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Review Article

Kombucha tea in cancer care: A review of its anti-cancer potential and role in integrative oncology

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Abstract

Objective: The burden of cancer prevalence and mortality poses challenges to global cancer care delivery, particularly impacting low- and middle-income countries in accessing evidence-based cancer prevention, treatment, and supportive care. Integrative oncology integrates traditional, complementary, and integrative medicine with standard cancer therapies to enhance healthcare delivery. This study aims to evaluate the anti-cancer properties of kombucha tea across multiple cancer types.

Materials and Methods: Various databases, including PubMed, Science Direct, and Scopus, reviewed for recent research on kombucha tea's potential benefits and impact on cancer.

Results: Recent research developments highlight kombucha tea as a potential aid in enhancing cancer resistance and offering various health benefits.

Conclusion: Integrative oncology, complemented by the consumption of kombucha tea, presents a promising approach to addressing the complexities of cancer care. Further exploration and updates on kombucha tea anti-cancer properties against breast, lung, liver, colorectal, ovarian, uterine, and prostate cancers are warranted to enhance comprehensive understanding and potential therapeutic applications.

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Introduction

Integrative oncology, a field that combines conventional cancer therapies with complementary and alternative approaches, has gained momentum as patients and researchers alike seek holistic solutions to cancer care (Asgharzadeh and Binabaj 2023; Binabaj and Asgharzadeh ; Carlson et al. 2023). Among the various natural products being investigated for their therapeutic potential, kombucha tea, a fermented beverage made from tea, sugar, and a symbiotic culture of bacteria and

yeast, has emerged as a promising candidate (Farid 2023). The fermentation process involved in kombucha production results in the generation of a variety of bioactive compounds, including polyphenols, organic acids (e.g., acetic acid and gluconic acid), B vitamins, and antioxidants (Barakat et al. 2023; Kitwetcharoen et al. 2023; Martins et al. 2023). The fermentation process also produces small amounts of alcohol and carbonation, giving kombucha its distinct tangy flavor. It has been widely consumed for centuries in different cultures, believed to offer benefits like improved digestion, detoxification, and immune support (Antolak, Piechota and Kucharska 2021a; Ojo and de Smidt 2023). For instance, Rasouli et al. (2021) demonstrated enhanced cytotoxicity of kombucha when combined with doxorubicin on colorectal cancer cell lines, indicating possible synergistic effects. However, their study lacked *in vivo* confirmation, warranting further investigation into the clinical translatability of these effects.

The possible anticancer effects of kombucha stem from its rich composition of bioactive components (Sales et al. 2023). These include tea-derived polyphenols, known for their antioxidant and anti-inflammatory properties, and fermentation by-products like organic acids and probiotics that may modulate immune responses (Sanwal et al. 2023). Studies suggest that these compounds may interfere with cancer progression by inhibiting tumor cell proliferation, inducing apoptosis, and reducing angiogenesis (Jayabalan et al. 2011; Sharifudin ; Vīna et al. 2014). Early preclinical studies have indicated potential anticancer activity against various cancer types including breast, liver, colon, and prostate cancers (Ghandehari et al. 2023; Kaewkod et al. 2022; Rasouli et al. 2021b; Sales et al. 2023; Sharifudin ; Taupiqurrohman et al. 2024).

This review article aims to explore the anticancer potential of kombucha tea across multiple cancer types, examining the bioactive compounds involved, underlying mechanisms, and preclinical as well as clinical evidence supporting its use. By integrating kombucha into the broader context of cancer treatment, we seek to illuminate its role in enhancing conventional therapies and its potential as a complementary approach in oncology. Understanding the molecular pathways through which, kombucha may exert anticancer effects could open new avenues for research and therapeutic development in integrative oncology. Our objective is to clarify kombucha possible role as a complementary approach in integrative oncology and to highlight directions for future research.

Materials and Methods

To comprehensively evaluate the effects and potential benefits of kombucha tea on cancer, a systematic literature search was conducted using multiple reputable scientific databases. These include PubMed, ScienceDirect, and Scopus. The search included studies written in English. Keywords such as "kombucha," "kombucha tea", "fermented tea", "cancer", "antitumor", "anticancer", "polyphenols", and "cell proliferation" were used in various combinations using Boolean operators (AND/ OR).

Inclusion criteria were: (1) original research articles focused on kombucha and its effects on cancer cell lines or animal models, (2) articles discussing molecular mechanisms of action, (3) studies published in peer-reviewed journals. Reviews, editorials, and studies lacking relevant experimental data were excluded.

The titles and abstracts of all retrieved articles were screened for relevance, and full texts of potentially eligible studies were reviewed in detail. Data were extracted on study type, experimental model, type of cancer studied, key findings, and proposed mechanisms.

Results

Preparation methods and bioactive properties of Kombucha

Kombucha is a fermented beverage that has gained increasing attention for its potential health benefits, particularly in the context of integrative oncology. The base of kombucha consists of tea, typically black or green, which provides polyphenols that act as natural antioxidants. The tea is sweetened with sucrose which serves as the primary substrate for fermentation (Bortolomedi, Paglarini and Brod 2022; Emiljanowicz and Malinowska-Pańczyk 2020). The fermentation process involves two key microbial activities: yeasts metabolize the sucrose into glucose and fructose, converting these into ethanol, while acetic acid bacteria oxidize the ethanol into acetic acid and other organic acids (Amarasekara, Wang and Grady 2020; Kumar and Joshi 2016). This fermentation typically lasts between 7 to 14 days under aerobic conditions at 20-30°C. The resulting beverage is characterized by its mildly acidic taste, fizziness, and low alcohol content (usually less than 0.5% alcohol by volume (ABV) (Figure 1).

Kombucha bioactive profile is influenced by both the tea itself and the fermentation process. During fermentation, a variety of organic acids are produced, including acetic acid, gluconic acid, and lactic acid (Antolak, Piechota and Kucharska 2021b; Jakubczyk et al. 2020). Acetic acid, the most abundant of these, contributes to the beverage sour flavor and is responsible for its antimicrobial properties, which help preserve kombucha while inhibiting pathogenic microbes (de Miranda et al. 2022; Dutta and Paul 2019). Gluconic acid is believed to support detoxification, while lactic acid, produced by lactic acid bacteria, has probiotic properties that can improve gut health by maintaining a healthy balance of intestinal microflora. The production of small amounts of glucuronic acid, although debated, is of particular interest due to its role in the detoxification processes in the liver, where it binds with toxins and aids their excretion from the body (Emiljanowicz and Malinowska-Pańczyk 2020; Martínez Leal et al. 2018; Watawana et al. 2015).

