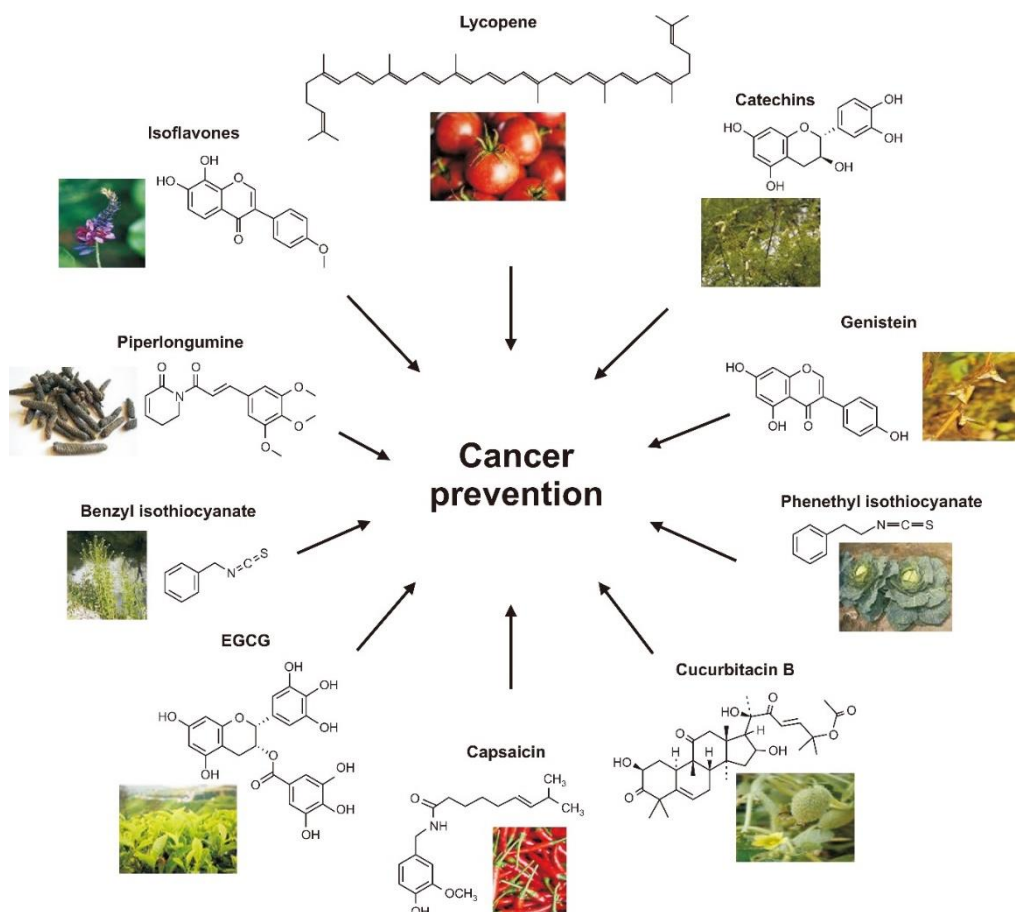
3. Tannins Tannins are polyphenolic composites that have luminous parcels. They're known for their capability to precipitate proteins and form complexes with essence ions. In the papaya, tannins contribute to the antimicrobial and antioxidant conditioning of the factory. They help inhibit the growth of bacteria and fungi, causing effective papaya in the treatment of infections. (4)

4. Saponins Saponins are glycosides that have cleaner-like parcels. They're known for their capability to produce stable lathers in waterless results. Saponins in papaya have been shown to have antimicrobial, anti-inflammatory, and anti-cancer parcels. They help strengthen the vulnerable system and cover against colorful conditions.

5. Glycosides Glycosides are composites that correspond to a sugar patch associated with a sugar-free patch. Glycosides similar to papain were linked in the papaya. Papain is a proteolytic enzyme that helps digestion and has anti-inflammatory and antimicrobial properties. It's generally used in the treatment of digestive diseases and crack mending.

