Proceedings of Anticancer Research, 2025, Volume 9, Issue 2
http://ojs.bbwpublisher.com/index.php/PAR
ISSN Online: 2208-3553
ISSN Print: 2208-3545

A Review of the Relationship between Tea Drinking and Breast Cancer

Jingjing Yu, Suriyakala Perumal Chandran*, Farra Aidah Jumuddin, Nurul Azmir Amir Hashim

Faculty of Medicine, Lincoln University College, Petaling Jaya 47301, Selangor, Malaysia

Corresponding author: Suriyakala Perumal Chandran, suriyakala@lincoln.edu.my

Abstract: The global incidence of breast cancer remains high and is increasing annually in some regions. Despite the variety of current treatments for breast cancer, the preventive and therapeutic effects are still limited due to the highly heterogeneous nature and complex biological mechanisms of breast cancer. In recent years, tea consumption has emerged as a research focus due to its possible anti-cancer properties. Numerous preclinical studies have demonstrated that regular tea intake could potentially curb the progression of breast cancer by influencing various biological mechanisms, including signaling pathways, cell cycle regulation, and immune system responses, among others. Nonetheless, the findings from epidemiological studies show considerable variability, and the connection between tea drinking and both the risk and outlook for breast cancer is shaped by numerous elements. These include the specific type of tea consumed, the quantity consumed, individual genetic variations, and environmental influences. This article summarizes the current research findings and delves into the connection between tea consumption and the risk as well as the prognosis of breast cancer among different regional populations. Meanwhile, it expounds on the potential molecular biological mechanisms behind it. The aim is to offer a theoretical foundation for the personalized prevention and treatment of breast cancer.

Keywords: Tea drinking; Breast cancer; Risk; Prognosis; Green tea; Black tea

Online publication: April 2, 2025

1. Introduction

Breast cancer stands as the most prevalent malignant tumor affecting women across the globe, with its incidence rising at a concerning pace. The latest statistics from the International Agency for Research on Cancer show that breast cancer continues to be the leading cause of cancer morbidity and mortality among women globally, with about 2.3 million new cases and 666,000 deaths in 2022 [1]. Breast cancer incidence is strongly associated with multiple factors, such as genetic elements, lifestyle choices, environmental exposures, and socioeconomic standing [2,3]. However, given the complexity of the etiology of breast cancer and its diverse clinical manifestations, its prevention and treatment still face many challenges.

In recent years, studies based on dietary patterns and lifestyle interventions have received widespread attention. Tea has become a research hotspot in this field due to its unique cultural value, rich bioactive components, and widespread global consumption. Based on different processing methods and sensory properties, tea is classified into six main types: green, white, yellow, oolong, red, and black tea [4]. Among them, black tea has the largest global production volume. Its main consumption areas include Europe, West Asia, and the United States. Green tea follows, ranking second in terms of production, and is mainly consumed in China and Japan. Oolong tea has a relatively lower production level and is predominantly consumed in the southeastern China and Taiwan region [5]. Tea is rich in various bioactive compounds, including polyphenols, amino acids, polysaccharides, and alkaloids, among others [6-8]. These active components endow tea with numerous beneficial qualities, including the ability to suppress bacteria, reduce inflammation, control blood sugar, regulate weight, and maintain cardiovascular health [9-11]. Numerous studies have shown the potential role of the active ingredients in tea in preventing and treating cancer [12-14], however, the results of related epidemiologic studies have not been agreed upon [15]. In the realm of breast cancer, the research results are equally inconsistent, and the link between tea intake and breast cancer remains ambiguous [16,17].

Consequently, the objective of this review is to fully combine the existing epidemiological findings with molecular biological processes in order to explore the intricate connection between tea intake and breast cancer, as well as to examine how the active compounds in tea influence the biological behavior of tumors, thereby providing new scientific insights into the prevention and management of breast cancer.

2. Association between tea consumption and breast cancer risk

2.1. Epidemiological research on tea intake and breast cancer risk across various regions

2.1.1. Europe

Before the 1990s, the epidemiological field on the association between tea intake and breast cancer risk was more limited, and the number of targeted studies was few. With the improvement of research methods and in-depth exploration of tea polyphenols and other components, the number of related studies is gradually increasing. In 1990, a Danish study on the link between dietary habits and the risk of breast cancer was conducted, analyzing questionnaires from 1,474 breast cancer patients. The findings indicated that tea intake was not significantly linked to the probability of developing breast cancer [18]. A forward-looking cohort study conducted in the Netherlands reached similar conclusions. The study focused on black tea and found that even after adjusting for confounding factors, groups that consumed tea more often (like five or more cups a day) had just a marginal uptick in the risk of breast cancer when compared to those who did not drink tea., but failed to achieve statistical significance (relative risk [RR] = 1.3; 95% confidence interval [CI]: 0.9–2.0). Further subgroup analysis considering vegetable and fruit intake likewise did not demonstrate any role of black tea consumption in reducing breast cancer risk [19]. A Swedish study based on a large breast cancer screening cohort similarly found no significant correlation between black tea intake and the incidence of breast cancer. The study included 1,271 breast cancer cases followed for nearly 10 years and demonstrated no meaningful correlation between tea consumption and the occurrence of breast cancer, either by general population, body mass index (BMI), or age. After adjusting for multiple covariates, there remained no statistically significant variation [20]. However, another Swedish study, centered around the Women's Lifestyle and Health (WLH) initiative, discovered that women who consumed more than one cup of tea daily faced a heightened risk of breast cancer when compared to those who did not drink tea (RR

= 1.19, 95% CI: 1.00–1.42) [21]. A French cohort study additionally analyzed the effects of Herbal tea (mainly *Tilia cordata*, *Mentha piperita*, and *Verbena officinalis*) and showed that women who consumed more than 150 ml of Herbal tea per day had a significantly lower risk of breast cancer (RR = 0.43; 95% CI: 0.20–0.94; *P*-trend = 0.04). However, no noteworthy link was observed between the consumption of regular tea (including black or green tea) and the risk of breast cancer [22]. It is essential to recognize that the study comprised only 95 breast cancer cases—a limited sample—and results should be viewed cautiously. Another French prospective cohort study followed 67,703 women for 11 years and ultimately included 2,868 cases of breast cancer. The findings indicated that tea intake did not have a meaningful correlation with breast cancer risk ($P = 0.22$). Although the cohort omitted details on tea varieties, the authors speculate that most participants drank traditional French black tea [23].

2.1.2. America

In a cohort study of postmenopausal women in Iowa, no notable link was found between tea consumption and breast cancer risk ($P = 0.28$). Compared to those who do not consume tea, the RR for women drinking two or more cups daily was 1.14 (95% CI: 0.92–1.41) [24]. However, only 9.5% of participants in the study reported drinking two or more cups of tea daily, which may limit the study's ability to detect potential associations. A major prospective cohort study utilizing the Nurses' Health Study II (NHS II) evaluated the link between tea, an important flavonol source, and breast cancer risk. The study participants showed an equal distribution in how often they consumed tea. No significant link was observed between tea intake (primarily black tea) and breast cancer risk over a follow-up period of nearly eight years. Compared to women consuming tea less than monthly, those drinking it two or more times daily showed a multivariable-adjusted hazard ratio of 1.02 (95% CI: 0.81–1.28; *P*-trend = 0.83) [25]. Another NHS-based cohort study, despite 22 years of follow-up and analysis of 5,272 breast cancer cases from 11 states, likewise did not show a connection between the quantity of tea consumed and the risk of breast cancer ($P = 0.25$) [26]. In addition, exploring a group of black women in the U.S. reached similar conclusions to the NHS cohort study [27]. However, a trend indicating a negative correlation between the risk of breast cancer and the consumption of green tea (P-trend < 0.01), but no significant overall association with black tea (P-overall = 0.25), was noted in a cohort of women with a familial breast cancer background in the U.S. and Puerto Rico. In terms of tea consumption, consuming five or more weekly servings of green or black tea may reduce breast cancer risk [28]. In a longitudinal study of Canadian females, no significant link was detected between tea consumption and the overall breast cancer risk (P-trend = 0.95). Statistically significant differences were also not observed across menopausal status, hormone replacement therapy, and BMI subgroups [29]. A case-control study carried out in Uruguay, South America, aimed at examining the relationship between mate tea consumption and the risk of breast cancer, as well as evaluating its synergistic effects with dietary antioxidants. The research indicated that a high consumption of mate tea was notably linked to a lower risk of breast cancer, especially in those consuming more than 1 liter per day (odds ratio [OR] = 0.38 and OR = 0.41) and long-term users (OR = 0.62 for both models). Notably, the consumption of mate tea was not associated with dietary antioxidant levels. For conventional tea (which the study hypothesized was black tea), the negative association with breast cancer was only significant in people with high levels of dietary antioxidant intake [30]. The impact of black tea and green tea on breast cancer has been investigated by researchers among Asian American groups, including women of Chinese, Japanese, and Filipino descent. The findings indicated that black tea intake had no significant correlation with breast cancer risk. In contrast, green tea consumption was linked to a notable decrease in the risk of developing breast cancer. This protective effect remained significant even after adjusting for diverse dietary and