In addition to organic acids, kombucha is rich in polyphenolic compounds, particularly catechins and flavonoids, which are derived from the tea used in its preparation. These polyphenols are known for their potent antioxidant properties which protect cells from oxidative damage by neutralizing free radicals (Antolak, Piechota and Kucharska 2021b). Green tea-based kombucha is especially rich in epigallocatechin gallate (EGCG), a catechin with well-documented anticancer effects (Dasgupta 2019; Farid 2023). During fermentation, the bioavailability of these polyphenols may increase, enhancing their antioxidant and anti-inflammatory activities. Polyphenols such as theaflavins and thearubigins, derived from black tea, also contribute to kombucha'shealth-promoting properties (Kitwetcharoen et al. 2023; Sanwal et al. 2023). These compounds not only exert antioxidant effects but have also been shown to regulate key cellular pathways involved in inflammation and apoptosis, which are crucial in cancer development and progression. Kombucha also contains probiotics, live microorganisms that confer various health benefits to the host, particularly related to gut health (Antolak, Piechota and Kucharska 2021a; da Anunciação et al. 2024; Kozyrovska et al. 2012; Vargas, Fabricio and Ayub 2021). The fermentation process produces a diverse microbial population, including species of *Acetobacter*, *Gluconacetobacter*, *Lactobacillus*, and *Saccharomyces* which are known to promote a balanced gut microbiome (Huang, Xin and Lu 2022). Emerging research suggests that maintaining gut health is critical in reducing chronic inflammation and modulating immune responses, both of which playing significant roles in cancer prevention and treatment. By promoting a

healthier gut environment, kombucha probiotics may help reduce systemic inflammation and improve immune function which are important aspects of integrative oncology approaches (Sales et al. 2023; Vázquez-Cabral et al. 2017; Villarreal-Soto et al. 2019).

Additionally, kombucha is a natural source of several B vitamins including thiamine (B1), riboflavin (B2), pyridoxine (B6), and cobalamin (B12) which are essential for metabolic processes, energy production, and maintaining nervous system health (de Miranda et al. 2022; Rezaldi et al. 2021). The microbial activity during fermentation enriches the B vitamin content, contributing to kombucha potential to support general health and well-being. Figure 2 provides a visual overview of the key bioactive components of kombucha including sugars, phenolic compounds, organic acids, and essential minerals.

The chemical complexity of kombucha and its diverse bioactive compounds including organic acids, polyphenols, probiotics, and vitamins, contribute to its proposed health benefits (Emiljanowicz and Malinowska-Pańczyk 2020) (Table 1). These properties have made kombucha a subject of interest in integrative oncology, as its antioxidant, anti-inflammatory, and detoxifying effects could complement conventional cancer therapies (Ahmed, Hikal and Abou-Taleb 2020; Chu and Chen 2006). However, while preclinical studies have demonstrated promising anticancer activities, further research is needed to fully understand the mechanisms by which kombucha may influence cancer prevention and treatment (Kahouli 2016; Salafzoon, Hosseini and Halabian 2018). As such, kombucha presents a unique and valuable subject for future investigation in the context of integrative cancer care.

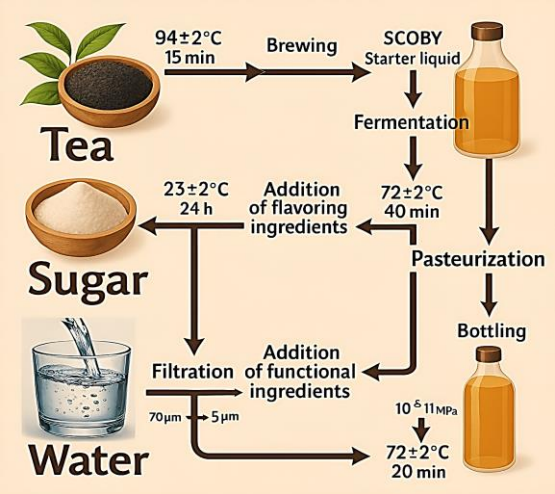

Figure 1. Flowchart illustrating the production process of kombucha tea. The process begins with brewing tea leaves at 94±2°C for 15 min, followed by cooling to 23±2°C. Sugar and water are added, and the mixture is inoculated with a SCOBY (Symbiotic Culture of Bacteria and Yeast) and starter liquid for fermentation. After reaching a pH ≤ 4.6 (typically pH 3.0±0.3), the fermented tea is filtered and pasteurized at 72±2°C for 40 min. Flavoring ingredients may be added, and secondary fermentation is performed at 23±2°C for 24 hr. The beverage then undergoes further filtration (from 70 µm to 5 µm), optional addition of functional ingredients, and carbonation at 10°C and 1.1 MPa before final bottling and pasteurization.

Table 1. Bioactive compounds and health benefits of Kombucha

Bioactive compound	Source	Health benefits	Reference
Polyphenols (e.g., EGCG)	Tea leaves	Antioxidant, anti-inflammatory, anticancer	(Antolak, Piechota and Kucharska 2021b; Kitwetcharoen et al. 2023)
Acetic acid	Fermentation	Antimicrobial, detoxification	(Dutta and Paul 2019)
Gluconic acid	Fermentation	Liver detoxification	(Emiljanowicz and Malinowska-Pańczyk 2020)
Probiotics (e.g. Lactobacillus)	SCOBY	Gut microbiota modulation, immune enhancement	(Huang, Xin and Lu 2022; Vargas, Fabricio and Ayub 2021)
B Vitamins (e.g. B12)	Fermentation	Metabolic support, energy production	(Rezaldi et al. 2021)