6. Fenics Phenolic composites are known for their antioxidant exertion. They help protect cells from oxidative stress and reduce the threat of habitual conditions. Papaya contains colorful phenolic composites, including caffeic acid and ferulic acid, which contribute to its antioxidants and anti-cancer parcels.

7. Vitamins Papaya is a rich source of introductory vitamins, including vitamin C, vitamin A, and vitamin E. Vitamin C is a strong antioxidant that helps strengthen the vulnerable system and cover from infection. Vitamin A is important for vision and skin health, while vitamin E helps protect cells from oxidative damage. (4)





DETAIL OVERVIEW OF PHYTOCONSTITUENT OF PAPAYA

ALKALOID

Papaya: A Natural Treasure in Cancer Therapy

Papaya, scientifically referred to as *Carica papaya* Linn., is a tropical fruit cherished for its abundant bioactive compounds. Among these, alkaloids stand out as particularly promising for their potential in combating cancer. Alkaloids are natural organic molecules containing nitrogen and are celebrated for their wide array of medicinal uses. The alkaloid most noteworthy in papaya is carpaine, widely recognized for its therapeutic properties. (5)

Carpaine: Papaya's Notable Alkaloid

Carpaine, a bitter compound present in papaya leaves, seeds, and latex, offers numerous pharmacological benefits. Known for its anti-inflammatory, antimicrobial, and cardiogenic properties, it has recently gained attention for its anticancer potential, establishing itself as a strong contender in cancer treatment. (6)

How Carpaine Fights Cancer

Carpaine's anticancer effectiveness lies in its interaction with various biological pathways and molecular targets. Here are the primary ways it combats cancer:

1. **Halting Cancer Cell Growth:** Carpaine disrupts the cell cycle by targeting cyclin-dependent kinases (CDKs), essential regulators of cell division. This disruption effectively prevents the proliferation of cancer cells.
2. **Inducing Apoptosis:** Apoptosis, or programmed cell death, is critical for eliminating cancer cells. Carpaine triggers apoptotic pathways by enhancing pro-apoptotic proteins and reducing anti-apoptotic proteins, facilitating the controlled destruction of cancer cells.
3. **Neutralizing Oxidative Stress:** Oxidative stress, caused by an imbalance of free radicals and antioxidants, significantly contributes to cancer development. Carpaine's antioxidant properties help counteract free radicals, shielding cells from damage and reducing the likelihood of mutations.
4. **Reducing Inflammation:** Chronic inflammation is a known catalyst for cancer. Carpaine's potent anti-inflammatory properties suppress the production of pro-inflammatory cytokines and enzymes, thus inhibiting cancer cell growth. (7)

Flavonoids in Papaya: A Closer Look

Papaya is also rich in flavonoids, a group of polyphenolic compounds renowned for their antioxidant, anti-inflammatory, and anticancer properties. Key flavonoids found in papaya include quercetin, kaempferol, and myricetin. These compounds are primarily located in the leaves, fruits, and seeds.

Key Flavonoids in Papaya

1. **Quercetin:** With powerful antioxidant and anti-inflammatory effects, quercetin is widely studied for its ability to inhibit the growth of cancer cells. It helps shield cells from oxidative damage and modulates pathways involved in cancer progression.
2. **Kaempferol:** This flavonoid exhibits notable anticancer activity, inducing apoptosis in cancer cells and curbing their proliferation. Its anti-inflammatory and antioxidant properties further amplify its therapeutic value.
3. **Myricetin:** Known for its significant antioxidant and anticancer benefits, myricetin promotes apoptosis in cancer cells, reduces inflammation, and safeguards cells from oxidative stress. (8)

Flavonoids in papaya function through multiple biological mechanisms:

1. **Inhibiting Cancer Cell Proliferation:** Compounds like quercetin and kaempferol block CDKs and other regulators of the cell cycle, effectively halting cancer cell growth.