other potential confounding factors, and breast cancer risk was further reduced with increasing green tea intake. In addition, the research also examined the relationship between consumption of green tea and soy products with breast cancer risk, showing that green tea's protective benefits were predominantly observed in individuals with low soy consumption [31].

2.1.3. Asia

A Japanese study pooled data from two prospective cohorts of 35,004 women, 222 of whom were diagnosed with breast cancer. The findings indicated no notable link between green or black tea intake and breast cancer occurrence. Unlike studies in Asian American populations, when stratified by soybean soup intake, women consuming five or more cups of green tea daily showed no significant difference in breast cancer risk compared to those drinking less than one cup daily, irrespective of soy soup consumption [32]. In their large-scale cohort study, Iwasaki *et al.* [33] refined green tea intake into nine dose groups (from < 1 cup/week to ≥ 10 cups/day), the results showed that no significant correlation with breast cancer risk was observed for either total green tea intake or grouping by tea type (Sencha, Bancha, and Genmaicha). In addition, studies of oolong tea and black tea also showed consistent results. Conversely, a case-control study of Japanese women found that green tea consumption was linked to a lower breast cancer risk, yet this was only evident in women who drank it 2–3 times a week (adjusted OR = 0.63; 95% CI: 0.43–0.93) [34]. Among Chinese Singaporean women, no statistically significant links were found between the consumption of green and black tea and breast cancer risk. To further validate the effect of gene-environment interaction on breast cancer risk, the researchers performed a stratified analysis based on angiotensin-converting enzyme (*ACE*) genotypes. The results found that the frequency of green tea consumption was significantly negatively associated with breast cancer risk (*P*-trend = 0.039) and had a dose-response relationship in women harboring high-activity *ACE* genotypes, whereas women harboring low-activity *ACE* genotypes did not show such an association. Green tea intake exhibited a statistically significant interaction with the *ACE* genotype in influencing breast cancer risk (*P*-interaction = 0.01), but this result was not observed in black tea [35]. Another study by the same team further evaluated the interaction of green tea intake with *MTHFR*/*TYMS* genotype and folate intake level on breast cancer risk. The findings indicated that among women with high-activity *MTHFR*/*TYMS* genotypes and lower folate intake, a significant inverse relationship was observed between green tea intake and breast cancer risk relative to other subgroups (OR = 0.44; 95% CI: 0.22–0.89) [36]. Both studies highlight the potential value of combining diet with an individual's genetic background in breast cancer prevention. A retrospective case-control study conducted in southeastern China found that green tea consumption was significantly associated with a reduced breast cancer risk when compared to women who did not drink tea. Those who consumed ≥ 750 g of dry tea annually, based on the amount of tea consumed, had a 39% lower risk of developing breast cancer than non-tea drinkers (adjusted OR = 0.61; 95% CI: 0.48–0.78). Breast cancer risk decreased with increasing duration and frequency of consumption, showing a clear dose-response relationship [37]. However, in a large prospective cohort study involving around half a million adults in China, no significant link was identified between tea intake and breast cancer risk in the researchers' findings (*P* = 0.267). The study covered 10 different geographic regions in China and included a total of 1,552 breast cancer cases [38].

While multiple epidemiological studies have investigated the link between tea intake and breast cancer risk, no consistent findings have been reached. Most studies show no significant correlation between tea intake and breast cancer risk, and results vary widely across geographic regions and populations. For instance, in Europe and the Americas, most studies have not identified a correlation between the intake of green or black tea and the

risk of breast cancer, whereas an increased association has been observed in studies conducted in Asia. However, there were also differences in results between different types of studies, such as cohort studies and case-control studies in Japan, from the same countries in the same region. This phenomenon may be related to the limitations of the studies. First, tea drinking preferences vary by region and cultural background, with black tea predominantly consumed in Europe and North America, mate tea in parts of South America, and more green tea in Asia. The biological mechanisms of action of the main active ingredients of different tea classes may have varying effects on breast cancer risk, which may lead to biased results. Some studies incorporated in this paper did not distinguish among tea categories, and homogenized analyses may dilute or confound the actual effects of specific tea categories on breast cancer risk. Secondly, although many studies have made substantial adjustments for various influencing factors, such as dietary habits and lifestyle behaviors, there are still potential factors that have not been measured or adequately considered, which could influence the precision and applicability of the findings. In addition, some studies suffered from self-reporting bias, measurement error of tea drinking frequency, multiple attribution, and lack of stratified analysis of breast cancer subtypes, which may mask potential associations among study subjects. Notably, studies of gene-environment interactions suggest that tea consumption may influence breast cancer development through interactions with individual genotypes, emphasizing the combined effects of dietary factors and genetic background and revealing that tea consumption may have the potential to personalize breast cancer prevention.

2.2. Impact of menopause and hormone receptor status on the link between tea intake and breast cancer risk

It is widely recognized that the onset and progression of breast cancer are strongly linked to menopausal and hormone receptor conditions. Green tea intake may affect estrogen metabolism or binding in different menopausal states, which in turn affects breast cancer risk [39]. Therefore, numerous studies have examined the association between tea intake and breast cancer risk across various menopausal statuses and hormone receptor profiles.

A study conducted using a Swedish mammography cohort revealed that black tea consumption was significantly linked to an increased risk of breast cancer overall, particularly for estrogen receptor-positive/progesterone receptor-positive (ER+/PR+) tumors (P-trend < 0.007). Compared with non-tea drinkers, women who drank ≥ 2 cups of tea per day had a 36% increased risk of ER+/PR+ tumors; the relationship remained unchanged regardless of menopausal status, hormone use in postmenopausal women, or BMI (P for interaction ≥ 0.10 for all) [40]. This is generally consistent with the conclusion of another study based on the WLH cohort above, which also found that among postmenopausal women, women who drank 1 cup of tea per day had a 24% increased risk of breast cancer (P-value = 0.007) [21]. Although the study did not specify the type of tea consumed, it was hypothesized that black tea was predominantly consumed, taking into account the context of the study and tea culture. However, in the French prospective study cohort, when analyzed based on menopause stage and hormonal receptor profile, no significant association was identified between black tea consumption and breast cancer risk [23]. Another multicenter European prospective cohort study evaluated the link between tea consumption and the risk of developing breast cancer in different menopausal states. The study involved 10 European countries with a mean follow-up of 11 years, and a total of 1,064 premenopausal and 9,134 postmenopausal breast cancers were diagnosed. Tea consumption does not appear to have a statistically significant impact on the risk of developing breast cancer, regardless of menopausal status. For premenopausal breast cancer, the adjusted hazard ratio (HR) associated with high tea consumption was 0.98 (95% CI: 0.77–1.26), while for postmenopausal breast cancer, it was 0.95 (95% CI:

0.88–1.03). Analyzed by hormone receptor status, again, no significant differences were found [41].

