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Can Black Tea and Green Tea Prevent Cancer? Novel Drug Delivery Approaches

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Abstract

Green tea and black tea, derived from *Camellia sinensis*, are polyphenol-rich beverages known for their health benefits. Green tea is abundant in epigallocatechin gallate (EGCG), a potent antioxidant with anticancer properties, while black tea, produced through fermentation, contains theaflavins and thearubigins, which helps reduce oxidative stress and support DNA repair. Both teas contain polyphenols that regulate tumor initiation, progression, and metastasis. Green tea has shown protective effects against esophageal, colorectal, and gynecologic cancers, while black tea exhibits anti-angiogenic and chemo-preventive properties. Combining both teas may enhance their anticancer potential, though factors like preparation methods, dosage, and genetic variability influence their efficacy. Various studies based on drug delivery systems using *Camellia sinensis* components have been added to this article to provide examples of approaches for future studies. Advances in nanotechnology are improving the bioavailability of tea polyphenols, facilitating their integration into cancer prevention and treatment strategies. Further research is needed to establish optimal consumption guidelines.

Key Words: *Camellia sinensis*, cancer prevention, anti cancer, drug delivery

1. Introduction

1.1.Green tea and black tea properties

Green tea and black tea, derived from the *Camellia sinensis* plant, are among the most consumed beverages worldwide (Khan & Mukhtar, 2019; Cabrera et al., 2006). Widely enjoyed in many countries, *Camellia sinensis* boasts numerous health benefits attributed to its rich composition of bioactive compounds (Bursalioglu, 2019). Green tea is a non-fermented type of tea and contains higher levels of catechins compared to black

tea (Cabrera et al., 2006). These catechins have been shown to possess strong antioxidant properties in both cell culture and animal studies (Khan & Mukhtar, 2019). EGCG (Epigallocatechin gallate) is the most extensively studied polyphenol in green tea, known for its antioxidant and antiviral properties (Khan & Mukhtar, 2019; Mhatre et al., 2021) . Moreover, the polyphenol content of green tea has been associated with various health benefits, including support for oral health, weight management, and anti-inflammatory effects (Cabrera et al., 2006; Xing et al., 2019). Figure 1 presents a photograph of several active ingredients found in *Camellia sinensis*.

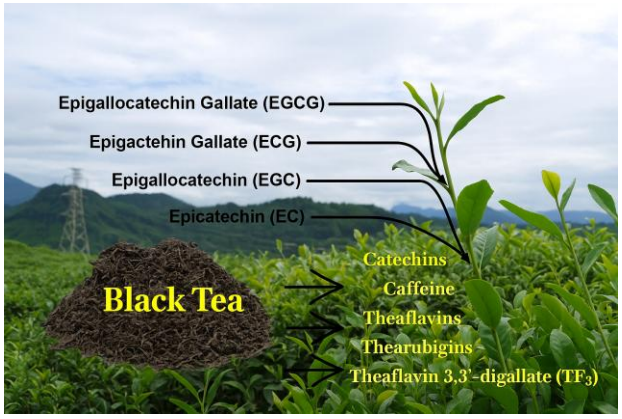

Figure 1. The image is associated with certain contents of the *Camellia sinensis* plant. This figure was originally drawn by the authors.

Black tea, on the other hand, contains unique bioactive compounds such as theaflavins and thearubigins, which are formed through the oxidation of polyphenols during fermentation (Tenore et al., 2015; Khan & Mukhtar, 2019). The composition of black tea makes it particularly effective in reducing oxidative stress caused by radiation and lowering blood pressure (Korystova et al., 2021; Mahdavi-Roshan et al., 2020). Additionally, black tea exhibits stronger antibacterial properties and a greater impact on reducing oral biofilms compared to green tea (Fernández et al., 2022). Polyphenols like theaflavin-3,3'-digallate (TF3) in black tea have shown potential antiviral effects, particularly against SARS-CoV-2 (Mhatre et al., 2021). Furthermore, black tea's fermentation products are effective in reducing cholesterol and triglyceride levels, making it a promising option for addressing conditions related to metabolic syndrome (Tenore et al., 2015).