2. **Triggering Apoptosis:** Flavonoids activate apoptosis pathways by increasing pro-apoptotic proteins and reducing anti-apoptotic ones, facilitating the controlled death of cancer cells.
3. **Combating Oxidative Stress:** These compounds neutralize free radicals, preventing oxidative damage that could lead to cancer mutations.
4. **Suppressing Inflammation:** Flavonoids like quercetin and kaempferol mitigate inflammation by inhibiting the production of pro-inflammatory cytokines and enzymes, which are crucial for cancer progression. (9)

Tannins in Papaya: Potential Cancer Allies

Papaya also contains tannins, including hydrolyzable tannins and condensed tannins, which contribute to its medicinal properties.

Key Types of Tannins

1. **Hydrolyzable Tannins:** These tannins break down into simpler compounds like gallic acid and ellagic acid. They exhibit strong antioxidant and anticancer properties by protecting cells from oxidative stress and curbing cancer cell growth.
2. **Condensed Tannins:** Also known as proanthocyanidins, these tannins are polymers of flavonoid units. They are known to inhibit cancer proliferation and promote apoptosis. (10)

Mechanisms of Tannins in Cancer Treatment

1. **Blocking Cancer Cell Growth:** Tannins target CDKs and other cell cycle regulators, effectively halting the division of cancer cells.
2. **Inducing Apoptosis:** They activate apoptotic pathways, increasing pro-apoptotic proteins while reducing anti-apoptotic ones to eliminate cancer cells.
3. **Reducing Oxidative Stress:** Tannins act as powerful antioxidants, neutralizing free radicals and preventing cellular damage that could lead to cancer development. (11)

Phenolics in Papaya: A Natural Ally in Cancer Treatment

Papaya (*Carica papaya* Linn.), a tropical fruit celebrated for its myriad health benefits, is rich in bioactive compounds. Among these, phenolic compounds have emerged as key contributors in the realm of cancer therapy. Phenolics are a diverse group of plant-derived chemicals characterized by hydroxyl groups attached to aromatic rings. Known for their potent antioxidant, anti-inflammatory, and anticancer properties, these compounds are primarily found in papaya's leaves, fruit, and seeds. Below, we delve into the types of phenolics in papaya, their medicinal applications, and the mechanisms underlying their anticancer effects. (12)

Types of Phenolic Compounds in Papaya

Papaya contains several types of phenolic compounds, each playing a unique role in its therapeutic benefits:

1. **Phenolic Acids:** Phenolic acids, such as gallic acid and caffeic acid, are abundant in papaya. These compounds are renowned for their ability to protect cells against oxidative stress and curb the proliferation of cancer cells, making them highly significant in anticancer research.
2. **Flavonoids:** Among the notable flavonoids found in papaya are quercetin, kaempferol, and myricetin. These compounds exhibit impressive antioxidant capabilities and actively influence biological pathways linked to cancer progression.
3. **Tannins:** Tannins, known for their astringent properties, contribute significantly to papaya's medicinal value. They exhibit strong antioxidant activity, inhibit cancer cell growth, and induce apoptosis (programmed cell death), positioning them as vital anticancer agents. (13)



Mechanisms of Anticancer Activity

The phenolic compounds in papaya combat cancer through various biological mechanisms. Here are the key ways in which they exert their therapeutic effects:

- 1. Restricting Cancer Cell Growth:** Phenolics disrupt the cell cycle by targeting cyclin-dependent kinases (CDKs) and other molecules essential for cell division. This interruption halts the proliferation of cancer cells and prevents tumor growth.
- 2. Inducing Apoptosis:** Apoptosis, the process of programmed cell death, is crucial for eliminating cancer cells. Phenolic compounds in papaya activate apoptotic pathways by enhancing pro-apoptotic proteins and suppressing anti-apoptotic proteins, ensuring the controlled destruction of cancerous cells.
- 3. Neutralizing Oxidative Stress:** Oxidative stress arises from an imbalance between free radicals and antioxidants, often contributing to cancer development. Papaya's phenolics counteract oxidative stress by neutralizing free radicals, protecting healthy cells from damage, and reducing the likelihood of mutations that lead to cancer.
- 4. Reducing Inflammation:** Chronic inflammation is a significant risk factor for cancer. Papaya's phenolics possess anti-inflammatory properties that help suppress the production of pro-inflammatory cytokines and enzymes. This reduces inflammation and impedes cancer cell growth. (14)