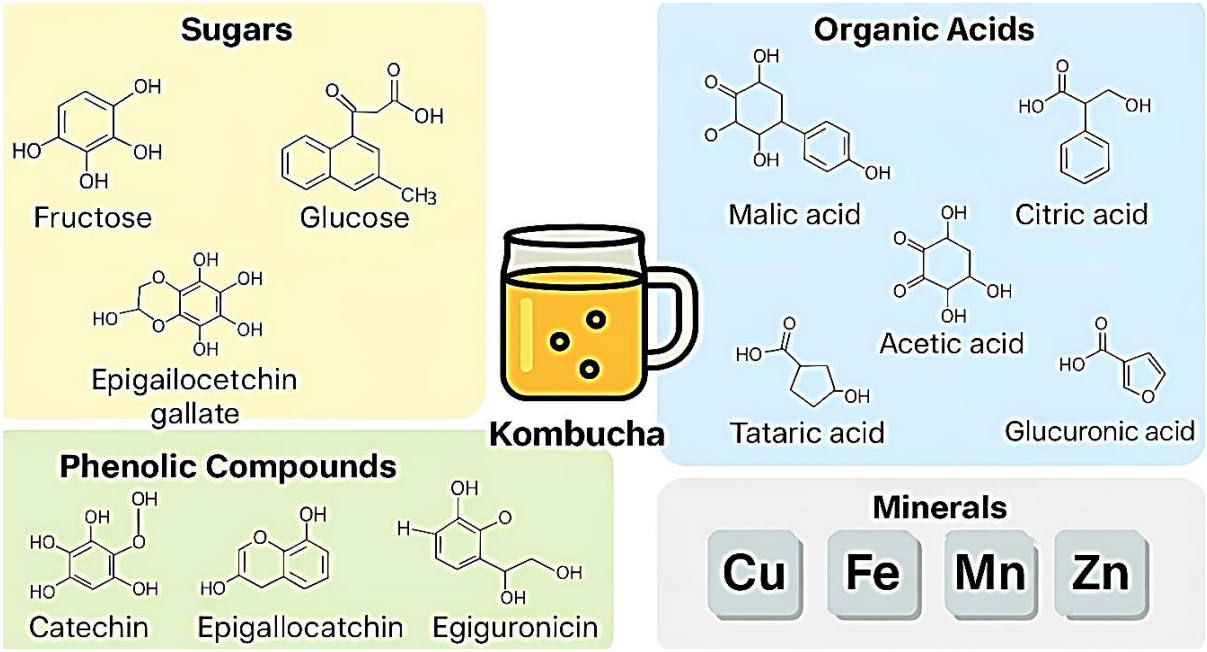

Figure 2. The main biochemical components of kombucha including sugars, organic acids, phenolic compounds, and essential minerals. Kombucha contains a variety of bioactive compounds such as simple sugars (glucose, fructose, and sucrose), organic acids (e.g. acetic acid, lactic acid, and glucuronic acid), phenolic compounds (e.g. catechin, epicatechin, and epigallocatechin gallate), and essential minerals (e.g. copper, iron, manganese, and zinc) which contribute to its health benefits.

Anticancer mechanism of Kombucha

Kombucha exhibits multiple anticancer properties through various biological mechanisms. These effects are largely due to its rich content of polyphenols, organic acids, probiotics, and vitamins. Although prior reviews (Antolak, Piechota and Kucharska 2021a; Jayabalan et al. 2011) emphasize kombucha antioxidant capacity, a recent work (Kitwetcharoen et al. 2023) has highlighted strain-specific bioavailability and metabolite diversity that influence anti-proliferative efficacy. Thus, assuming universal mechanisms across studies may be misleading. Instead of analyzing these mechanisms separately for each cancer type, this section presents a unified overview of the core biological actions through which kombucha may exert its anticancer effects (Kitwetcharoen et al. 2023).

Antioxidant activity

Oxidative stress, caused by an imbalance between free radicals and antioxidants, is a critical factor in cancer development and progression. Kombucha is rich in tea-derived polyphenols—especially catechins, theaflavins, and EGCG—that act as potent antioxidants. These compounds scavenge reactive oxygen species (ROS), prevent lipid peroxidation, and protect DNA from oxidative damage.

In vivo and *in vitro* studies have demonstrated that kombucha consumption leads to reduced levels of malondialdehyde (MDA)—a key marker of lipid peroxidation—and increased activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH). These findings suggest that kombucha can reduce systemic oxidative stress(Antolak, Piechota and Kucharska 2021b; Jayabalan et al. 2014; Mao et al. 2017).

Apoptosis induction

Apoptosis, or programmed cell death, is a key protective mechanism that eliminates damaged or malignant cells.

Cancer cells often evade apoptosis, leading to uncontrolled growth. Kombucha has been shown to restore apoptotic signaling in cancer cells by upregulating pro-apoptotic genes (e.g. P53, tumor necrosis factor-alpha (TNF-α)) and downregulating anti-apoptotic markers. Studies in ovarian and colorectal cancer cell lines show that kombucha, especially when delivered via nanoparticles or in combination with chemotherapeutic drugs, increases the proportion of cells in the sub-G1 phase and enhances DNA fragmentation. This supports the hypothesis that kombucha contributes to cancer suppression through apoptosis modulation (Jayabalan et al. 2014; Rasouli et al. 2021a; Rasouli et al. 2021b).

Inhibition of angiogenesis

Angiogenesis, the formation of new blood vessels, is essential for tumor growth and metastasis. Kombucha exerts anti-angiogenic effects by inhibiting key mediators such as vascular endothelial growth factor (VEGF), hypoxia-inducible factor 1-alpha (HIF-1α), interleukin (IL)-8, and cyclooxygenase-2 (COX-2). It also downregulates matrix metalloproteinases (MMP-2 and MMP-9), which facilitate tumor invasion and metastasis. In prostate and ovarian cancer models, kombucha-treated cells exhibited suppressed migration and reduced expression of angiogenesis-related genes. These findings demonstrate kombucha potential to disrupt tumor vascularization and limit cancer cell dissemination (Rasouli et al. 2021b; Srihari et al. 2013).

Anti-inflammatory effects

Chronic inflammation is a hallmark of cancer, contributing to tumor initiation, progression, and immune evasion. Kombucha shows strong anti-inflammatory properties by decreasing the levels of pro-inflammatory cytokines such as Interleukin (IL)-1β, IL-6, and TNF-α, while increasing the expression of anti-inflammatory cytokines like IL-10. In studies involving ovarian cancer cell lines, kombucha-loaded nanoparticles significantly modulated cytokine profiles, leading to reduced tumor-promoting inflammation. This immunoregulatory activity plays an important role in creating a tumor-suppressive microenvironment (Costa et al. 2022; Fraiz et al. 2024; Su et al. 2023; Villarreal-Soto et al. 2019).

