

## Herbal and Botanical Review

# Potential Benefits of Green Tea in Prostate Cancer Prevention and Treatment: A Comprehensive Review

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**ABSTRACT** Prostate cancer is a prevalent and debilitating disease that necessitates effective prevention and treatment strategies. Green tea, a well-known beverage derived from the *Camellia sinensis* plant, contains bioactive compounds with potential health benefits, including catechins and polyphenols. This comprehensive review aims to explore the potential benefits of green tea in prostate cancer prevention and treatment by examining existing literature. Green tea possesses antioxidant, anti-inflammatory, and anti-carcinogenic properties attributed to its catechins, particularly epigallocatechin gallate. Epidemiological studies have reported an inverse association between green tea consumption and prostate cancer risk, with potential protection against aggressive forms of the disease. Laboratory studies demonstrate that green tea components inhibit tumor growth, induce apoptosis, and modulate signaling pathways critical to prostate cancer development and progression. Clinical trials and human studies further support the potential benefits of green tea. Green tea consumption has been found to be associated with a reduction in prostate-specific antigen levels, tumor markers, and played a potential role in slowing disease progression. However, challenges remain, including optimal dosage determination, formulation standardization, and conducting large-scale, long-term clinical trials. The review suggests future research should focus on combinatorial approaches with conventional therapies and personalized medicine strategies to identify patient subgroups most likely to benefit from green tea interventions.

**KEYWORDS** green tea, prostate cancer, prevention, treatment, epigallocatechin gallate, review

Prostate cancer is one of the most common types of cancer among men worldwide.<sup>(1)</sup> The impact of prostate cancer extends beyond its prevalence, as it can significantly affect the quality of life of affected individuals and their families.<sup>(2)</sup> Prostate cancer is characterized by a range of symptoms, including urinary problems, sexual dysfunction, and, in advanced stages, bone pain and other systemic manifestations.<sup>(3)</sup> Given the considerable impact of prostate cancer, there is an urgent need for effective prevention and treatment strategies.<sup>(4)</sup> Early detection through regular screening and timely intervention can greatly improve outcomes for patients.<sup>(5,6)</sup> Additionally, advancements in treatment options have led to better management of localized and advanced prostate cancer, including surgery, radiation therapy, hormonal therapy, chemotherapy, and emerging targeted therapies.<sup>(7-9)</sup>

However, despite these advancements, challenges remain in preventing and effectively treating prostate cancer. Not all cases are detected early, and some may become resistant to conventional therapies.<sup>(10-12)</sup> Nowadays, there is a growing interest in complementary

and alternative medicine for managing a wide variety of diseases.<sup>(13,14)</sup> In particular, there is a significant effort to explore complementary approaches that can enhance existing treatment strategies or provide alternative options for prevention and management.<sup>(15-17)</sup>

Green tea, derived from the *Camellia sinensis* plant, has been widely studied for its bioactive compounds with potential health benefits.<sup>(18,19)</sup> These compounds, such as catechins and polyphenols, have shown promising effects in laboratory and preclinical studies, suggesting their potential role in inhibiting tumor growth, inducing cancer cell death, and modulating various cellular processes involved in

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prostate cancer development and progression.<sup>(20-22)</sup>

The aim of this comprehensive review is to explore the potential benefits of green tea in prostate cancer prevention and treatment. By examining the existing literature, we aim to summarize the current knowledge regarding the effects of green tea and its bioactive components on prostate cancer.

### Green Tea and Prostate Cancer: An Overview

Green tea is a popular beverage originating from the leaves of the *Camellia sinensis* plant.<sup>(23)</sup> It has been consumed for centuries in many Asian countries and has gained attention globally for its potential health benefits.<sup>(24,25)</sup> Green tea undergoes minimal oxidation during its production, which helps to preserve its natural compounds and unique properties.<sup>(26,27)</sup> Green tea contains various bioactive components, including polyphenols, catechins, flavonoids, and alkaloids.<sup>(28,29)</sup> Among these, the most abundant and well-studied bioactive compounds are epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC), and epigallocatechin gallate (EGCG).<sup>(24,30)</sup> EGCG, in particular, has been extensively investigated for its potential health-promoting properties, including its anticancer effects.<sup>(31,32)</sup>