Mechanisms of Action of Papaya Leaf Extracts in Cancer Treatment

Cancer, a complex disease defined by the uncontrolled growth of abnormal cells, often requires aggressive treatments like chemotherapy and radiation. While effective, these treatments can result in severe side effects. This has driven researchers to explore natural alternatives, such as papaya leaf extract, for their potential anticancer properties. Derived from *Carica papaya*, papaya leaves have a long history in traditional medicine and have shown promising results against various forms of cancer. Their effectiveness is attributed to their rich content of bioactive compounds, including flavonoids, alkaloids, saponins, and phenolic compounds. These components work through multiple mechanisms to inhibit tumor growth, strengthen the immune system, and halt cancer progression. (15)

1. Inducing Apoptosis (Programmed Cell Death)

One of the primary ways papaya leaf extract combats cancer is by inducing apoptosis, the body's natural process of programmed cell death. In healthy individuals, apoptosis helps eliminate damaged or dysfunctional cells. However, cancer cells often evade this process, enabling their uncontrolled growth.

Papaya leaf extract contains compounds, such as flavonoids and alkaloids, that re-establish this balance by triggering apoptotic pathways in cancer cells. These compounds stimulate pro-apoptotic proteins like Bax and caspases, which dismantle cancer cells from the inside. At the same time, they suppress anti-apoptotic proteins like Bcl-2, which cancer cells rely on to evade death. This dual action forces cancer cells to undergo apoptosis, curbing tumor growth. Furthermore, studies suggest that papaya leaf extract specifically targets cancer cells while leaving healthy cells unharmed. This selective nature makes it a promising, less toxic alternative to traditional chemotherapy, which often harms healthy cells alongside cancerous ones. (14)

2. Inhibiting Cancer Cell Growth (Anti-Proliferative Effects)

Another critical mechanism is the ability of papaya leaf extract to suppress the rapid division of cancer cells, a hallmark of tumor growth.

The bioactive compounds in papaya leaves interfere with the cell cycle, which governs cell division and growth. These compounds arrest cancer cells at certain checkpoints, effectively halting their progression. Research has shown that papaya leaf extract can inhibit essential enzymes like cyclins and cyclin-dependent kinases (CDKs), disrupting the cycle necessary for cancer cell proliferation. Additionally, phenolic compounds and flavonoids in the extract inhibit angiogenesis—the formation of new blood vessels that supply tumors with nutrients. Without adequate blood flow, tumors struggle to grow and may even shrink. (13)



3. Boosting the Immune System

The immune system plays a critical role in recognizing and eliminating cancerous cells. However, many cancers develop mechanisms to evade immune detection, compromising the body's natural defense.

Papaya leaf extract has been shown to enhance immune function by stimulating the production of cytokines, such as interferon-gamma (IFN- γ) and interleukins (IL-2 and IL-12). These cytokines activate immune cells like natural killer (NK) cells and T-cells, which are essential for targeting and destroying cancer cells. Additionally, papaya leaf extract has demonstrated immune-boosting properties in dengue fever by increasing platelet counts. This benefit could extend to cancer patients, particularly those undergoing chemotherapy, which often weakens the immune system. By restoring immune function, papaya leaf extract can improve overall treatment outcomes. (10)