Both green tea and black tea have been found to reduce the negative effects of obesity on male reproductive health, with black tea demonstrating a stronger impact in this regard (Han et al., 2020). Additionally, the antihypertensive effects of green tea have been observed to be more pronounced compared to black tea, especially with regular consumption (Mahdavi-Roshan et al., 2020). The distinct bioactive properties of catechins in green tea and fermentation-derived compounds in black tea highlight their complementary health benefits (Xing et al., 2019; Korystova et al., 2021).

2. Method

2.1. Examples from the literature on the anti-cancer effects of green tea and black tea

Tea is one of the three most consumed nonalcoholic beverages, and its global consumption has increased significantly in recent years (FAO 2019). These drinks, which are a beautiful gift of nature, play a beneficial role in health as well as flavor and pleasure. Green and black tea, derived from *Camellia sinensis*, have been extensively studied for their potential health benefits, particularly in cancer prevention. These teas contain polyphenols such as catechins and theaflavins, which have demonstrated potent antioxidant and anti-inflammatory properties, crucial in inhibiting cancer progression (Beltz et al., 2006; Chung, 1999; Farhan, 2022; Filippini et al., 2020). Epigallocatechin gallate (EGCG), a key catechin in green tea, has been shown to interfere with cancer cell proliferation as well as to induce apoptosis and regulate signaling

pathways associated with tumor growth and metastasis (Almatroodi et al., 2020).

Epidemiological studies suggest that regular green tea consumption is linked to a reduced risk of esophageal, colorectal, and gynecologic cancers (Abe & Inoue, 2021; Zhao et al., 2021; Ohishi et al., 2022). These protective effects are attributed to green tea polyphenols targeting pathways involved in tumor initiation, promotion, and progression. They modulate gene expression by downregulating oncogenes and upregulating tumor suppressor genes, thereby creating an inhospitable environment for cancer cell growth (Zhao et al., 2014).

Black tea, while less researched compared to green tea, contains unique polyphenolic compounds, including theaflavins and thearubigins, which exhibit significant antioxidative and chemo-preventive properties. These compounds help reduce oxidative stress, suppress angiogenesis, and inhibit matrix metalloproteinases, which play roles in tumor invasion and metastasis. Black tea polyphenols also support DNA repair mechanisms and protect against carcinogen-induced DNA damage, making them valuable in cancer prevention strategies (Singh et al., 2017; Bag & Bag, 2018; Sharma, et al., 2018; Kager, et al., 2010).

Studies combining green and black teas have shown complementary effects in preclinical and clinical research. Green tea catechins have been linked to delayed cancer onset and reduced recurrence rates, particularly in colorectal adenomas, while black tea polyphenols exhibit preventive effects against oral cancers through molecular pathways like the epidermal growth factor receptor (EGFR) pathway (Khan & Mukhtar, 2019; Nimbalkar, et al., 2022; Yoon, et al., 2012). These findings highlight the importance of integrating different tea types into dietary interventions for comprehensive cancer prevention. The anticancer mechanisms of tea polyphenols are diverse. They act as both antioxidants and pro-oxidants depending on the microenvironment, selectively targeting cancer cells while sparing normal cells (Yang & Wang, 2016; Rogovskii, et al., 2019; Lambert & Forester, 2013). Cell cycle, apoptosis and angiogenesis constitute the main points of the process in tumor development. Additionally, tea polyphenols induce cell cycle arrest, promote apoptosis, and inhibit angiogenesis all of which are critical processes in preventing tumor growth and metastasis (Khan & Mukhtar, 2010; Beltz, et al., 2006; Daniel et al., 2005). Epigenetic modulation is a process that regulates gene expression without changing the DNA sequence, through mechanisms such as DNA methylation, histone modification and non-coding RNAs. Epigenetic modulation by tea polyphenols, including alterations in DNA methylation and histone modification, further enhances their chemo-preventive potential (Nandakumar et al., 2011; Meeran et al., 2010). Emerging evidence suggests that tea polyphenols enhance the efficacy of conventional cancer therapies. For example, combining green tea catechins with chemotherapy drugs has demonstrated synergistic effects in reducing tumor size and improving patient outcomes (Rahmani et al., 2015; Fujiki et al., 2012).