Epidemiological studies have explored the relationship between green tea consumption and prostate cancer incidence, progression, and overall risk reduction.<sup>(33,34)</sup> However, findings have been somewhat mixed, several studies suggest a potential protective effect of green tea against prostate cancer.<sup>(35,36)</sup> Some population-based studies have observed an inverse association between green tea consumption and the risk of developing prostate cancer.<sup>(35,36)</sup> These studies have indicated that individuals who regularly consume green tea may have a lower incidence of prostate cancer compared to those who consume it less frequently or not at all. Furthermore, there is evidence suggesting that green tea may play a role in reducing the risk of advanced or aggressive forms of prostate cancer.<sup>(37,38)</sup> Some studies have reported associations between green tea consumption and decreased risk of advanced prostate cancer or slower disease progression.<sup>(39,40)</sup> However, additional research is needed to confirm and further elucidate these findings.

The potential mechanisms by which green tea may exert protective effects against prostate

cancer are still under investigation. The bioactive components of green tea, especially EGCG, have been shown to possess antioxidant, anti-inflammatory, and anti-carcinogenic properties. They can modulate signaling pathways involved in cell growth, apoptosis, angiogenesis, and metastasis, which are crucial in prostate cancer development and progression.<sup>(41,42)</sup>

### Anticancer Properties of Green Tea

Green tea contains a range of bioactive components that contribute to its potential health benefits.<sup>(43)</sup> The most abundant and well-studied bioactive compounds in green tea are catechins, a type of flavonoid.<sup>(44,45)</sup> The major catechins found in green tea include EC, ECG, EGC, and EGCG.<sup>(30,46)</sup> Among these, EGCG is considered the most potent and extensively studied. It is estimated that EGCG accounts for about 50%–75% of the total catechin content in green tea.<sup>(47)</sup> These catechins possess strong antioxidant activity, which helps to protect cells from oxidative damage caused by free radicals.<sup>(48)</sup> Additionally, they have been shown to have anti-inflammatory, antimicrobial, and anticancer properties.<sup>(49)</sup>

### Antioxidant Properties

Green tea is rich in polyphenols, particularly catechins, which possess potent antioxidant properties.<sup>(50)</sup> These antioxidants help neutralize harmful free radicals in the body, which can cause DNA damage and contribute to the development and progression of cancer, including prostate cancer. By reducing oxidative stress and DNA damage, green tea's antioxidants may help protect against prostate cancer.<sup>(51)</sup>

### Anti-inflammatory Effects

Chronic inflammation has been implicated in various stages of cancer development, including prostate cancer.<sup>(52)</sup> Green tea and its bioactive components have demonstrated anti-inflammatory effects by inhibiting pro-inflammatory cytokines, enzymes, and signaling pathways. By modulating inflammation, green tea may help suppress the growth and progression of prostate cancer cells.<sup>(53,54)</sup>

### Antiangiogenic Activity

Angiogenesis is crucial for tumor growth and metastasis.<sup>(55)</sup> Green tea polyphenols, particularly EGCG, have shown antiangiogenic properties by inhibiting the production of vascular endothelial growth factor (VEGF) and other factors involved in blood vessel formation.<sup>(20,56)</sup> By inhibiting angiogenesis,

green tea may help limit the blood supply to prostate tumors, thus impeding their growth and spread.<sup>(57)</sup>

### Modulation of Cell Signaling Pathways

Green tea and its bioactive components can interfere with several signaling pathways involved in cancer cell growth and survival.<sup>(58)</sup> For instance, EGCG has been shown to inhibit the activation of nuclear factor-kappa B (NF- $\kappa$ B), a transcription factor involved in inflammation and cell proliferation.<sup>(59)</sup> Additionally, green tea compounds can influence other pathways, such as PI3K/AKT, Mitogen-activated protein kinase (MAPK), and Wnt/ $\beta$ -catenin, which play roles in prostate cancer development and progression.<sup>(60,61)</sup> MAPK pathway plays a vital role in cell proliferation and survival. Green tea polyphenols can modulate this pathway, controlling the aberrant cell growth in prostate cancer.<sup>(62)</sup> Dysregulation of the Wnt/ $\beta$ -catenin pathway is common in cancers, including prostate cancer. Green tea compounds can interfere with this pathway, potentially preventing uncontrolled cell division and tumor formation. NF- $\kappa$ B is a transcription factor involved in inflammation and cell proliferation.<sup>(63)</sup> EGCG has been shown to inhibit NF- $\kappa$ B activation, curb the inflammatory responses and unchecked cell growth in prostate cancer.<sup>(64-66)</sup>