Modulation of cell signaling and receptor pathways

Kombucha polyphenols and organic acids affect various molecular signaling pathways that are critical in cancer biology. These include the Wnt/β-catenin pathway (implicated in colorectal cancer), FasL/CD95-mediated apoptosis, and TNF signaling. Additionally, kombucha has shown effects on hormone receptors, which may be particularly relevant for hormone-dependent cancers such as breast and prostate cancer. By regulating these signaling pathways, kombucha contributes to reduced proliferation, enhanced cell cycle arrest, and increased susceptibility of cancer cells to therapy (Clarissa 2021; Jayabalan et al. 2014; Srihari et al. 2013).

Detoxification and liver protection

Glucuronic acid and gluconic acid, by-products of fermentation, support liver detoxification by binding to toxins and facilitating their excretion. Kombucha has demonstrated hepatoprotective effects in thioacetamide (TAA)-induced liver injury models, significantly lowering liver enzyme levels aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) and improving histopathological markers of damage. These detoxification capabilities not only protect against carcinogen-induced liver damage but may also enhance systemic elimination of harmful compounds, contributing to cancer prevention (Barakat 2022; Hyun et al. 2016).

Gut microbiota modulation

Kombucha is a natural probiotic beverage containing beneficial bacteria such as *Acetobacter*, *Lactobacillus*, and *Saccharomyces*. These microorganisms support gut health, modulate the immune system, and reduce chronic inflammation—factors closely linked to colorectal and systemic cancers. Emerging evidence suggests that kombucha-derived probiotics improve short-chain fatty acid (SCFA) production, increase cytokine levels such as interferon-gamma (IFN-γ) and IL-2, and promote gut microbial diversity. These effects contribute to both cancer prevention and enhanced immune surveillance (Costa et al. 2022; Ecklu-Mensah et al. 2024; Kozyrovska et al. 2012).

Breast cancer

Breast cancer (BC) is the leading cause of cancer-related mortality among women worldwide (Hashemzehi et al. 2018). One of the most significant challenges in treating BC is the migration and metastasis of cancer cells, which often leads to poor patient outcomes (Izdebska et al. 2023). BC metastasizes to various organs including the bone, lungs, liver, and brain, a phenomenon referred to as metastatic heterogeneity (Liang et al. 2020). Among the various BC subtypes, triple-negative breast cancer (TNBC) is considered the most aggressive, often associated with a worse prognosis (Izdebska et al. 2023). Current treatment modalities such as surgery, chemotherapy, radiation therapy, and hormone therapy are widely used; however, these approaches frequently result in severe side effects and often fail to provide sufficient therapeutic efficacy (Barzaman et al. 2020).

Recent studies have explored the potential benefits of natural compounds in cancer therapy. In a mouse model of BC, ginger-based kombucha reduced tumor volume and improved survival rate. The study also reported changes in antioxidant enzyme activity (SOD and GSH) in tumor tissues (Salafzoon, Mahmoodzadeh Hosseini and Halabian 2017). Kombucha ginger tea contains bioactive components which are also present in ginger, along with the main constituents of kombucha itself (Mousavi et al. 2020). In the aforementioned study, the antioxidant enzyme activity in tumor tissues was evaluated. SOD activity and GSH levels were found to decrease, although no changes were observed in catalase activity. Additionally, MDA levels, a marker of lipid peroxidation, were reduced in tumor tissues, indicating lower oxidative damage to cell membranes. In the group that received kombucha (15% kombucha in water), findings were similar to those in the ginger kombucha group, except for an observed increase in catalase activity. The significant reduction in SOD levels in both the liver and kidneys, along with a reduction in tumor tissue, suggests a decrease in superoxide anion production following kombucha consumption. This is particularly relevant, as BC progression is associated with elevated superoxide anion generation due to enhanced aerobic respiration (Salafzoon, Mahmoodzadeh Hosseini and Halabian 2017).

Interestingly, no significant changes were observed in liver catalase activity, and both groups exhibited increased catalase activity in the kidneys. This may suggest a limited systemic antioxidant effect of kombucha consumption. Moreover, the maintenance of GSH levels in the liver across both groups indicates that kombucha tea may protect against the depletion of liver GSH. Furthermore, reduced MDA levels in both the liver and kidneys support the hypothesis that kombucha may mitigate lipid peroxidation and subsequent cellular damage (Salafzoon, Hosseini and Halabian 2018). In conclusion, ginger-based kombucha may offer modest antioxidant effects in breast cancer by modulating several key antioxidant factors. These findings suggest the potential role of kombucha as a complementary approach to managing oxidative stress associated with BC progression (Table 2) (Salafzoon, Hosseini and Halabian 2018).

Lung cancer

Lung cancer (LC) is a malignant tumor and a leading cause of mortality worldwide, ranking as the second most prevalent cancer (Frankell et al. 2023). LC is pathologically classified into two main types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) [45, 46]. NSCLC which includes adenocarcinoma (AD), squamous cell carcinoma (SCC), and large cell carcinoma (LCC), accounts for approximately 80-85% of lung cancer cases, while SCLC constitutes the remaining 10-15% (Bunn Jr 2012; Zhenhua, Hongyu and Jun 2022). Current LC treatments include surgery, radiotherapy, chemotherapy, and targeted drug therapy. Around 80% of LC patients undergo chemotherapy alone or in combination with radiotherapy. However, these treatments can lead to severe side effects, including lung fibrosis and pneumonitis, particularly with chemotherapeutic agents like bleomycin (Bunn Jr 2012; Zhenhua, Hongyu and Jun 2022). This underscores the need for new therapeutic strategies and the improvement of existing treatment protocols. Chronic lung conditions that often lead to LC are associated with prolonged oxidative stress, immunosuppression, and recurrent lung infections, highlighting the role of these factors in disease progression. Fermented black tea kombucha (BTK) has gained attention for its physiologically active components. Notably, BTK contains a significantly higher concentration of theophylline—a xanthine bronchodilator—than regular black tea (BT). While a cup of BT contains 0.014 mg of theophylline, BTK offers 1.44 mg per cup, which may contribute to its therapeutic effects for patients requiring theophylline treatment, such as those with asthma (Leiter, Veluswamy and Wisnivesky 2023).