Despite these promising findings, several challenges remain. Factors such as variations in tea preparation methods, individual genetic differences, and optimal dosages significantly influence the effectiveness of tea polyphenols in cancer prevention. High-temperature brewing has been associated with enhanced catechin bioavailability, but excessive consumption may lead to adverse effects, including hepatotoxicity in sensitive individuals. Addressing these variables is essential for maximizing the benefits of tea in cancer prevention. (Wang et al., 2010; Lambert & Forester, 2013; Yang, et al., 2009; Fujiki, et al., 2018; Chow et al., 2005; Sarma et al., 2008). These studies are also given in Table 1.

Table 1. The protective effects of green tea and black tea against cancer.

Tea Type	Active İngredient	İmpact of Cancer Prevention	References
Green tea/black tea	catechins theaflavins	these teas possess significant antioxidant and anti-inflammatory properties, which renders them of considerable importance in the prevention of cancer progression.	Beltz et al., 2006; Chung, 1999; Farhan, 2022; Filippini et al., 2020
Green tea	EGCG	induces apoptosis and may be involved in regulating signalling pathways associated with tumour growth and metastasis	Almatroodi et al., 2020
Green tea	polyphenols	they affect tumor initiation, promotion, and progression pathways by gene modulations.	Zhao et al., 2014
Black tea	polyphenols	support DNA repair mechanisms and protect against DNA damage	Bag & Bag, 2018; Sharma, et al. 2018;
Green tea	catechins	protection colorectal adenomas	Khan & Mukhtar, 2019
Black tea	polyphenols	preventive effects against oral cancers	Nimbalkar, et al. 2022; Yoon, et al. 2012
Green tea /black tea	polyphenols	preventing tumor growth and metastasis.	Beltz, et al. 2006; Daniel et al. 2005
Green tea /blac k tea	polyphenols	chemo-preventive effects due to epigenetic modulation	Nandakumar et al. 2011; Meeran et al. 2010
Green tea	catechins	using with chemotherapy drugs has synergistic effects	Rahmani et al., 2015; Fujiki et al., 2012

3. Novel drug delivery approaches

Drug delivery systems are innovative approaches developed to ensure effective and controlled delivery of therapeutic agents to target areas. Overcoming the limitations of traditional methods, these systems enable drugs to overcome biological barriers, target-specific release, and reduce side effects through carriers such as liposomes, nanoparticles, and biocompatible polymers. For example, the liposomal formulation of *Rosmarinus officinalis* (rosemary) extract significantly increased skin permeability compared to conventional forms, providing a high absorption rate in a short time of 160 minutes (Aslan & Kurt, 2021). Similarly, liposome-gel systems containing Estradiol/Estriol developed for women in menopause offered ease of transdermal application with their alcohol-free structures and low toxicity, while ensuring homogeneous distribution to the skin

(Aslan & Aytekin, 2023). The therapeutic potential of liposomes is not limited to skin permeability. The utilisation of liposome carrier systems has been demonstrated to reduce the toxicity of certain volatile oils (Özdemir et al., 2018) and to increase the antifungal activities of some essential oils (Yazıcı et al., 2011) Furthermore, the employment of herbal formulations has been documented to accelerate wound healing (Gunal et al., 2019; Gunal et al., 2021)) and enhance the kinetic stability of plants obtained by maceration(Kurt et al., 2025), as in nanoemulsion formulations (Kurt & Aslan 2025).

They also hold promise in neurological diseases thanks to their ability to cross the blood-brain barrier. Liposomal resveratrol's more effective suppression of penicillin-induced epileptic seizures compared to the free form is an example of this (Ethemoglu et al., 2017). In addition, chitin, a natural polymer, provides the advantage of use in wound healing carrier systems with its antimicrobial properties and biocompatibility (Mehrabani et al., 2018), while liposomes modified with terpenes have increased treatment sensitivity by improving GLUT1 receptor targeting in cancer cells (Wang et al., 2021). Nanotechnology-based systems have created an important turning point in cancer treatment. Although nanoparticles accumulate in tumor tissues with enhanced permeation and retention (EPR) effect, they are weak in reaching metastatic lymph nodes. Dual-target nanosystems such as enzyme-sensitive DMSN@Pla-Lipo developed to solve this problem both increase penetration in the primary tumor and optimize drug delivery to lymphatic metastases (Yuan et al., 2025). In breast cancer treatment, PTX-loaded nanostructured lipid carriers (NLC) have increased treatment safety by reducing normal cell toxicity while showing target-specific effect (Attar et al., 2025). The use of natural components plays a critical role in drug delivery systems in terms of both stability and efficacy. Herceptin complexes with (-)-Epigallocatechin-3-O-gallate (EGCG) have shown promising results in cancer treatment, while tannic acid and therapeutic protein combinations have shown promising results in cardiovascular diseases (Chung et al., 2014; Shin et al., 2018). In addition, gel formulations of liposomal postbiotics have created a new perspective in pharmaceutical applications by providing ease of use while maintaining antimicrobial activity (Gokce & Aslan, 2024).