### Induction of Apoptosis and Cell Cycle Arrest

Apoptosis, or programmed cell death, is a crucial mechanism for eliminating damaged or cancerous cells.<sup>(67)</sup> Green tea polyphenols have been found to induce apoptosis and cell cycle arrest in prostate cancer cells by regulating key molecules involved in these processes.<sup>(20)</sup> This can help prevent uncontrolled cell growth and the formation of tumors.

### Mitochondrial Dysfunction and Caspase Activation

Tea polyphenols, especially EGCG, induce mitochondrial dysfunction in prostate cancer cells.<sup>(68)</sup> This disruption of the mitochondria, the powerhouse of the cell, hampers energy production and triggers apoptotic pathways, leading to cell death.<sup>(69)</sup> EGCG activates various caspases, including caspase-3 and -9.<sup>(70)</sup> Caspases are key enzymes in apoptosis, orchestrating the dismantling of cellular components and ensuring the orderly demise of cancerous cells.<sup>(71)</sup>

### Inhibition of Survival Pathways and Antiinvasive Effects

By inhibiting NF- $\kappa$ B pathway, tea polyphenols

inhibit the survival signals, curbing the uncontrolled growth of prostate cancer cells.<sup>(63,72)</sup> EGCG impedes the invasion of prostate cancer cells by downregulating matrix metalloproteinases (MMPs),<sup>(73)</sup> which facilitate the breakdown of extracellular matrix, a crucial step in cancer cell invasion and metastasis.<sup>(74)</sup> By suppressing MMPs, tea polyphenols mitigate the invasive potential of prostate cancer cells.<sup>(75)</sup>

### Modulation of miRNA Expression and Epigenetic Alterations

Tea polyphenols, particularly EGCG, modify miRNA expression profiles.<sup>(75)</sup> Altered miRNA expression can influence cancer-related pathways as a potential therapeutic target.<sup>(76)</sup> EGCG has the ability to reverse epigenetic alterations, including DNA methylation and histone modifications.<sup>(77)</sup> Restoring normal epigenetic patterns can reinstate the control over gene expression, hinder the aberrant growth of prostate cancer cells.<sup>(78)</sup>

The combined effects of green tea's antioxidant, anti-inflammatory, antiangiogenic properties, and its ability to modulate key signaling pathways contribute to its potential anticancer effects, including its relevance to prostate cancer prevention and treatment.<sup>(79)</sup> Table 1 summarizes mechanisms of action of green tea in prostate cancer.

### Green Tea and Prostate Cancer Prevention

Several review studies have synthesized the available evidence regarding the potential role of green tea in prostate cancer prevention and progression. A systematic review and meta-analysis by Guo, et al<sup>(35)</sup> found that green tea consumption was associated with a reduced risk of developing prostate cancer. The study reported a significant inverse association between green tea intake and prostate cancer incidence, particularly for advanced or aggressive forms of the disease.

*In vivo* and *in vitro* studies have provided insights into the mechanisms underlying the potential anticancer effects of green tea in prostate cancer. In terms of tumor growth inhibition, a study by Khan, et al<sup>(80)</sup> investigated the effects of EGCG on the growth of human prostate cancer cells implanted in mice. They observed a significant reduction in tumor volume and weight in the EGCG-treated group compared to the control group. This effect was attributed to the inhibition