Interestingly, regular kombucha consumption has been linked to a lower incidence of cancer in some populations, and there have been reports of successful cancer treatments involving kombucha. Subsequent studies suggest that long-term kombucha consumption may enhance the immune system's anticancer defenses. It is hypothesized that kombucha modulates the immune response and inhibits cancer proliferation, particularly in the early stages of tumor growth. This effect is attributed to the synergistic action of various kombucha symbiosis products, including glucuronic acid (GlcUA), lactic acid, acetic acid, and natural antibiotic compounds (Vīna et al. 2014). Kombucha has also been shown to regulate cell proliferation and exert anticarcinogenic effects, especially in hormone-dependent tumors (Sinir, Tamer and Suna 2019). Polyphenolic compounds present in kombucha are known to influence tumor cell transformation and inhibit the growth of cancer cells both *in vitro* and *in vivo* (Table 2). Recent research has identified several potential anticancer compounds in kombucha and elucidated their mechanisms of action. For instance, kombucha has been found to affect the viability and invasiveness of various cancer cell lines including human lung carcinoma, osteosarcoma, and renal carcinoma cells (Cho et al. 2024). The inhibition of MMPs which play a crucial role in tumor metastasis, is one of the key anticancer actions of kombucha. This inhibition occurs in a concentration-dependent manner (Vīna et al. 2014). Malonate and vitexin, compounds isolated from kombucha ethyl acetate fraction, have been experimentally demonstrated to possess cytotoxic and anti-invasive properties, potentially contributing to kombucha anticancer effects (Mahmoudi et al. 2016) .

Additionally, folic acid (vitamin B9), a component of kombucha, has been reported to modulate the cell cycle and regulate cell proliferation, further supporting its role in cancer prevention and development (Sinir, Tamer and Suna 2019).

These findings suggest that kombucha could play a complementary role in cancer prevention and therapy by influencing

critical cellular processes involved in tumor progression.

Liver cancer

Hepatocellular carcinoma (HCC), the most common type of primary liver cancer, remains one of the leading causes of cancer-related mortality globally. Despite advances in preventive measures such as hepatitis vaccinations, novel blood tests, and improved imaging technologies, the global burden of HCC remains significant (Sun et al. 2023). Chronic liver diseases, including cirrhosis and cancer, contribute to approximately 3.5% of all deaths worldwide annually (Bedewy and El-Kassas 2023). HCC comprises three primary forms: hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma, and mixed carcinoma, with HCC being the most prevalent, accounting for over 80% of primary liver cancers (Zhao et al. 2023).

While some HCC patients initially respond to chemotherapy, the long-term prognosis remains poor (Yu et al. 2023). Radiation lobectomy, a targeted radiation approach to induce liver hypertrophy and tumor control, has demonstrated limited success, with only 30-40% of patients achieving complete tumor regression in colorectal liver metastases. The role of tumor biology in this variable response remains unclear (Andel et al. 2023).

In animal models of chemically-induced liver injury, kombucha administration has been shown to improve liver enzyme profiles and reduce tissue damage, suggesting both therapeutic and protective effects on the liver (Kabiri and Mahzooni 2013). Additionally, other studies have reported that kombucha may improve liver function in nonalcoholic fatty liver disease models and reduce hepatic steatosis (Lee et al., 2019). Furthermore, kombucha has shown cytotoxic activity against human hepatocellular carcinoma (HepG2) cell lines, indicating a potential antiproliferative effect (Deghrigue et al., 2023; El Nady et al., 2023).

These findings highlight the potential of kombucha as a complementary therapy in liver disease, offering both protective and therapeutic benefits against liver damage and associated metabolic disorders (Table 2).

Colorectal cancer

The microbial composition of kombucha, including its symbiotic culture of bacteria and yeast (SCOBY), plays a crucial role in the production of bioactive compounds during fermentation. The predominant bacteria in SCOBYs, such as *Gluconacetobacter* and *Acetobacter*, undergo metabolic adaptations depending on the type of tea used, generating different metabolites that contribute to kombucha therapeutic effects (Cardoso et al. 2020; Costa et al. 2022; De Filippis et al. 2018; Jakubczyk et al. 2020). *Acetobacter*, a key player in kombucha fermentation, oxidizes ethanol and sugars into acetic acid, resulting in a lower pH and a higher concentration of organic acids, which may enhance kombucha therapeutic properties (Costa et al. 2022). Recent studies have highlighted kombucha anticancer potential. For example, kombucha prepared from black tea contains bioactive compounds such as dimethyl 2-(2-hydroxy-2-methoxypropylidene) malonate and vitexin, which exhibit cytotoxic effects against human renal carcinoma (786-O) and human osteosarcoma (U2OS) cells. In colorectal cancer (HCT-116) cell lines, kombucha demonstrated anticancer activity, particularly when combined with chemotherapeutic agents like doxorubicin. This combination increased the proportion of cells in the G0/G1 phase, suggesting enhanced antitumor efficacy compared to doxorubicin alone (Konikoff and Gophna 2016).

Kombucha anticancer effects are attributed to its ability to induce apoptosis, a regulated form of cell death that is critical in cancer suppression. The mitochondrial pathway of apoptosis induced by kombucha tea is summarized in Figure 3. Kombucha

increases the expression of pro-apoptotic proteins (Bax, P21, and P53) and decreases Bcl-2, leading to cytochrome C release, caspase activation, and subsequent apoptosis. Chemotherapeutic agents, such as cisplatin, doxorubicin, and 5-fluorouracil (5-FU), rely on apoptotic pathways, including TNF-α and Fas ligand (FasL/CD95/Apo1), to eliminate cancer cells. Studies have shown that kombucha prepared with plant extracts such as *Aegle marmelos* (KA) enhances the antioxidant activity, phenolic compounds, and flavonoid content compared to traditional kombucha (KT). These kombucha blends exhibit increased anticancer activity due to higher levels of organic acids like glucuronic acid, ascorbic acid, and succinic acid, which have been shown to inhibit cancer cell proliferation and promote apoptosis in colorectal cancer cells (Shahbazi et al. 2018).