The impact of green tea was explored in a case-control study conducted in Shanghai, China, which included 3,454 cases and 3,474 individuals in the control group. The results showed that individuals who habitually drank green tea experienced a modest decrease in the risk of developing breast cancer (OR = 0.88; 95% CI: 0.79–0.98). In premenopausal women, the duration, frequency, and quantity of green tea intake were all linked to a lower likelihood of developing breast cancer. In postmenopausal women, the relationship was only associated with older age at initiation and lower intake [42]. A separate investigation examining a cohort of Chinese women in Hong Kong revealed that the risk of developing breast cancer was not influenced by the specific type of tea consumed (including green, black, oolong, and other teas), but rather depended on the menopausal status of the women and the hormone receptor status of the tumors. In premenopausal women, the intake of tea was linked to a lower likelihood of developing breast cancer (OR = 0.62; 95% CI: 0.40–0.97). Conversely, in postmenopausal women, tea consumption appeared to correlate with a heightened risk of the disease (OR = 1.40; 95% CI: 1.00–1.96). Similar trends were observed among green tea drinkers. Further stratified analysis based on ER status found that post-menopausal ER-green tea drinkers had the most increased risk of breast cancer (OR = 2.99; 95% CI: 1.26–7.11) [43]. A case-control study conducted in a hospital setting in Nagano Prefecture, Japan, concluded that there was no notable association between the intake of green tea and the risk of developing breast cancer. The study did not stratify analyses by menopausal status and did not obtain statistically significant results when stratified by different hormone receptor status [44]. In another prospective study based on public health centers in Japan, menopausal status had no significant effect on green tea and breast cancer risk [33].

Among U.S. women with a familial predisposition to breast cancer, the consumption of green tea was linked to a notably reduced risk of ER+ breast cancer. In particular, a 19% reduction in the risk of ER+ breast cancer (95% CI: 0.68–0.97) was observed among women who consumed at least five cups of green tea per week. No meaningful correlation was identified between green tea intake and the likelihood of developing ER- breast cancer. Among postmenopausal women, an enduring negative correlation was also observed between green tea intake and the risk of breast cancer, with the trend reaching statistical significance (P-trend < 0.01). However, no correlation was observed in black tea [28]. In a study focusing on African American women in the U.S., researchers observed a potential link between tea consumption and an increased risk of breast cancer among postmenopausal participants (incidence rate ratio [IRR] = 1.44, 95% CI: 0.89–2.34). However, this association fell short of achieving statistical significance. Further stratification by ER/PR status also showed no significant association [27]. Herbal tea, which contains flavonoids, quercetin, and kaempferol, is more commonly consumed in the Mexican region than green and black tea. Herbal tea demonstrated protective benefits in premenopausal females, especially when consumed less than 3 cups per week (OR = 0.41; 95% CI: 0.18–0.92). However, in women after menopause, the association was not significant [45]. In addition, a case-control study from Wisconsin, Massachusetts, and New Hampshire found that among women under 50 years of age, those who consumed at least three cups of tea each day had a 37% lower risk of breast cancer than non-tea drinkers (adjusted OR = 0.63, 95% CI: 0.44–0.89), and a significant trend indicating an increased effect with higher consumption was observed (P-trend = 0.01) [46].

Research data on the effects of menopause and ER/PR expression on tea intake and breast carcinoma risk are still limited, and published findings lack consistency. However, in some of the studies where associations have been observed, green tea consumption appears to show a potential correlation with reduced breast carcinoma risk among premenopausal individuals as well as ER+ women, such as the research conducted in Shanghai, China, and the U.S. Cohort Study on women with hereditary breast cancer risk. In contrast, black tea intake appears to be

linked to a heightened risk of breast cancer, particularly among postmenopausal women and those with ER+/PR+ subtypes, as evidenced by findings from the Swedish Mammography Cohort Study and the WLH Cohort Study. Findings from multiple cross-sectional studies suggest that green tea consumption might be negatively correlated with blood estrogen concentrations, while black tea consumption appears to show a positive correlation with blood estrogen levels [47], suggesting that tea's effect on endogenous hormones may be an important factor contributing to these differential outcomes. Yet, it is necessary to note that this trend in risk relationships has not been consistently confirmed in all studies. For example, neither the French prospective study cohort nor the multicenter European prospective cohort study detected a substantial link between the consumption of black tea and the risk of breast cancer. This may be related to differences in population characteristics, tea drinking habits, type and quality of tea, as well as study design and statistical methods across studies. Consequently, additional high-quality, large-sample, multicenter investigations are required to delve deeper into this intricate relationship.

3. Relationship between tea intake and breast cancer outcomes

3.1. Effect of tea consumption on survival and recurrence of breast cancer patients

Currently, limited epidemiological research exists on the impact of tea intake on breast cancer outcomes. In 1998, a Japanese investigation initially examined this connection and observed that an increased intake of green tea before diagnosis correlated with markedly better outcomes for individuals diagnosed with stage I and II breast cancer, although this effect was not seen in those with stage III disease [48]. A separate investigation conducted by Japan's Aichi Cancer Center revealed that drinking at least three cups of green tea each day prior to diagnosis was associated with a reduced likelihood of breast cancer recurrence (HR = 0.69; 95% CI = 0.47–1.00). However, this protective benefit was observed exclusively in patients diagnosed with stage I breast cancer [49]. Seely *et al.* [50] conducted a meta-analysis combining data from two studies, revealing a pooled RR of 0.75 (95% CI: 0.47–1.19; $P = 0.22$) for breast cancer recurrence across all stages. However, when diving into subgroup analysis, the findings painted a clearer picture: the pooled RR for stage I and II breast cancer dropped to 0.56 (95% CI: 0.38–0.83; $P = 0.004$). This suggests that green tea consumption might play a role in reducing the risk of recurrence, particularly in the early stages of breast cancer. A cohort study from Sweden analyzed the relationship between black tea consumption and breast cancer mortality and showed no significant correlation between black tea consumption and breast cancer-specific and total mortality. Moreover, this finding was not influenced by factors such as hormone receptor classification, cancer stage at the time of diagnosis, or tobacco usage (all $P > 0.05$) [51]. A study based on a US NHS cohort explored the relationship between tea intake and survival after breast cancer diagnosis. A total of 1,054 breast cancer-related and 2,501 overall deaths were documented over a follow-up period spanning up to 30 years. The findings indicated that drinking tea after a breast cancer diagnosis was linked to reduced overall mortality. Specifically, breast cancer patients who regularly consumed more than three cups of tea daily experienced a 26% lower risk of dying from any cause (HR = 0.74; 95% CI: 0.58–0.95; P-trend = 0.04). Nevertheless, no link was found between tea intake and mortality specifically related to breast cancer. Following a stratified analysis based on estrogen receptor status and molecular subtypes, the association between tea consumption and both overall and breast cancer-specific mortality lost its significance [52]. This indicates that increased tea intake might be linked to improved overall survival in breast cancer survivors. In another prospective cohort study involving patients diagnosed with triple-negative breast cancer, women who regularly consumed tea after diagnosis had not only a lower all-cause mortality rate (HR = 0.57; 95% CI: 0.34–

0.93), but also a lower recurrence/disease-specific mortality rate (HR = 0.54; 95% CI: 0.31–0.96). However, no interaction with menopausal status was observed [53]. A study conducted in Guangzhou, China, examined the link between tea intake and survival rates prior to and following a breast cancer diagnosis. The results indicated that no significant link was detected between tea intake and progression-free survival, regardless of whether it was before or after diagnosis. However, when delving deeper into the analysis by tea consumption category, it was discovered that the consumption of oolong tea had no significant correlation with the risk of breast cancer progression (HR = 1.32; 95% CI: 0.60–2.90). On the flip side, other teas, primarily green teas, markedly reduced the likelihood of progression (HR = 0.52; 95% CI: 0.29–0.91). In addition, those who drank tea ≥ 7 times per week had a better prognosis (HR = 0.30; 95% CI: 0.11–0.84), but the concentration of tea intake was not linked to the progression risk [54].