A number of studies have indicated the potential of green and black tea to offer protection against cancer, thereby raising hopes that they may also possess therapeutic properties and reduce side effects. A significant number of studies have evaluated the components of the *Camellia sinensis* plant in terms of their therapeutic efficacy, with a view to identifying cancer-protective properties. The search for new methods of cancer treatment has also led to a growing interest in substances with anti-carcinogenic properties, with various studies being conducted using different drug delivery systems. The potential for these studies to inform the development of new treatment modalities is significant. Advances in nanotechnology, such as nanodelivery systems, have further improved the bioavailability and therapeutic efficiency of tea polyphenols, paving the way for their clinical application in cancer treatment (Jiang et al., 2021; Almatroodi, et al., 2020). Xiong and colleagues conducted a study to ascertain the efficacy of delivering anticancer proteins (e.g. Herceptin) using micellar nanocomplexes (MNCs) containing green tea catechin derivatives. The MNCs demonstrated significant toxicity towards breast cancer cells by inducing apoptosis, while showing no toxicity towards normal human cells. Furthermore, MNCs are unlikely to induce kidney toxicity (Xiong et

al., 2023). Bae and colleagues reported the findings of research conducted on micellar nanocomplexes. These nanocomplexes, which consist of a conjugate of hyaluronic acid and EGCG, in addition to cisplatin, have been shown to facilitate targeted drug delivery in ovarian cancer via CD44 receptors. The antioxidant property of EGCG has been demonstrated to reduce the organ toxicity of cisplatin, while the core-structured design of the nanocomplex has been shown to allow for high drug accumulation in the tumour. The basis of this system being a safe and effective chemotherapy strategy is attributable to its green tea catechin composition (Bae et al., 2017). Chung et al., 2014) reported that micellar nano-complexes formed by the gradual self-assembly of EGCG derivative and anticancer protein Herceptin can solve traditional problems associated with drug carriers by demonstrating both carrier and therapeutic effects. This structure, with Herceptin-EGCG oligomers in the core and PEG-EGCG in the shell, provides longer blood circulation, targeted tumour accumulation and effective tumour shrinkage compared to free Herceptin in mouse models. The anticancer and protective properties of EGCG enhance therapeutic efficacy while eliminating carrier toxicity concerns, thus demonstrating the potential of 'bifunctional' nanotherapeutics in cancer treatment (Chung et al., 2014).

Bae et al., 2022) reported the findings of a study on the design of bone marrow-targeted nanotherapeutics based on green tea catechins. Green tea catechins-based bone marrow-targeted micellar nano-complexes have been shown to enhance the anti-leukaemic effect of sorafenib in the treatment of acute myeloid leukaemia (AML) by targeting mTOR, the survival signal of leukaemic cells. The nanocomplex demonstrated a 11-fold higher accumulation in the bone marrow compared to free sorafenib, effectively clearing leukaemic cells in the bone marrow in a mouse model derived from an AML patient. (Bae et al., 2022). The investigation by Haratifar and colleagues sought to ascertain whether the antiproliferative effect of EGCG, the main component of green tea, would be preserved through its nanoencapsulation with casein micelles. The study revealed that EGCG encapsulated in casein micelles exhibited a comparable level of inhibition of HT-29 cancer cell proliferation to that of free EGCG, thereby confirming that bioaccessibility was not diminished. of EGCG (Haratifar et al., 2014). A study on Sunitinib-loaded micellar nanocomplex (SU-MNC) was reported by Yongvongsoontorn and colleagues.SU-MNC was constructed using poly(ethylene glycol)-conjugated epigallocatechin-3-O-gallate (PEG-EGCG) as a carrier. The study concluded that SU-MNC specifically inhibited vascular endothelial growth factor-induced proliferation of endothelial cells and exhibited minimal toxicity against normal kidney cells (Yongvongsoontorn et al., 2019). Almatroodi and colleagues conducted a study on the potential to overcome poor bioavailability through nanotechnology-based strategies such as encapsulation, liposomes, micelles, nanoparticles and various other formulations. Although EGCG, the main component of green tea, has antioxidant and anticancer properties, it suffers from low bioaccessibility; therefore, nanoencapsulation methods play an important role in overcoming this problem by increasing the effectiveness of clinical doses and increasing its potential in cancer treatment (Almatroodi et al., 2020).