4. Reducing Oxidative Stress (Antioxidant Properties)

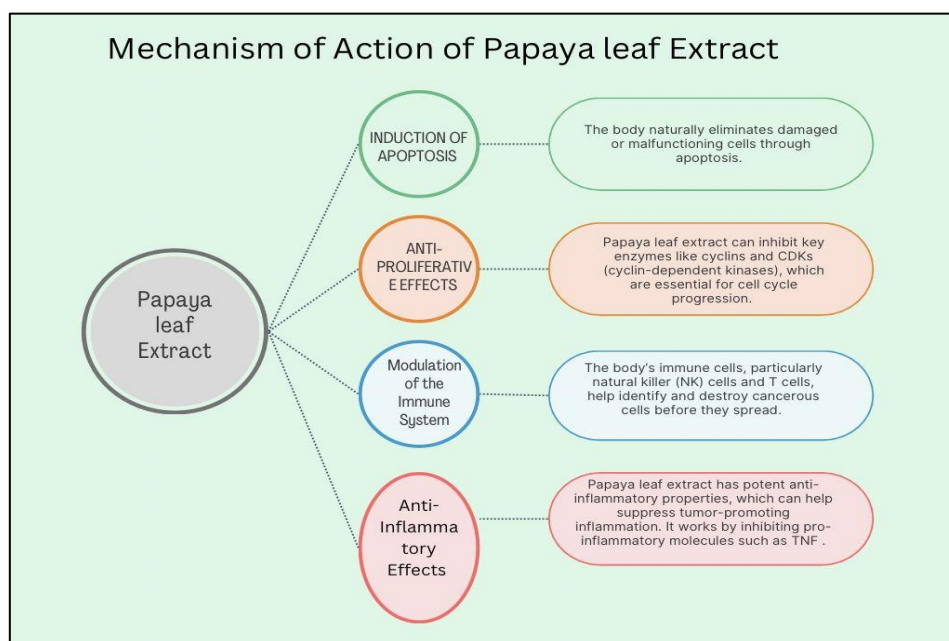
Oxidative stress, caused by an imbalance between free radicals and antioxidants, is a significant factor in cancer development. Free radicals can damage DNA, leading to mutations that transform normal cells into cancerous ones.

Rich in antioxidants such as flavonoids, vitamin C, and beta-carotene, papaya leaves neutralize harmful free radicals and reduce oxidative stress. This protective action minimizes DNA damage and lowers the risk of cancer initiation and progression. Moreover, antioxidants in papaya leaves have been found to enhance the efficacy of chemotherapy and radiation by reducing their oxidative side effects, such as fatigue and tissue damage. (16)

5. Reducing Cancer-Related Inflammation (Anti-Inflammatory Effects)

Chronic inflammation is a major contributor to cancer progression, as it creates an environment conducive to tumor growth by providing nutrients and facilitating metastasis.

Papaya leaf extract exhibits potent anti-inflammatory effects, inhibiting key pro-inflammatory molecules like tumor necrosis factor-alpha (TNF- α) and nuclear factor kappa B (NF- κ B). These molecules are crucial for cancer cell survival and spread. By suppressing inflammation, papaya leaf extract not only slows tumor growth but also alleviates common symptoms in cancer patients, such as pain, swelling, and fatigue. (17)





Conclusion

Papaya leaves, derived from the *Carica papaya* plant, have garnered attention as a natural approach to fight against cancer. These leaves are packed with potent bioactive compounds, including flavonoids, alkaloids, and phenolic substances, which work together to deliver impressive anticancer benefits. Their mechanisms include inducing apoptosis (a natural process of programmed cell death), inhibiting the rapid multiplication of cancer cells, fortifying the immune system, alleviating oxidative stress, and curbing inflammation.

What truly sets papaya leaf extract apart is its remarkable ability to distinguish between healthy and cancerous cells, selectively targeting the latter. This precision makes it a compelling complementary option alongside traditional treatments like chemotherapy and radiation, which often come with harsh side effects. Additionally, its immune-boosting qualities hold promise in enhancing the body's resilience, particularly for patients undergoing taxing cancer therapies.

While preclinical studies and laboratory findings are encouraging, there is a crucial need for more clinical trials to validate the safety, effectiveness, and appropriate dosages for human use. Moving forward, research should prioritize uncovering the exact molecular mechanisms that drive its anticancer properties, optimizing extraction methods for maximum efficacy, and assessing how it integrates with existing cancer treatments.

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