The link between tea intake and breast cancer outcomes is still unclear. ER and menopausal status seem to have little impact on their correlation, whereas the variety of tea consumed may play a role in this relationship. There may be an association between green tea intake and improved prognosis and reduced risk of breast cancer progression in patients with early-stage breast cancer. However, there are fewer relevant studies on black tea. The existing research did not identify a meaningful link between black tea consumption and breast cancer mortality, necessitating further investigation into its possible effects. In addition, most studies have focused primarily on the impact of tea consumption on patient survival after breast cancer diagnosis, and few studies have examined the impact of tea consumption prior to diagnosis. This somewhat limits a comprehensive assessment of the potential role of tea consumption in early intervention for breast cancer.

3.2. Effects of tea consumption on health and functional status of breast cancer patients

As the survival of breast cancer patients continues to lengthen, the assessment of their prognosis has gradually shifted from survival alone to a more comprehensive perspective. On a basis of traditional indicators such as survival and mortality, quality of life (QoL) has also been included as an important consideration [55]. A multicenter cohort study assessed the association between tea consumption and QoL in breast cancer patients through patient-reported outcomes (PROs). The study found that at one year after diagnosis, patients in all groups experienced a decrease in overall QoL and an increase in fatigue and pain. However, tea intake was not found to have a meaningful association with QoL, anxiety, depression, fatigue, or pain reported by breast cancer patients. Plus, studies have not observed significant associations between tea consumption and breast cancer recurrence-free survival, distant disease-free survival, and overall survival [56]. Thus, existing evidence indicates that tea intake does not seem to substantially enhance the survival or quality of life of individuals with breast cancer.

It has been shown that breast cancer treatment may have an impact on cognitive function [57]. Common cognitive impairments include decreased memory, attention, information processing speed, and so on [58]. Although cognitive impairment gradually resolves after cancer treatment, these cognitive dysfunctions may persist for some cancer survivors [59]. A large prospective cohort study demonstrated that consistent tea intake was linked to better cognitive performance, especially in delayed memory ($P = 0.04$). Tea drinkers had a more significant improvement in delayed memory at 18 and 36 months post-diagnosis than non-tea drinkers, with a mean improvement score of 1.91 (compared to 1.43 for non-tea drinkers), which was of small to moderate clinical significance (Cohen's $d = 0.46$) [60]. This suggests that tea consumption may contribute to cognitive recovery in breast cancer patients after treatment.

4. Potential anticancer mechanisms of tea drinking

Polyphenols are the key bioactive constituents in tea, mainly including flavonoids, flavonols, phenolic acids, and others [61]. Tea polyphenols (TP), commonly known as catechins, are a class of flavonoids with the basic structure of α-phenylbenzopyranes, which can be mainly divided into the following four types: epigallocatechin gallate (EGCG), epicatechin gallate (ECG), epigallocatechin (EGC), and epicatechin (EC) [62]. Due to the rich content of EGCG in tea and the numerous related studies, this paper will focus on the anticancer mechanism of EGCG and cover the related contents of other components.

4.1. Inhibition of signaling pathways and oxidative stress regulation

Approximately 15–20% of breast cancer patients exhibit *HER-2* gene overexpression, and this abnormal expression is typically strongly associated with poor patient prognosis [63]. EGCG can inhibit the phosphorylation of HER-2, which in turn inhibits the activation of Stat3 as well as the promoter activity of c-fos and cyclin D1, and decreases the intracellular cyclin D1 and Bcl-XL protein levels, thereby inhibiting the growth of HER-2 positive breast cancer cells. In addition, EGCG enhanced the inhibitory effect of paclitaxel on such breast cancer cells [64]. In ER+/PR+ breast cancer cells, EGCG can also exert the same inhibitory effect. It promotes the separation of Hsp90 from progesterone receptor B (PR-B) by activating the p38MAPK/CK2 signaling pathway, leading to the translocation of PR-B to the nucleus and the recruitment of NCoR and HDAC1 co-repressor complexes at the half-progestin-responsive element site on the ERα promoter, which inhibits the transcriptional activity and expression level of the *ERα* gene. In addition, EGCG significantly inhibited ERα-associated genomic and non-genomic signaling pathways [65]. HBP1 is a transcriptional repressor that inhibits the transcriptional activation of the Wnt signaling pathway, and its mutation is associated with the proliferation of breast cancer cells. EGCG can increase the expression level of HBP1 protein by increasing the stability of HBP1 mRNA, inhibit the activity of the Wnt signaling pathway, and reduce the proliferation and invasiveness of breast cancer cells [66]. Proline dehydrogenase (PRODH) is a key enzyme involved in proline metabolism within cells and supports cancer cell survival and growth by promoting proline metabolism. EGCG significantly suppresses the expression of PRODH and its regulatory proteins in triple-negative breast cancer (TNBC) cell lines. Similarly, in patient-derived xenograft mouse models, EGCG markedly downregulates PRODH expression and inhibits tumor growth [67]. Kaempferol (Kaem) is a natural flavonoid phytoestrogen widely found in tea and other plants. Triclosan (TCS), a synthetic antimicrobial agent with estrogenic activity, promotes the proliferation of MCF-7 breast cancer cells through activation of the non-genomic ER signaling pathway associated with IGF-1R. Kaem can significantly impede the growth of cancer cells caused by TCS or induced 17β-estradiol (E2) by regulating the expression of cell cycle-related genes (such as the down-regulation of cyclin D1 and cyclin E) as well as apoptosis-related genes (such as the up-regulation of Bax). In a xenograft breast cancer mouse model, Kaem also significantly inhibited tumor growth induced by E2 or TCS. This suggests that Kaem has the potential to mitigate the risk of breast cancer triggered by endogenous and exogenous estrogens by inhibiting ER and IGF-1R signaling pathways [68].

Green tea catechins (GTCs), the primary bioactive compounds in green tea, may help prevent carcinogenesis by reducing oxidative stress-induced processes. Low-dose exposure to environmental carcinogens triggers an increase in reactive oxygen species (ROS) levels in mammary cells, which activates the ERK pathway, resulting in cell growth and DNA impairment. GTCs significantly inhibit this process at non-cytotoxic concentrations and continue to exert their effects under prolonged exposure conditions, as well as preventing cells from gaining cancer-related traits, including decreased reliance on growth factors, the ability to grow independently of

anchorage, and enhanced migratory ability [69]. Green tea extract (GTE) also possesses antioxidant activity, which effectively scavenges free radicals at low concentrations, significantly reduces H_2O_2-induced ROS levels, and inhibits serum MMP-2 and MMP-9 activities in breast cancer patients in a concentration-dependent manner. It offers additional evidence supporting tumor progression inhibition via antioxidant mechanisms [70].

4.2. Suppression of tumor microenvironment and angiogenesis

It was found that TNBC cell-secreted factors can induce adipose-derived mesenchymal stem/stromal cells (ADMSC) to exhibit inflammatory and cancer-associated adipocyte (CAA)-like phenotypes, which were characterized by the increased expression of CAA-associated cytokines (such as CCL2, CCL5, etc.) and immunomodulatory factors (such as COX2, HIF-1α, etc.), and the expression of Snail was upregulated. EGCG could effectively inhibit the *CAA* gene expression induced by TNBC cell secretion factors, as well as the activation state of Smad2 and NF-κB. This suggests that EGCG is able to prevent the inflammatory response and the formation of CAA-like phenotype in ADMSC triggered by TNBC cell-secreted factors [71].

Tumor growth relies on angiogenesis, a process primarily stimulated by vascular endothelial growth factor (VEGF), a key mediator of angiogenesis [72]. A previous study found that both GTE and its single catechin component effectively restricted the growth of breast cancer cells and vascular endothelial cells and reduced tumor vessel density in mice [73]. Further studies showed that GTE and EGCG could reduce VEGF secretion in breast cancer cells and endothelial cells by inhibiting VEGF promoter activity and RNA transcription. GTE may also be involved in the inhibitory effect on VEGF by decreasing the transcription of c-fos and c-jun RNA and the expression of protein kinase C [74]. Polyphenon E (PolyE), a standardized green tea extract, can block STAT3 activation by suppressing STAT3 phosphorylation and its dimerization with STAT1. This mechanism downregulates the expression levels of VEGF and MMP-9, thereby inhibiting angiogenesis and breast cancer cell migration [75]. Fibroblast growth factors (FGFs) also play a key role in tumor angiogenesis and tumor growth. gTE and EGCG not only reduce the transcriptional levels of acidic and basic fibroblast growth factor (bFGF) in endothelial cells and breast cancer cells, but also decrease the bFGF protein levels in cells in a dose-dependent manner [76].