**Table 1. Mechanisms of Action of Green Tea in Prostate Cancer**

Mechanism	Details
Antioxidant properties	Green tea's polyphenols, especially EGCG, neutralize harmful free radicals, reducing oxidative stress and DNA damage
Anti-inflammatory effects	Inhibits pro-inflammatory cytokines, enzymes, and pathways, modulating inflammation and suppressing cancer cell growth
Antiangiogenic activity	Inhibits angiogenesis by reducing production of VEGF and other pro-angiogenic factors, limiting blood supply to tumors, hindering tumor growth and metastasis
Modulation of cell Signaling pathways	Interferes with pathways like NF- $\kappa$ B, PI3K/AKT, MAPK, and Wnt/ $\beta$ -catenin, which are crucial in cancer development, inhibiting proliferation and promoting apoptosis
Induction of apoptosis and cell cycle arrest	Green tea polyphenols induce apoptosis and arrest cell cycle in prostate cancer cells, preventing uncontrolled growth and tumor formation
Epigenetic regulation	Influences DNA methylation and histone acetylation, affecting gene expression, potentially preventing or slowing down prostate cancer progression
Inhibition of PI3K/AKT pathway	EGCG inhibits the PI3K/AKT pathway, vital for cell survival and growth, suppressing proliferation and survival of prostate cancer cells
Modulation of AR signaling	Interferes with AR signaling, either by suppressing AR expression or inhibiting its activity, impacting the growth of prostate cancer cells
Oxidative stress and antioxidant defense	Counters oxidative stress, supporting cellular homeostasis and inhibiting cancer progression
Synergistic effects with other treatments	Enhances efficacy of chemotherapy and radiation therapy, potentially overcoming drug resistance and promoting cancer cell death

Notes: EGCG: epigallocatechin gallate; VEGF: vascular endothelial growth factor; MAPK: mitogen-activated protein kinase; AR: androgen receptor

of cell proliferation and the promotion of apoptosis.

Regarding apoptosis induction, studies have shown that green tea catechins can modulate various signaling pathways involved in cell death. Siddiqui, et al<sup>(81)</sup> demonstrated that EGCG can induce apoptosis in prostate cancer cells by activating the caspase cascade, which plays a crucial role in the apoptotic process. The regulation of the cell cycle by green tea components has also been investigated. Gupta, et al<sup>(82)</sup> demonstrated that EGCG can arrest prostate cancer cells at the G<sub>0</sub>/G<sub>1</sub> phase by downregulating cyclin-dependent kinases (CDKs) and cyclins, key regulators of the cell cycle progression. A study by Deb, et al<sup>(83)</sup> demonstrated that EGCG can inhibit the migration

and invasion of prostate cancer cells by suppressing the expression of MMPs, enzymes involved in the breakdown of extracellular matrix during metastasis.

### Green Tea and Prostate Cancer Treatment

Studies have explored the potential therapeutic benefits of green tea in the treatment of prostate cancer, with a focus on its impact on key factors such as prostate cancer cell proliferation, apoptosis induction, and sensitization to conventional treatments like chemotherapy or radiation therapy.

### Impact on Prostate Cancer Cell Proliferation

Green tea and its bioactive components have been investigated for their ability to inhibit prostate cancer cell proliferation.<sup>(84)</sup> In a study by Thangapazham, et al,<sup>(85)</sup> treatment with EGCG led to a significant reduction in the growth of prostate cancer cells *in vitro*. This suggests that green tea compounds may slow down the progression of prostate cancer by impeding the proliferation of cancer cells.

### Induction of Apoptosis in Prostate Cancer Cells

One of the hallmarks of successful cancer treatment is the induction of apoptosis, or programmed cell death, in cancer cells. Green tea catechins, particularly EGCG, have demonstrated the ability to induce apoptosis in prostate cancer cells.<sup>(86,87)</sup> These findings suggest that green tea compounds may have a direct cytotoxic effect on prostate cancer cells, promoting their death and potentially inhibiting tumor growth.

Gupta, et al<sup>(88)</sup> investigated the mechanisms of green tea polyphenols (GTP)-induced apoptosis in human prostate cancer cells with or without p53 suppression. GTP treatment activated distinct pathways, including p53-dependent activation of p21/waf1 and Bax, and Fas upregulation through the c-jun-N-terminal kinase pathway. Both pathways converged to induce mitochondrial dysfunction, cytochrome C release, and caspase activation, leading to cell death. GTP also inhibited the survival pathway mediated by Akt, particularly in cells with p53 suppression. Furthermore, GTP inhibited class I histone deacetylase protein, increased accessibility of transcription factors to the promoters of p21/waf1 and Bax. These findings reveal specific molecular mechanisms targeted by GTP, suggesting its potential as a chemopreventive or therapeutic strategy for prostate cancer, regardless of p53 status.