The interaction between green tea and liposomes was conducted by Andrade and colleagues. The study found that green tea extract (GTE) increased membrane fluidity by binding to biomembranes through hydrophobic and electrostatic interactions in liposome models. However, the presence of cholesterol reduced this interaction and limited the anti-lipid peroxidation effect,

which may affect the effectiveness of GTE (Andrade et al., 2021). A study was conducted on the subject of skin penetration of catechins. The process of skin penetration of catechins is challenging due to their lipophilic nature. However, the use of carriers such as liposomes, micelles and polymeric nanoparticles has been shown to improve bioavailability by increasing skin hydration and supporting follicular transport. This is promising in terms of applications in skin cancer and anti-aging (Aljuffali et al., 2022). Liang et al. reported the development of micellar nanocomplexes (MNC) with high stability (88% drug loading) by combining doxorubicin (DOX) and polyethylene glycol (PEG)-EGCG conjugate. This approach addressed the problems of low drug loading and instability in the bloodstream, which hindered the success of nanomedicine in the clinic. In mouse models of liver cancer, MNCs showed significant tumour suppression effect even at low doses while minimising unwanted side effects, compared to free DOX and liposomal DOX (Liang et al., 2018). In the study by Jin et al., a nano-micelle composite was developed, consisting of a cationic lipopolymer functionalised with catechin and serum albumin. Cationic liposomes have been shown to increase the bioavailability of catechins by accumulating in the lung microvasculature due to electrostatic effects. Albumin contributes to long-term in vivo retention as a biocompatible anti-plasma sorbent.

The physicochemical and antitumour properties of the nano-micellar complexes have been confirmed by detailed analyses, suggesting that this system could be a promising tool in the treatment of lung diseases (Jin et al., 2024). Fang and colleagues was reported that liposomes with added anionic components (deoxycholic acid) accelerated drug release but did not significantly increase skin deposition when applied topically. However, liposomes provided greater drug delivery to solid tumours compared to catechins in free form. The gallic acid ester in the structure of EGCG significantly improved tissue uptake, while (+)-catechin and (-)-epicatechin isomers differed in their accumulation in skin and tumour (Fang et al., 2005). De Pace and colleagues developed the EGCG encapsulated chitosan-coated nanoliposomes (CSLIPO-EGCG) system, which consists of chitosan-coated nanoliposomes. This system was developed to address the problems of instability and poor absorption in the body of EGCG, the main component of green tea. The CSLIPO-EGCG system has been shown to induce apoptosis in MCF7 breast cancer cells by providing higher intracellular uptake compared to free EGCG. The biocompatible and degradable nature of the system offers an innovative strategy for breast cancer treatment by providing chemoprevention at doses where conventional EGCG is ineffective (De Pace et al., 2013).

A liposome-based system to enhance the intra-tumour distribution of EGCG, the main component of green tea, was developed by Fang and colleagues. The accumulation of EGCG in basal cell carcinoma (BCCs) tissue was increased 20-fold by liposomes containing deoxycholic acid (DA) and 15% ethanol compared to the free form, resulting in a marked improvement. The liposomes, in addition to their protective effect against EGCG degradation, exhibited the capacity to induce BCCs cell death even at low concentrations.The efficacy of this system was further demonstrated through its application in melanoma and colon tumours, thereby substantiating the potential of modified liposomes as a targeted therapeutic agent through intra-tumour injection (Fang et al., 2006).