4.3. Suppression of cancer cell invasion and metastasis

Epithelial-mesenchymal transition (EMT) is a key process that promotes cancer cell invasion and metastasis. Studies have shown that EGCG can inhibit EMT in breast cancer cells by activating FOXO3a, which induces an increase in the expression of ERα, and then up-regulates epithelial marker genes (such as E-cadherin and MTA3) and down-regulates mesenchymal marker genes (such as Snail) [77]. Matrix metalloproteinases (MMPs), primarily responsible for breaking down the extracellular matrix, are crucial in tumor progression and metastasis. Both TP and EGCG significantly downregulate *MMP-9* gene expression and enzyme activity to inhibit cellular matrix degradation. They can also diminish cytoplasmic and nuclear β-catenin buildup by decreasing AKT phosphorylation levels, thereby down-regulating genes regulated by β-catenin/Tcf (e.g., c-myc and AKT1) and further inhibiting the proliferation and invasion of tumor cells [78]. For the enhanced MMP-9 expression and activity induced by epidermal growth factor (EGF), EGCG could significantly reduce the expression and activity of MMP-9 by blocking the phosphorylation of FAK, PI3K, and ERK, which in turn inhibited the binding of NF-κB and AP-1 transcription factors to the MMP-9 promoter. Not only that, EGCG also inhibited the interaction of integrin α5β1 with extracellular matrix fibronectin, further weakening the synergistic induction of MMP-

9 overexpression by EGF and fibronectin [79]. In addition, EGCG has an inhibitory effect on the Rac1 pathway, which decreases VASP expression and thus suppresses the migration and invasion capabilities of MCF-7 cells [80].

4.4. Inhibition of cellular metabolic mechanisms

The expression of fatty acid synthase (FAS) is significantly upregulated in cancer cells compared to normal cells, and inhibition of FAS expression has been shown to selectively inhibit cancer cell growth [81]. Studies have shown that extracts from both green and black tea, especially EGCG and TF-3 therein, significantly inhibit the protein and mRNA expression of FAS. Both can block PI3K/Akt signaling pathway activation by inhibiting EGF binding to EGFR, thereby impairing the binding capacity of nuclear transcription factor Sp-1 to DNA. Since Sp-1 cannot effectively bind to the promoter region of the *FAS* gene, this process inhibits the abnormally high expression of FAS in the MCF-7 breast cancer cell line, exerting its potential anticancer and lipid-lowering effects [82]. In addition, the glycolytic pathway occupies an important position in the metabolism of cancer cells. EGCG can significantly inhibit the glycolytic process by decreasing the activity and mRNA expression of key enzymes of glycolysis (such as hexokinase), as well as by decreasing the expression of HIF1α and GLUT1, thereby decreasing the uptake of glucose and the synthesis of ATP [83].

4.5. Enhancement of anti-tumor immunomodulation

Myeloid-derived suppressor cells (MDSCs) are a heterogeneous class of myeloid cells that can inhibit the function of T cells through a variety of mechanisms, thereby promoting tumor growth and metastasis. EGCG was found to significantly inhibit the proliferation of 4T1 breast cancer cells. In *in vivo* experiments, EGCG notably diminished the buildup of MDSCs in the peripheral blood, spleen, and tumor tissues of 4T1 tumor-bearing mice and increased the proportion of $CD4^+$ and $CD8^+$ T cells, thus enhancing anti-tumor immune responses. In an *in vitro* assay, EGCG effectively inhibited the survival and proliferation of MDSCs by down-regulating classical signaling pathways (such as Arg-1/iNOS/Nox2/NF-κB/STAT3) as well as regulating non-classical pathways (such as ECM-receptor interactions and adhesion patch formation) in MDSCs. Meanwhile, the expression of nine key genes in MDSCs was restored. This provides new insights into the role of EGCG in anti-tumor immunity [84].

4.6. Impact on epigenetic regulation

Tissue inhibitors of matrix metalloproteinases (TIMPs) are a group of naturally occurring proteins whose main function is to inhibit the activity of MMPs. GTP and EGCG can significantly induce TIMP-3 expression in breast cancer cells through epigenetic pathways, thereby inhibiting the activity of MMP-2 and MMP-9 and decreasing the ability of cell invasion. Specifically, GTP and EGCG reduce the modification of H3K27 trimethylation in the TIMP-3 promoter region and increase the level of H3K9/18 acetylation by decreasing the protein expression of EZH2 and class I HDACs, which in turn induces the expression of TIMP-3 and restores the balance between MMP and TIMP [85]. Signal peptide-CUB-EGF domain-containing protein 2 (SCUBE2) is an oncogene whose expression is usually down-regulated in tumor tissues, and one of the main reasons for the down-regulation is the hypermethylation of its promoter region. It was found that EGCG could significantly upregulate SCUBE2 by decreasing the methylation of the SCUBE2 promoter through decreasing the activity of DNA methyltransferase (DNMT), while enhancing E-cadherin levels and reducing vimentin levels, thereby suppressing the migration and invasion of breast cancer cells [86].

4.7. Cell cycle arrest and pro-apoptotic regulation

Growth factors regulate normal cell cycle protein homeostasis and promote cell progression from G1 to S phase, a process that involves accumulation of cell cycle proteins, reduction of CDK inhibitors, activation of CDK, and phosphorylation of pRB [87]. EGCG can inhibit cyclin D1-associated pRB kinase activity and its phosphorylation by inducing the expression of p21(CIP1/WAF1/SDI1), thereby inhibiting the entry of MCF10A mammary epithelial cells into the S-phase under the stimulation of EGF, which in turn affects the progression of the cell cycle. Notably, the inducing effect of EGCG on p21 was dependent on EGF signaling, which increased p21 expression approximately three-fold in the presence of EGF, but no notable effect was observed in the absence of EGF [88].

EGC, which is structurally similar to ECGC, inhibits breast cancer cell growth by inducing apoptosis, has no effect on cell cycle progression, and has no impact on the proliferation of healthy mammary epithelial cells. EGC-induced apoptosis involves the Fas signaling pathway and correlates with a decrease in the levels of the Bcl-2 protein and an increase in the levels of the Bax protein [89]. Telomerase, a reverse transcriptase that maintains the integrity of chromosome ends (telomeres), is activated in more than 90% of breast cancers, and its increased activity correlates with a poor prognosis [90]. EGCG can inhibit cell proliferation and induce apoptosis by inhibiting mRNA and protein expression of telomerase reverse transcriptase and down-regulating telomerase activity in MCF-7 breast cancer cell lines [91]. Survivin belongs to the family of apoptosis-inhibiting proteins, which have the function of inhibiting apoptosis as well as regulating cell division. TP can induce apoptosis in breast cancer cells by down-regulating survivin expression. In a nude mouse transplantation tumor model, TP significantly reduced the volume of the tumor and the expression level of survivin protein in tumor tissues [92]. As the main active component of TP, EGCG can inhibit survivin promoter activity by suppressing the AKT signaling pathway, leading to significant down-regulation of survivin mRNA and protein levels. This process further activates caspase-9, which ultimately induces apoptosis in breast cancer cells [93]. The pro-apoptotic effects of theaflavins were more pronounced in breast cancer cells expressing functional p53. Specifically, theaflavins promote the translocation of Bax to mitochondria by up-regulating the expression of p53 and the pro-apoptotic protein Bax, resulting in the disruption of mitochondrial membrane potential, cytochrome c release, caspase cascade activation, and subsequent apoptosis induction [94]. This mechanism is similar to the anti-tumor mechanism of Ziyang tea polyphenol extract (ZTP). In addition to this, ZTP-treated MCF-7 cells produce excessive ROS, which play a key role in ZTP-induced apoptosis [95]. ZIP9 (SLC39A9) is a membrane androgen receptor that induces apoptosis upon binding to androgen. Studies have shown that both (-)-epicatechin and (+)-catechin have a high affinity for ZIP9, but their mechanisms of action are different: (-)-epicatechin exhibits significant agonist activity at low concentrations, whereas (+)-catechin exhibits antagonistic effects. In MDA-MB-468 breast cancer cells, (-)-epicatechin induces apoptosis by activating the ZIP9 signaling pathway, decreasing intracellular cAMP production, and increasing free zinc levels [96]. Deoxycytidine triphosphate deaminase (DCTD) is an enzyme involved in DNA metabolism that indirectly affects DNA synthesis and repair, mainly by regulating the balance of the nucleotide pool. Teadenol B, a chemical derived from microbial fermented tea, is able to inhibit the growth of cancer cells by inducing early and late apoptosis of MDA-MB-231 cells. In MDA-MB-231 cells, the transformation of autophagy marker LC3-I to LC3-II was significantly increased after teadenol B treatment, while the level of SQSTM protein was decreased, suggesting that teadenol B has a significant autophagy induction effect [97].