### Sensitization to Chemotherapy or Radiation Therapy

In addition to its direct effects on prostate cancer cells, green tea has also shown promise in sensitizing cancer cells to conventional treatments such as chemotherapy or radiation therapy.<sup>(54)</sup> For instance, a study by Siddiqui, et al<sup>(89)</sup> demonstrated that EGCG sensitized prostate cancer cells to the effects of radiation therapy. The combination of EGCG and radiation therapy resulted in enhanced cell death compared to radiation therapy alone. Similarly, other studies have reported synergistic effects between green tea components and chemotherapy drugs, such as docetaxel or cisplatin, leading to increased cancer cell death.<sup>(90,91)</sup> These findings suggest that green tea may enhance the efficacy of conventional treatments and potentially overcome drug resistance in prostate cancer cells.

### Clinical Evidence and Human Studies

Clinical trials and human studies investigating the effects of green tea in prostate cancer prevention and treatment have provided valuable insights into its potential benefits.

In a randomized controlled trial (RCT) conducted by Henning, et al,<sup>(92)</sup> 97 male patients with prostate cancer who were scheduled for radical prostatectomy were assigned to receive either 6 cups of brewed green tea or water daily for 3–8 weeks before surgery. The study found that green tea consumption resulted in a significant reduction in prostate-specific antigen (PSA) levels and tumor markers, suggesting a potential role in slowing disease progression.

Another study by Bettuzzi, et al<sup>(93)</sup> evaluated the effects of a green tea extract capsule in men with high-grade prostate intraepithelial neoplasia (PIN), a precursor to prostate cancer. The participants received green tea extract or a placebo for 1 year. The study found that green tea extract led to a reduction in the incidence of prostate cancer in men with high-grade PIN.

A systematic review and meta-analysis by Guo, et al<sup>(94)</sup> examined 7 observational studies and 3 RCTs and found that green tea consumption was associated with a reduced risk of developing prostate cancer. The results of this study demonstrated a dose-response relationship between green tea intake and the risk of prostate cancer. While the highest *versus* lowest category comparison did not show statistical significance, there was a trend of reduced prostate

cancer incidence with each 1 cup/day increase of green tea. The dose-response meta-analysis further revealed that higher green tea consumption, specifically more than 7 cups/day, was linearly associated with a decreased risk of prostate cancer. Additionally, the study found that green tea catechins were effective in preventing prostate cancer, with a relative risk of 0.38. This study provides systematic and quantitative evidence supporting the association between green tea intake and prostate cancer risk, emphasizing the potential benefits of higher green tea consumption and the effectiveness of green tea catechins in prostate cancer prevention.

Elham Sharifi-Zahabi, et al<sup>(95)</sup> in a systematic review and meta-analysis of RCTs evaluated the effects of green tea consumption on prostate-specific antigen (PSA) levels. A total of 7 studies were included in the meta-analysis. The overall analysis indicated that green tea did not have a significant impact on PSA levels (weighted mean difference:  $-0.60$  ng/mL; 95% confidence interval:  $-1.32, 0.12$  ng/mL;  $P=0.104$ ). However, subgroup analysis based on geographical location showed that green tea significantly reduced PSA levels in the USA population compared to non-USA populations. The study concluded that green tea consumption did not have a significant effect on PSA levels overall, further consistent clinical trials with larger sample sizes are needed to draw more conclusive findings due to the heterogeneity among the included studies.

### Crucial Consideration: Dosage of Tea Polyphenols in Cancer Prevention

Determining the appropriate dosage of tea polyphenols is a pivotal factor in optimizing their potential for cancer prevention. The relationship between dosage and efficacy is multifaceted, which could be influenced by various factors such as the type of tea consumed, the concentration of polyphenols, and individual differences in metabolism.