Furthermore, polysaccharides extracted from kombucha have demonstrated immuno-enhancing properties in preclinical models. In immunocompromised mice treated with cyclophosphamide (CTX), kombucha-derived polysaccharides significantly increased the levels of key cytokines, including IFN-γ, IL-2, IL-4, IL-10, and TNF-α, indicating enhanced immune function. These polysaccharides also modulated gut microbiota composition, increasing the synthesis of short-chain fatty acids (SCFAs), which are known to exert anti-inflammatory and immunomodulatory effects (Table 2) (Konikoff and Gophna 2016; Nakayama et al. 2012).

Taken together, kombucha demonstrates promising anticancer and immunomodulatory properties, suggesting its potential as a complementary therapeutic agent for colorectal cancer treatment.

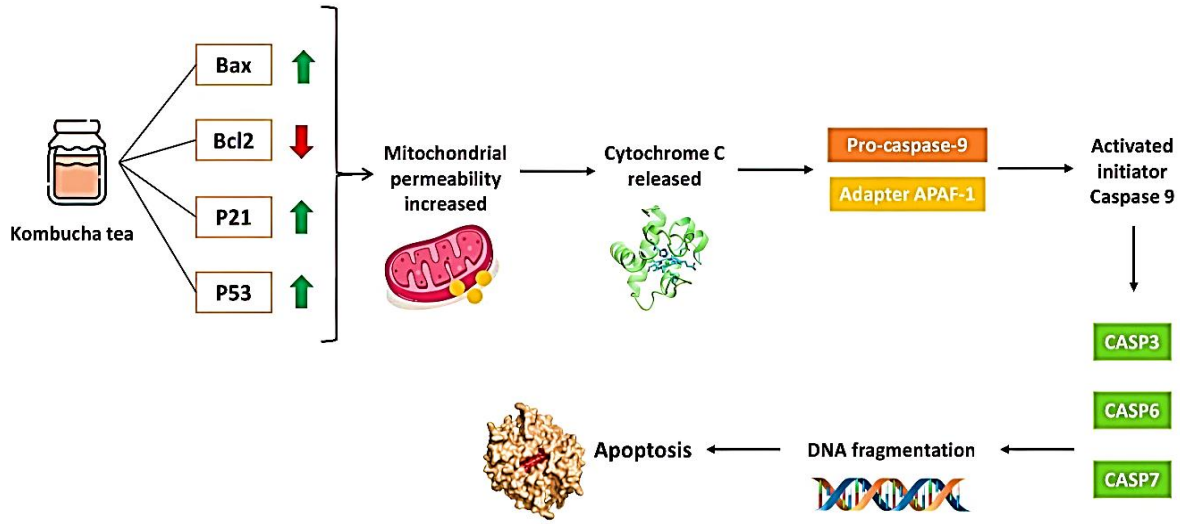

Figure 3. Proposed mechanism of kombucha tea-induced apoptosis in cancer cells via the mitochondrial pathway. Kombucha tea upregulates pro-apoptotic proteins (Bax, P21, and P53; green arrows) and downregulates the anti-apoptotic protein Bcl-2 (red arrow), leading to increased mitochondrial membrane permeability. This results in the release of cytochrome C, which, together with APAF-1 and pro-caspase-9, activates initiator caspase 9. Subsequently, executioner caspases (caspase-3, -6, and -7) are activated, leading to DNA fragmentation and apoptosis.

Ovarian cancer

Ovarian cancer (OC), which includes primary tumors of the ovary, fallopian tubes, and peritoneum, is the second most prevalent cancer of the female reproductive system and remains one of the deadliest cancers affecting women globally (Mohamadian et al. 2022). OC can arise from various ovarian tissues, including the epithelium, stroma, and germ cells, with high-grade serous carcinoma of the ovarian epithelium being the most common subtype. This aggressive form accounts for 70% of cases diagnosed at advanced stages,

often posing significant challenges in treatment due to cancer metastasis and migration (Izdebska et al. 2023).

Despite advances in debulking surgery and platinum-based chemotherapy, approximately 80% of patients with advanced-stage OC experience disease relapse within two years of treatment (Koole et al. 2021). Given the limitations of current therapies, particularly in advanced cases, the identification of novel therapeutic strategies is critical. One such promising area is nanotechnology, which has shown potential in improving drug delivery, targeting, and overall therapeutic efficacy in cancer treatments. Nanoparticles (NPs) can enhance the pharmacokinetic and pharmacodynamic properties of cancer therapies, making them attractive for augmenting existing treatment modalities like surgery and chemotherapy. Recent studies have explored the use of kombucha extract-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles (KFE-PNPs) as a novel therapeutic option for OC. In a study PLGA nanoparticles synthesized from kombucha demonstrated anticancer activity in human OC cell lines (A2780) (Ghandehari et al. 2023). These NPs exhibited enhanced CAT gene expression, as confirmed by FRAP and ABTS assays. Additionally, they showed anti-inflammatory properties by decreasing the expression of IL-6 and IL-1β, while increasing the expression of the anti-inflammatory cytokine IL-10 (Izdebska et al. 2023). This is significant, as IL-6 and IL-1β are known to promote tumor progression, survival, and metastasis, while IL-10 can inhibit cancer cell invasion and support immune regulation. These findings suggest that kombucha-loaded nanoparticles could reduce tumor progression by modulating inflammatory pathways and cytokine expression. Further research by Pandey et al. supported the anti-inflammatory potential of PLGA-NPs, showing a reduction in pro-inflammatory factors like TNF-α, IL-1β, and IL-6, along with an increase in IL-10 levels. This cytokine regulation by kombucha-loaded NPs indicates a promising anti-cancer mechanism through immune modulation, making these NPs a potential candidate for future OC therapies (Pandey, Samota and Sanches Silva 2023). Another study evaluated the cytotoxic, pro-apoptotic, and anti-angiogenic effects of kombucha extract-loaded PLGA nanoparticles (KFE-PNPs) on the A2780 human OC cell line. The nanoparticles formed stable particles with a zeta potential of −26.27 mV and a particle size of 288.32 nm, indicating their suitability for biomedical applications. The encapsulation efficiency (%EE) of kombucha extract in PLGA-NPs was 71%. KFE-PNPs exhibited selective cytotoxicity against OC cells (IC50 < 200 µg/mL) compared to normal human fibroblasts (HFF) (IC50 > 500 µg/mL). Increased apoptotic cell populations confirmed the pro-apoptotic effects, enhanced sub-G1 phase cell percentages in flow cytometry, and elevated expression of apoptotic genes such as P53 and TNF-α (Nakayama et al. 2012).