Besides, the dose of EGCG determined the pattern of MCF-7 cell death: low-dose (10–50 μM) EGCG induced apoptosis by increasing ROS generation, activating c-Jun N-terminal kinase and caspase-9/3, decreasing

mitochondrial membrane potential, and increasing the Bax/Bcl-2 ratio; whereas, high-dose (100–400 μM) EGCG mainly induced cell necrosis by decreasing intracellular ATP levels [98].

4.8. Improving drug resistance

Multidrug resistance (MDR) is one of the common and unresolved challenges in the treatment of malignant tumors and has several manifestations. One of these manifestations is the overexpression of p-glycoprotein (Pgp), which decreases the intracellular concentration of a drug by mediating the transport of the drug to the extracellular compartment and expelling the chemotherapeutic agent out of the cell [99]. TP was able to reverse MDR by inhibiting the activity of Pgp. Assessment of Pgp activity can be accomplished by assaying cellular uptake of the Pgp substrate ^{99m}Tc-tetrofosmin. At a concentration of 500 μg/mL, TP increased the uptake of ^{99m}Tc-tetrofosmin by adriamycin-resistant cell line MCF-7/Adr cells by 16-fold, whereas the conventional MDR modulator, quinidine, increased by only 4-fold at a concentration of 200 μM, suggesting that TP has a significant potential for the reversal of Pgp-mediated resistance [100]. In terms of tamoxifen resistance, EGCG inhibits ERK signaling pathway activity by reducing EGFR expression and phosphorylation levels, leading to reduced cell proliferation and invasion. In addition, EGCG can significantly reduce the expression of matrix metalloproteinases (MMP-2 and MMP-9) and its inducer EMMPRIN, increase the level of tissue inhibitors of metalloproteinases (TIMP-1 and TIMP-2), inhibit the activity of MMP, and multi-target the invasion and metastasis ability of tamoxifen-resistant breast cancer cells [101].

4.9. Synergistic mechanism

Through *in vivo* and *in vitro* experimental studies, the combined use of GTE and tamoxifen has a synergistic anticancer effect on breast cancer. GTE can enhance the antitumor activity of tamoxifen by down-regulating ER-α expression, blocking ER-dependent transcription, and inhibiting estrogen-induced MAPK signaling pathways. This combined therapy more effectively suppresses breast cancer cell growth and enhances apoptosis compared to either drug individually [102]. The combination of EGCG and HDAC inhibitors significantly enhanced ERα reactivation, making ERα-breast cancer cells sensitive to estradiol and tamoxifen. This effect activates ERα transcription primarily by modulating the histone acetylation and methylation status of the ERα promoter and decreasing the binding of the transcriptional repressor complex in this region, thus providing a potential therapeutic strategy for hormone-resistant breast cancer [103]. 5-aza-20-deoxycytidine (5-aza 20 dC) is a DNA methyltransferase inhibitor with the ability to induce DNA demethylation, but it can trigger cytotoxicity at higher doses. Combination therapy with low concentrations of EGCG and 5-aza 20 dC significantly inhibited breast cancer cell growth, with better results than monotherapy and no significant toxicity to normal breast epithelial cells. The combination therapy enhanced cell cycle arrest and apoptosis by down-regulating cycle-related genes and anti-apoptotic genes and up-regulating pro-apoptotic genes. In addition, this combination treatment reduced the expression of DNMT1, DNMT3b, and HDAC1, inducing DNA hypomethylation and histone modification changes [104]. A similar epigenetic regulatory mechanism was observed when GTP was combined with thiosulfonamide in broccoli buds [105]. Although the anti-angiogenic drug sunitinib has shown significant efficacy in the treatment of many cancers, it suffers from drug resistance and a narrow therapeutic window. It was found that the combination of EGCG and sunitinib could reduce VEGF secretion while down-regulating IRS-1 levels and inhibiting the MAPK signaling pathway. This combination can effectively reduce tumor size and inhibit tumor angiogenesis, thus enhancing the anti-tumor effect of sunitinib [106].

5. Conclusion

Although preclinical studies provide some theoretical support for the potential of tea consumption in breast cancer prevention and treatment, the results of epidemiologic studies still fail to draw consistent conclusions. This discrepancy may be closely related to the complex interplay of tea-drinking habits, tea types, genetic diversity, and multiple confounding factors. Future studies should pay more attention to the heterogeneity of different populations and explore the biological mechanisms of various components of tea. Through a comprehensive analysis of molecular biology, genetics, and epigenetics, the exact function and potential mechanisms of tea intake in preventing and treating breast cancer were additionally explored to provide a more accurate scientific basis for the personalized prevention and treatment of breast cancer.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Bray F, Laversanne M, Sung H, et al., 2024, Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin, 74(3): 229–263.

[2] Lundqvist A, Andersson E, Ahlberg I, et al., 2016, Socioeconomic Inequalities in Breast Cancer Incidence and Mortality in Europe: A Systematic Review and Meta-Analysis. Eur J Public Health, 26(5): 804–813.

[3] Lukasiewicz S, Czeczelewski M, Forma A, et al., 2021. Breast Cancer Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies: An Updated Review. Cancers (Basel), 13(17): 4287.

[4] Luo Q, Luo L, Zhao J, et al., 2024, Biological Potential and Mechanisms of Tea's Bioactive Compounds: An Updated Review. J Adv Res, 65: 345–363.

[5] Yuan JM, Sun C, Butler LM, 2011, Tea and Cancer Prevention: Epidemiological Studies. Pharmacol Res, 64(2): 123–135.

[6] Yue Y, Chu GX, Liu XS, et al., 2014, TMDB: A Literature-Curated Database for Small Molecular Compounds Found from Tea. BMC Plant Biol, 14: 243.

[7] Tang GY, Meng X, Gan RY, et al., 2019, Health Functions and Related Molecular Mechanisms of Tea Components: An Update Review. Int J Mol Sci, 20(24): 6196.

[8] Liu Y, Zhao G, Li X, et al., 2020, Comparative Analysis of Phenolic Compound Metabolism among Tea Plants in the Section Thea of the Genus Camellia. Food Res Int, 135: 109276.

[9] Ramadan G, El-Beih NM, Talaat RM, et al., 2017, Anti-Inflammatory Activity of Green Versus Black Tea Aqueous Extract in a Rat Model of Human Rheumatoid Arthritis. Int J Rheum Dis, 20(2): 203–213.

[10] Brimson JM, Prasanth MI, Kumaree KK, et al., 2022, Tea Plant (Camellia sinensis): A Current Update on Use in Diabetes, Obesity, and Cardiovascular Disease. Nutrients, 15(1): 37.

[11] Liu S, Zhang Q, Li H, et al., 2022, Comparative Assessment of the Antibacterial Efficacies and Mechanisms of Different Tea Extracts. Foods, 11(4): 620.

[12] Farhan M, 2022, Green Tea Catechins: Nature's Way of Preventing and Treating Cancer. Int J Mol Sci, 23(18): 10713.