### Optimal Dosage Range

Studies exploring the optimal dosage of tea polyphenols have yielded valuable insights. It is essential to strike a balance, ensuring a dosage that is both safe and effective. For instance, a moderate daily consumption of green tea, often ranging from 3 to 5 cups, has been associated with potential health benefits, including cancer prevention.<sup>(96)</sup> However,

higher dosages, typically exceeding 5 cups per day, might be necessary to achieve notable effects in cancer prevention.<sup>(96)</sup>

### Bioavailability Challenges

The body's ability to absorb and utilize polyphenols varies among individuals, and this bioavailability significantly impacts the effective dosage.<sup>(97)</sup> Factors such as gastrointestinal absorption, metabolism, and excretion processes play a crucial role. Research suggests that the bioavailability of tea polyphenols can be enhanced by consuming tea with certain foods or substances, thereby improving their absorption in the body.<sup>(98)</sup>

While tea polyphenols offer potential health benefits, excessive consumption may lead to adverse effects. High doses, especially in supplement form, might interact with medications or negatively impact certain individuals. Hence, a cautious approach is essential, and consultation with healthcare professionals is advised, particularly for individuals with existing health conditions or those on specific medications.<sup>(99,100)</sup>

### Direct Absorption and Distribution of Tea Polyphenols into Prostate Tissues: Current Insights

Research has indicated that tea polyphenols, including EGCG and other catechins, can indeed be absorbed and distributed into prostate tissues. Studies conducted both *in vitro* and *in vivo* have demonstrated the presence of these compounds in prostate cells after oral consumption of green tea extracts.<sup>(47)</sup> This suggests that tea polyphenols have the potential to directly interact with prostate cells, influencing various cellular processes.

The absorption of tea polyphenols involves complex mechanisms within the gastrointestinal tract. These compounds are absorbed through the intestinal epithelial cells and enter the bloodstream, allowing them to reach various organs and tissues, including the prostate. Studies have explored the role of specific transporters and carriers in facilitating the absorption of tea polyphenols, shedding light on the molecular processes involved.<sup>(101,102)</sup> Upon absorption, tea polyphenols are distributed throughout the body, including prostate tissues. Research has shown that these compounds can accumulate in the prostate gland, potentially reaching concentrations that are

biologically relevant for exerting their effects.<sup>(38)</sup>

### Limitations and Challenges

While clinical trials and human studies provide valuable evidence, there are several limitations and challenges associated with translating preclinical and epidemiological findings to clinical practice. One challenge is the variability in the bioavailability and metabolism of green tea components among individuals. Factors such as the form of green tea consumed, dosage, preparation method, and genetic differences can influence the absorption and effectiveness of the bioactive compounds. Standardization of green tea products and dosages remains a challenge in clinical research. Moreover, the optimal dose and duration of green tea consumption for prostate cancer prevention and treatment are still not well-established. Clinical trials have used different dosages and forms of green tea, making it difficult to compare results and determine the most effective regimen. Additionally, confounding factors and limitations of observational studies can affect the interpretation of epidemiological evidence. Factors such as lifestyle, dietary patterns, and other health behaviors can influence the observed associations between green tea consumption and prostate cancer risk.

Furthermore, clinical trials evaluating the effects of green tea face challenges such as small sample sizes, short duration of treatment, and variations in study design. Large-scale, long-term clinical trials with standardized protocols are needed to provide more robust evidence.

### Potential Mechanisms and Future Directions

The effects of green tea on prostate cancer are thought to involve various mechanisms, including interactions with specific molecular targets and modulation of signaling pathways.

#### Epigenetic Regulation

Green tea and its bioactive compounds, such as EGCG, have been shown to influence epigenetic modifications, including DNA methylation and histone acetylation.<sup>(103)</sup> These modifications can affect gene expression, including genes involved in prostate cancer development and progression.

Epigenetic changes, including DNA methylation, histone modifications, and miRNA regulation, play

a significant role in prostate cancer. A previous study suggests that green tea catechins, particularly EGCG, have the potential to reverse these epigenetic alterations and serve as a promising strategy for cancer prevention and therapy.<sup>(117)</sup> Evidence indicates that EGCG can act as an epigenetic modulator and modify miRNA expression, leading to the inhibition of prostate carcinogenesis. Furthermore, the study suggests that combining green tea catechins with existing chemotherapeutic agents may enhance their effects and reduce side effects.