As a result, drug delivery systems have the potential to further increase treatment success when integrated with personalized medicine and combination therapies. The use of biocompatible materials allows for

the development of sustainable and safe formulations, while multifunctional nanosystems open the door to a new era in metastasis control. Research in this area will continue to shape the future of the pharmaceutical industry and provide transformative solutions for treating diseases. A description of all stages of this compilation work is shown in figure 2.

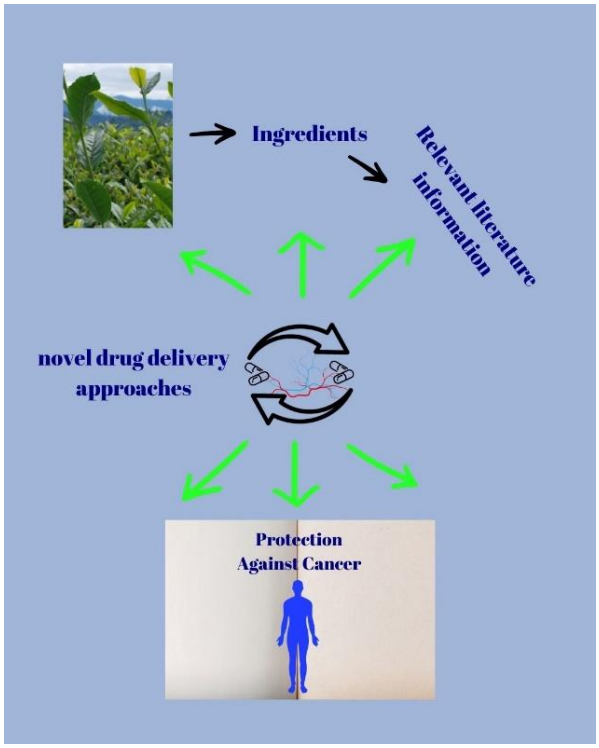

Figure 2. visualisation of the basic stages of the study on the anticancer content of the *Camellia sinensis* plant ingredients and next generation drug transport systems approach**.** This figure was originally drawn by the authors.

4. Conclusion

Green and black teas represent valuable natural resources for cancer prevention. Their polyphenolic compounds, particularly catechins and theaflavins, modulate key processes involved in carcinogenesis, including tumor initiation, progression, and metastasis (Beltz et al., 2006; Chung, 1999; Farhan, 2022; Filippini et al., 2020). Green tea, rich in EGCG, has shown protective effects against esophageal, colorectal, and gynecologic cancers (Abe & Inoue, 2021; Zhao et al., 2021; Ohishi et al., 2022), while black tea's theaflavins and thearubigins exhibit antioxidative, anti-angiogenic, and DNA repair-supporting properties (Bag & Bag, 2018; Sharma, et al., 2018). Combining both teas may enhance their anticancer potential, as their complementary mechanisms target multiple pathways in cancer development (Beltz et al., 2006; Chung, 1999; Farhan, 2022; Filippini et al., 2020; Daniel et al., 2005; Nandakumar et al., 2011; Meeran et al., 2010). Advances in nanotechnology, such as nanodelivery systems, are improving the bioavailability and therapeutic efficiency of tea polyphenols, facilitating their integration into cancer prevention and treatment strategies (Jiang et al., 2021; Almatroodi, et al., 2020). However, factors like preparation methods, dosage, and genetic variability significantly influence their efficacy. High-temperature brewing may enhance catechin bioavailability, but excessive consumption could lead to adverse effects, including hepatotoxicity in sensitive individuals (Almatroodi et al., 2020; Chung et al., 2014; Bae et al., 2022). Continued research is essential not only to establish optimal consumption guidelines but also to understand individual variability and improve delivery mechanisms. By addressing these knowledge gaps, researchers can unlock the full therapeutic potential of green and black teas, making them an integral part of dietary recommendations for comprehensive cancer prevention and treatment (Almatroodi et al., 2020; Chung et al., 2014; Bae et al., 2022; Ohishi et al., 2022).

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Author Contribution
All authors shared equal tasks at all stages of the study.

Conflicts of Interest
Authors declare no conflicts of interests.

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