[13] Mao X, Xiao X, Chen D, et al., 2019, Tea and Its Components Prevent Cancer: A Review of the Redox-Related Mechanism. Int J Mol Sci, 20(21): 5249.

[14] Khan N, Mukhtar H, 2018, Tea Polyphenols in Promotion of Human Health. Nutrients, 11(1): 39.

[15] Boehm K, Borrelli F, Ernst E, et al., 2009, Green Tea (Camellia sinensis) for the Prevention of Cancer. Cochrane Database Syst Rev, 2009(3): CD005004.

[16] Najaf Najafi M, Salehi M, Ghazanfarpour M, et al., 2018, The Association Between Green Tea Consumption and Breast Cancer Risk: A Systematic Review and Meta-Analysis. Phytother Res, 32(10): 1855–1864.

[17] Ogunleye AA, Xue F, Michels KB, 2010, Green Tea Consumption and Breast Cancer Risk or Recurrence: A Meta-Analysis. Breast Cancer Res Treat, 119(2): 477–484.

[18] Ewertz M, Gill C, 1990, Dietary Factors and Breast-Cancer Risk in Denmark. Int J Cancer, 46(5): 779–784.

[19] Goldbohm RA, Hertog MG, Brants HA, et al., 1996, Consumption of Black Tea and Cancer Risk: A Prospective Cohort Study. J Natl Cancer Inst, 88(2): 93–100.

[20] Michels KB, Holmberg L, Bergkvist L, et al., 2002, Coffee, Tea, and Caffeine Consumption and Breast Cancer Incidence in a Cohort of Swedish Women. Ann Epidemiol, 12(1): 21–26.

[21] Oh JK, Sandin S, Strom P, et al., 2015, Prospective Study of Breast Cancer in Relation to Coffee, Tea and Caffeine in Sweden. Int J Cancer, 137(8): 1979–1989.

[22] Hirvonen T, Mennen LI, de Bree A, et al., 2006, Consumption of Antioxidant-Rich Beverages and Risk for Breast Cancer in French Women. Ann Epidemiol, 16(7): 503–508.

[23] Fagherazzi G, Touillaud MS, Boutron-Ruault MC, et al., 2011, No Association between Coffee, Tea or Caffeine Consumption and Breast Cancer Risk in a Prospective Cohort Study. Public Health Nutr, 14(7): 1315–1320.

[24] Zheng W, Doyle TJ, Kushi LH, et al., 1996, Tea Consumption and Cancer Incidence in a Prospective Cohort Study of Postmenopausal Women. Am J Epidemiol, 144(2): 175–182.

[25] Adebamowo CA, Cho E, Sampson L, et al., 2005, Dietary Flavonols and Flavonol-Rich Foods Intake and the Risk of Breast Cancer. Int J Cancer, 114(4): 628–633.

[26] Ganmaa D, Willett WC, Li TY, et al., 2008, Coffee, Tea, Caffeine and Risk of Breast Cancer: A 22-Year Follow-Up. Int J Cancer, 122(9): 2071–2076.

[27] Boggs DA, Palmer JR, Stampfer MJ, et al., 2010, Tea and Coffee Intake in Relation to Risk of Breast Cancer in the Black Women's Health Study. Cancer Causes Control, 21(11): 1941–1948.

[28] Zhang D, Nichols HB, Troester M, et al., 2020, Tea Consumption and Breast Cancer Risk in a Cohort of Women with Family History of Breast Cancer. Int J Cancer, 147(3): 876–886.

[29] Arthur R, Kirsh VA, Rohan TE, 2018, Associations of Coffee, Tea and Caffeine Intake with Risk of Breast, Endometrial and Ovarian Cancer among Canadian Women. Cancer Epidemiol, 56: 75–82.

[30] Ronco AL, Stefani ED, Mendoza B, et al., 2016, Mate and Tea Intake, Dietary Antioxidants and Risk of Breast Cancer: A Case-Control Study. Asian Pac J Cancer Prev, 17(6): 2923–2933.

[31] Wu AH, Yu MC, Tseng CC, et al., 2003, Green Tea and Risk of Breast Cancer in Asian Americans. Int J Cancer, 106(4): 574–579.

[32] Suzuki Y, Tsubono Y, Nakaya N, et al., 2004, Green Tea and the Risk of Breast Cancer: Pooled Analysis of Two Prospective Studies in Japan. Br J Cancer, 90(7): 1361–1363.

[33] Iwasaki M, Inoue M, Sasazuki S, et al., 2010, Green Tea Drinking and Subsequent Risk of Breast Cancer in a Population-Based Cohort of Japanese Women. Breast Cancer Res, 12(5): R88.

[34] Mizoo T, Taira N, Nishiyama K, et al., 2013, Effects of Lifestyle and Single Nucleotide Polymorphisms on Breast Cancer Risk: A Case-Control Study in Japanese Women. BMC Cancer, 13: 565.

[35] Yuan JM, Koh WP, Sun CL, et al., 2005, Green Tea Intake, ACE Gene Polymorphism and Breast Cancer Risk among Chinese Women in Singapore. Carcinogenesis, 26(8): 1389–1394.

[36] Inoue M, Robien K, Wang R, et al., 2008, Green Tea Intake, MTHFR/TYMS Genotype and Breast Cancer Risk: The Singapore Chinese Health Study. Carcinogenesis, 29(10): 1967–1972.

[37] Zhang M, Holman CD, Huang JP, et al., 2007, Green Tea and the Prevention of Breast Cancer: A Case-Control Study in Southeast China. Carcinogenesis, 28(5): 1074–1078.

[38] Li X, Yu C, Guo Y, et al., 2019, Association between Tea Consumption and Risk of Cancer: A Prospective Cohort Study of 0.5 Million Chinese Adults. Eur J Epidemiol, 34(8): 753–763.

[39] Fuhrman BJ, Pfeiffer RM, Wu AH, et al., 2013, Green Tea Intake is Associated with Urinary Estrogen Profiles in Japanese-American Women. Nutr J, 12: 25.

[40] Larsson SC, Bergkvist L, Wolk A, 2009, Coffee and Black Tea Consumption and Risk of Breast Cancer by Estrogen and Progesterone Receptor Status in a Swedish Cohort. Cancer Causes Control, 20(10): 2039–2044.

[41] Bhoo-Pathy N, Peeters PH, Uiterwaal CS, et al., 2015, Coffee and Tea Consumption and Risk of Pre- and Postmenopausal Breast Cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) Cohort Study. Breast Cancer Res, 17(1): 15.

[42] Shrubsole MJ, Lu W, Chen Z, et al., 2009, Drinking Green Tea Modestly Reduces Breast Cancer Risk. J Nutr, 139(2): 310–316.

[43] Li M, Tse LA, Chan WC, et al., 2016, Evaluation of Breast Cancer Risk Associated with Tea Consumption by Menopausal and Estrogen Receptor Status among Chinese Women in Hong Kong. Cancer Epidemiol, 40: 73–78.

[44] Iwasaki M, Mizusawa J, Kasuga Y, et al., 2014, Green Tea Consumption and Breast Cancer Risk in Japanese Women: A Case-Control Study. Nutr Cancer, 66(1): 57–67.

[45] Torres-Sanchez L, Lopez-Carrillo L, Lopez-Cervantes M, et al., 2000, Food Sources of Phytoestrogens and Breast Cancer Risk in Mexican Women. Nutr Cancer, 37(2): 134–139.

[46] Kumar N, Titus-Ernstoff L, Newcomb PA, et al., 2009, Tea Consumption and Risk of Breast Cancer. Cancer Epidemiol Biomarkers Prev, 18(1): 341–345.

[47] Wu AH, Yu MC, 2006, Tea, Hormone-Related Cancers and Endogenous Hormone Levels. Mol Nutr Food Res, 50(2): 160–169.

[48] Nakachi K, Suemasu K, Suga K, et al., 1998, Influence of Drinking Green Tea on Breast Cancer Malignancy among Japanese Patients. Jpn J Cancer Res, 89(3): 254–261.