### Inhibition of PI3K/AKT Pathway

The PI3K/AKT pathway is frequently dysregulated in prostate cancer and plays a crucial role in cell survival and growth.<sup>(104)</sup> Green tea catechins, particularly EGCG, have been found to inhibit this pathway, thereby suppress the proliferation and survival of prostate cancer cells.<sup>(20)</sup>

### Modulation of Androgen Receptor Signaling

The androgen receptor is a key player in prostate cancer growth and progression.<sup>(105)</sup> Green tea compounds have been reported to interfere with androgen receptor (AR) signaling, either by suppressing AR expression or inhibiting its activity, thus potentially impact the growth of prostate cancer cells.<sup>(106)</sup>

### Oxidative Stress and Antioxidant Defense

Green tea's antioxidant properties help counteract oxidative stress, which is implicated in prostate cancer development.<sup>(107)</sup> By reducing oxidative damage and supporting antioxidant defense mechanisms, green tea may help maintain cellular homeostasis and inhibit cancer progression.<sup>(108)</sup>

### Anti-inflammatory Effects

Chronic inflammation has been associated with prostate cancer development and progression.<sup>(109)</sup> Green tea's anti-inflammatory properties can modulate inflammatory signaling pathways, such as NF- $\kappa$ B and cyclooxygenase 2, potentially reduce inflammation-driven cancer processes.<sup>(110)</sup>

While there has been significant research on green tea and prostate cancer, there are several areas that warrant further investigation. It is crucial to determine the most effective dosage, formulation, and bioavailability of green tea compounds for prostate cancer prevention and treatment. Future studies should explore different

dosing regimens, standardized formulations, and methods to enhance bioavailability. Conducting well-designed clinical trials with larger sample sizes and longer follow-up periods is necessary to validate the therapeutic benefits of green tea in prostate cancer. These trials can help determine the optimal treatment protocols, assess long-term effects, and evaluate potential interactions with other medications.

Investigating the potential synergistic effects of green tea with other treatments, such as chemotherapy, radiation therapy, or targeted therapies, is an area of interest. Combinatorial approaches may enhance treatment efficacy, reduce side effects, and overcome drug resistance in prostate cancer.

It is important to explore the role of individual genetic variations and biomarkers in determining the response to green tea treatment. Personalized medicine approaches can help identify patient subgroups that may benefit the most from green tea interventions and optimize treatment strategies. Further mechanistic studies are needed to elucidate the specific molecular targets and signaling pathways influenced by green tea compounds. Understanding these mechanisms will help refine therapeutic approaches and identify potential novel targets for intervention.

### Conclusions

This comprehensive review has highlighted the potential benefits of green tea in prostate cancer prevention and treatment. The findings from epidemiological studies suggest an inverse association between green tea consumption and prostate cancer risk, particularly for advanced or aggressive forms of the disease. Laboratory studies have elucidated potential mechanisms, including the modulation of molecular targets and signaling pathways, inhibition of tumor growth, induction of apoptosis, and sensitization to conventional treatments.

Though the evidence from clinical trials and human studies is still evolving, initial findings demonstrate promising results. Green tea consumption has shown potential in reducing prostate-specific antigen levels, inhibiting tumor markers, and impacting disease progression. However, challenges remain, such as determining optimal dosage, formulation, and long-term effects, as well as standardizing protocols for clinical trials.

Future research efforts should focus on well-designed clinical trials with larger sample sizes and longer follow-up periods to provide more robust evidence. Combinatorial approaches, incorporating green tea with conventional therapies or targeted agents, hold promise in improving treatment efficacy and overcoming drug resistance. Personalized medicine approaches, considering individual genetic variations and biomarkers, may help identify patient subgroups that are most likely to benefit from green tea interventions.

In conclusion, green tea and its bioactive components offer potential benefits in the prevention and treatment of prostate cancer. While further research is warranted to fully elucidate the optimal use of green tea in clinical practice, the available evidence suggests its role as a promising adjunctive therapy. Understanding the underlying mechanisms, conducting well-designed clinical trials, and exploring combinatorial and personalized medicine approaches will pave the way for the development of targeted and effective strategies in prostate cancer management.

### Conflict of Interest

None.

### Author Contributions

Liu GH and Yao ZQ designed the work and extracted the data. Chen GQ and Li YL analyzed the data. Liang B wrote the first draft of the manuscript. All authors critically read and approved the final version of the manuscript.

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