Additionally, KFE-PNPs demonstrated anti-angiogenic effects by reducing VEGF gene expression and decreasing blood vessel formation in the chick chorioallantoic membrane (CAM) assay. Since angiogenesis is essential for tumor growth and metastasis, the inhibition of VEGF-mediated pathways by KFE-PNPs suggests a viable strategy for halting OC progression. The upregulation of TNF-α, a multifunctional cytokine involved in immune regulation and apoptosis, further supports the cytotoxic and pro-apoptotic effects of kombucha-loaded NPs. Overall, these studies highlight the potential of kombucha extract-loaded PLGA nanoparticles as an innovative anticancer agent in OC. By inducing apoptosis, inhibiting angiogenesis, and modulating cytokine expression, KFE-PNPs may provide a new therapeutic approach for treating OC. Future research should focus on investigating the pharmacokinetics and pharmacodynamics of these nanoparticles

and conducting *in vivo* studies to confirm their safety and efficacy as anti-cancer agents (Table 2) (Nakayama et al. 2012).

Prostate cancer

Prostate cancer (PCa) is a hormone-dependent malignancy that originates as an androgen-sensitive lesion, driven by endogenous receptor signaling to promote cellular proliferation (Owen, Clayton and Pearson 2022; Srihari et al. 2013). It is a multifactorial disease, influenced by a combination of genetic, environmental, and physiological factors. Approximately 30% of prostate cancer cases are benign, while 40% are at moderate risk of metastasizing to distant organs such as the bones, pelvis, bladder, rectum, brain, and lumbar vertebrae (Sekhoacha et al. 2022). Current treatment options for PCa include active surveillance, chemotherapy, cryotherapy, and surgery, with the choice of therapy depending on disease stage and risk stratification. PCa can be broadly categorized into androgen-sensitive and non-androgen-sensitive types, which informs the selection of therapies such as hormone deprivation or radiation therapy. The highest incidence of prostate cancer is observed in African men, followed by European and Asian populations (Boehm et al. 2023).Hormonal dysregulation plays a critical role in the pathogenesis of prostate disorders, including benign prostatic hyperplasia (BPH) and PCa. BPH, often affecting older men, is characterized by prostate enlargement, which can obstruct the urethra, leading to significant urinary complications (Zhang et al. 2018).

In recent years, kombucha, a fermented tea beverage, has garnered attention for its purported health benefits, including its potential role in cancer prevention and treatment. Despite early claims, such as those by (Vīna et al. 2014), linking kombucha to immune stimulation, few studies offer molecular insights specific to prostate cancer. Recent work by (Srihari et al. 2013) reveals angiogenesis inhibition via VEGF and MMP suppression, yet the lack of comparative control groups in their assays limits generalizability. Anecdotal evidence suggests that regular kombucha consumption is associated with a low incidence of cancer, and some studies propose that kombucha may have therapeutic benefits in treating cancer, particularly through immune modulation and the inhibition of tumor progression. This effect is thought to be mediated by kombucha bioactive compounds, such as glucuronic acid (GlcUA), lactic acid, acetic acid, and antibiotic compounds, which may synergistically inhibit tumor growth, especially in hormone-dependent cancers. Kombucha anticancer effects have been attributed to its ability to regulate cell proliferation and modulate angiogenesis, a key process in tumor growth and metastasis. Specifically, polyphenolic molecules in kombucha have demonstrated significant effects on the transformation of tumor cells in both *in vitro* and *in vivo* studies. Recent research has identified that kombucha can inhibit stimulators of angiogenesis, such as HIF-1α, IL-8, VEGF, COX-2, and MMPs, such as MMP-2, which are critical in tumor invasion and metastasis (Srihari et al., 2013). These findings suggest that kombucha may have therapeutic potential in the treatment or prevention of prostate cancer. Notably, malonate and vitexin, compounds isolated from the ethyl acetate fraction of kombucha, have been experimentally validated as possessing cytotoxic and anti-invasive properties, further supporting kombucha potential as an anti-cancer agent (Vīna et al. 2014). While the anticancer properties of kombucha were once considered folklore, recent studies have begun to scientifically investigate its effects, particularly in liver and renal carcinoma cells. expanded upon these findings by exploring kombucha anti-angiogenic properties in the PC-3 human prostate cancer cell line. In their study, lyophilized kombucha extracts were prepared and fractionated using ethyl acetate before being tested for their effects on cell migration and angiogenic gene

expression. Kombucha treatment significantly inhibited the migration of PC-3 cells, as demonstrated by wound healing assays, where kombucha-treated cells (200 µg/mL and 400 µg/mL) exhibited reduced migration compared to control cells. Furthermore, kombucha treatment led to a significant decrease in the gene expression of angiogenic stimulators, including HIF-1α, VEGF, IL-8, and COX-2, in a dose-dependent manner. This suggests that kombucha inhibits angiogenesis, which is essential for tumor growth and metastasis. Additionally, kombucha treatment significantly reduced the expression of MMP-2 and MMP-9, enzymes involved in the degradation of the extracellular matrix and facilitation of tumor invasion. The downregulation of these molecules indicates that kombucha may possess anti-metastatic properties (Srihari et al. 2013) (Table 2). These findings underscore the potential of kombucha as an adjunct therapy in prostate cancer treatment, particularly through its anti-angiogenic, anti-invasive, and immune-modulatory effects. However, further studies are needed to confirm its efficacy and safety in clinical settings, particularly regarding its pharmacokinetics, pharmacodynamics, and long-term impact on prostate cancer progression.

Table 2. Potential effects of Kombucha on cancer

Cancer Type	Mechanism of Action	Key Findings	Reference
Breast Cancer	Antioxidant activity, apoptosis induction	Reduced oxidative damage in tumor tissues	(Salafzoon, Hosseini and Halabian 2018)
Lung Cancer	Immune modulation, MMP inhibition	Reduced cell invasion and tumor progression	(Vīna et al. 2014)
Liver Cancer	Anti-inflammatory, detoxification	Improved liver enzyme levels and reduced apoptosis	(Kabiri and Mahzooni 2013)
Colorectal Cancer	Apoptosis induction, immune enhancement	Enhanced efficacy with chemotherapeutics	(Konikoff and Gophna 2016)
Ovarian Cancer	Anti-angiogenic, pro-apoptotic	Decreased VEGF and increased TNF-α expression	(Ghandehari et al. 2023)
Prostate Cancer	Angiogenesis inhibition, immune regulation	Decreased expression of COX-2 and MMP-2	(Srihari et al. 2013)

Discussion

Kombucha tea, a fermented beverage rich in bioactive compounds with potent antioxidant properties, has gained attention for its therapeutic potential in mitigating oxidative stress—a key driver of cancer development and progression (Kitwetcharoen et al. 2023). While oxidative stress is widely acknowledged as a cancer hallmark (Mao et al. 2017), few studies have clarified whether kombucha antioxidant action exceeds that of unfermented tea (Cardoso et al. 2020) reported higher phenolic content in green tea kombucha versus black tea, suggesting differential effects. This study sheds light on the multifaceted anticancer mechanisms of Kombucha tea, as illustrated in Figure 4, demonstrating its broad therapeutic effects across various cancer types, including prostate, breast, colon, liver, and lung cancers. In prostate cancer, Kombucha tea's antioxidant components exhibit the ability to modulate androgen receptors, thereby suppressing androgen-driven tumor growth and proliferation (Kaewkod, Bovonsombut and Tragoolpua 2019). Similarly, in breast cancer, these antioxidants modulate estrogen receptors, curbing hormone-dependent cancer progression. In colon cancer, Kombucha tea demonstrates anti-angiogenic effects, inhibiting the formation of new blood vessels essential for tumor growth and metastasis (Rasouli et al. 2021a). Kaewkod et al. (2022) demonstrated kombucha-mediated apoptosis in HT-29 cells through caspase activation, but Rasouli et al. (2021) failed to replicate this in Caco-2 cells, highlighting strain and cell-line specificity that must be addressed in future studies. Its ability to

enhance detoxification pathways further aids in the elimination of carcinogenic substances, providing a protective mechanism against the progression of colon cancer (Kaewkod et al. 2022). For liver cancer, Kombucha tea's antioxidants are pivotal in enhancing liver detoxification processes and inhibiting the proliferation of cancer cell lines, including A549 and HepG2 (Lacerda et al. 2024). In lung cancer, the anti-inflammatory and antioxidant activities of kombucha components contribute to the downregulation of pro-inflammatory cytokines and oxidative damage, potentially impairing tumor cell survival and metastasis.

Collectively, these findings underscore kombucha tea's pleiotropic mechanisms in targeting multiple cancer pathways, including oxidative stress reduction, hormone receptor modulation, angiogenesis inhibition, apoptosis induction, and detoxification enhancement. However, variability in fermentation conditions, microbial composition, and tea substrate necessitates standardized protocols for reproducibility and clinical translation.

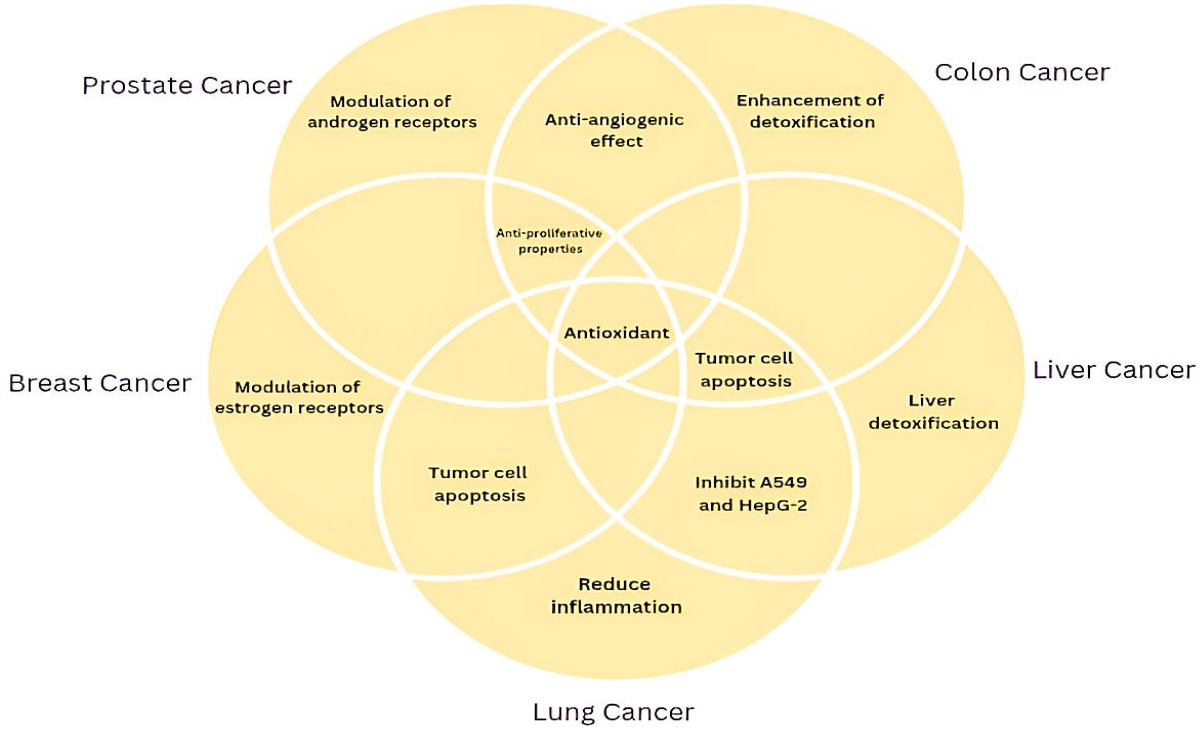

Figure 4. Venn diagram summarizing the proposed anticancer mechanisms of kombucha tea across different cancer types. The diagram illustrates both unique and shared effects of kombucha on prostate, breast, colon, liver, and lung cancers. Key mechanisms include modulation of hormone receptors, anti-angiogenic effects, enhancement of detoxification, antioxidant activity, induction of tumor cell apoptosis, inhibition of specific cancer cell lines (A549 and HepG2), reduction of inflammation, and anti-proliferative properties. Overlapping areas represent mechanisms common to multiple cancer types.

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Conflicts of interest

The authors have declared that there is no conflict of interest.

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