[49] Inoue M, Tajima K, Mizutani M, et al., 2001, Regular Consumption of Green Tea and the Risk of Breast Cancer Recurrence: Follow-Up Study from the Hospital-Based Epidemiologic Research Program at Aichi Cancer Center (HERPACC), Japan. Cancer Lett, 167(2): 175–182.

[50] Seely D, Mills EJ, Wu P, et al., 2005, The Effects of Green Tea Consumption on Incidence of Breast Cancer and Recurrence of Breast Cancer: A Systematic Review and Meta-Analysis. Integr Cancer Ther, 4(2): 144–155.

[51] Harris HR, Bergkvist L, Wolk A, 2012, Coffee and Black Tea Consumption and Breast Cancer Mortality in a Cohort of Swedish Women. Br J Cancer, 107(5): 874–878.

[52] Farvid MS, Spence ND, Rosner BA, et al., 2021, Post-Diagnostic Coffee and Tea Consumption and Breast Cancer Survival. Br J Cancer, 124(11): 1873–1881.

[53] Bao PP, Zhao GM, Shu XO, et al., 2015, Modifiable Lifestyle Factors and Triple-Negative Breast Cancer Survival: A Population-Based Prospective Study. Epidemiology, 26(6): 909–916.

[54] Zhang JY, Liao YH, Lin Y, et al., 2019, Effects of Tea Consumption and the Interactions with Lipids on Breast Cancer Survival. Breast Cancer Res Treat, 176(3): 679–686.

[55] Suzuki K, Morishita S, Nakano J, et al., 2024, Association between Quality of Life and Mortality Risk in Patients with

Breast Cancer: A Systematic Review and Meta-Analysis. Breast Cancer, 31(4): 552–561.

[56] Soldato D, Havas J, Crane TE, et al., 2022, Coffee and Tea Consumption, Patient-Reported, and Clinical Outcomes in a Longitudinal Study of Patients with Breast Cancer. Cancer, 128(19): 3552–3563.

[57] Ahles TA, Root JC, Ryan EL, 2012, Cancer- and Cancer Treatment-Associated Cognitive Change: An Update on the State of the Science. J Clin Oncol, 30(30): 3675–3686.

[58] Dietrich J, Monje M, Wefel J, et al., 2008, Clinical Patterns and Biological Correlates of Cognitive Dysfunction Associated with Cancer Therapy. Oncologist, 13(12): 1285–1295.

[59] Koppelmans V, Breteler MM, Boogerd W, et al., 2013, Late Effects of Adjuvant Chemotherapy for Adult Onset Non-CNS Cancer; Cognitive Impairment, Brain Structure and Risk of Dementia. Crit Rev Oncol Hematol, 88(1): 87–101.

[60] Huang Z, Shi Y, Bao P, et al., 2018, Associations of Dietary Intake and Supplement Use with Post-Therapy Cognitive Recovery in Breast Cancer Survivors. Breast Cancer Res Treat, 171(1): 189–198.

[61] Yan Z, Zhong Y, Duan Y, et al., 2020, Antioxidant Mechanism of Tea Polyphenols and its Impact on Health Benefits. Anim Nutr, 6(2): 115–123.

[62] Yang CS, Kim S, Yang GY, et al., 1999, Inhibition of Carcinogenesis by Tea: Bioavailability of Tea Polyphenols and Mechanisms of Actions. Proc Soc Exp Biol Med, 220(4): 213–217.

[63] Krishnamurti U, Silverman JF, 2014, HER2 in Breast Cancer: A Review and Update. Adv Anat Pathol, 21(2): 100–107.

[64] Masuda M, Suzui M, Lim JT, 2003, Epigallocatechin-3-Gallate Inhibits Activation of HER-2/neu and Downstream Signaling Pathways in Human Head and Neck and Breast Carcinoma Cells. Clin Cancer Res, 9(9): 3486–3491.

[65] De Amicis F, Russo A, Avena P, et al., 2013, In Vitro Mechanism for Downregulation of ER-α Expression by Epigallocatechin Gallate in ER+/PR+ Human Breast Cancer Cells. Mol Nutr Food Res, 57(5): 840–853.

[66] Kim J, Zhang X, Rieger-Christ KM, et al., 2006, Suppression of Wnt Signaling by the Green Tea Compound (-)-Epigallocatechin 3-Gallate (EGCG) in Invasive Breast Cancer Cells. Requirement of the Transcriptional Repressor HBP1. J Biol Chem, 281(16): 10865–10875.

[67] Lee WJ, Cheng TC, Yen Y, et al., 2021, Tea Polyphenol Epigallocatechin-3-Gallate Inhibits Cell Proliferation in a Patient-Derived Triple-Negative Breast Cancer Xenograft Mouse Model Via Inhibition of Proline-Dehydrogenase-Induced Effects. J Food Drug Anal, 29(1): 113–127.

[68] Kim SH, Hwang KA, Choi KC, 2016, Treatment with Kaempferol Suppresses Breast Cancer Cell Growth Caused by Estrogen and Triclosan in Cellular and Xenograft Breast Cancer Models. J Nutr Biochem, 28: 70–82.

[69] Rathore K, Choudhary S, Odoi A, et al., 2012, Green Tea Catechin Intervention of Reactive Oxygen Species-Mediated ERK Pathway Activation and Chronically Induced Breast Cell Carcinogenesis. Carcinogenesis, 33(1): 174–183.

[70] Latronico T, Petraglia T, Sileo C, et al., 2024, Inhibition of MMP-2 and MMP-9 by Dietary Antioxidants in THP-1 Macrophages and Sera from Patients with Breast Cancer. Molecules, 29(8): 1718.

[71] Gonzalez Suarez N, Fernandez-Marrero Y, Torabidastgerdooei S, et al., 2022, EGCG Prevents the Onset of an Inflammatory and Cancer-Associated Adipocyte-Like Phenotype in Adipose-Derived Mesenchymal Stem/Stromal Cells in Response to the Triple-Negative Breast Cancer Secretome. Nutrients, 14(5): 1099.

[72] Le Querrec A, Duval D, Tobelem G, 1993, Tumour Angiogenesis. Baillieres Clin Haematol, 6(3): 711–730.

[73] Sartippour MR, Heber D, Ma J, et al., 2001, Green Tea and its Catechins Inhibit Breast Cancer Xenografts. Nutr Cancer, 40(2): 149–156.

[74] Sartippour MR, Shao ZM, Heber D, et al., 2002, Green Tea Inhibits Vascular Endothelial Growth Factor (VEGF) Induction in Human Breast Cancer Cells. J Nutr, 132(8): 2307–2311.

[75] Leong H, Mathur PS, Greene GL, 2009, Green Tea Catechins Inhibit Angiogenesis Through Suppression of STAT3

Activation. Breast Cancer Res Treat, 117(3): 505–515.

[76] Sartippour MR, Heber D, Zhang L, et al., 2002, Inhibition of Fibroblast Growth Factors by Green Tea. Int J Oncol, 21(3): 487–491.

[77] Belguise K, Guo S, Sonenshein GE, 2007, Activation of FOXO3a by the Green Tea Polyphenol Epigallocatechin-3-Gallate Induces Estrogen Receptor Alpha Expression Reversing Invasive Phenotype of Breast Cancer Cells. Cancer Res, 67(12): 5763–5770.

[78] Thangapazham RL, Passi N, Maheshwari RK, 2007, Green Tea Polyphenol and Epigallocatechin Gallate Induce Apoptosis and Inhibit Invasion in Human Breast Cancer Cells. Cancer Biol Ther, 6(12): 1938–1943.

[79] Sen T, Chatterjee A, 2011, Epigallocatechin-3-Gallate (EGCG) Downregulates EGF-Induced MMP-9 in Breast Cancer Cells: Involvement of Integrin Receptor α5β1 in the Process. Eur J Nutr, 50(6): 465–478.

[80] Zhang Y, Han G, Fan B, et al., 2009, Green Tea (-)-Epigallocatechin-3-Gallate Down-Regulates VASP Expression and Inhibits Breast Cancer Cell Migration and Invasion by Attenuating Rac1 Activity. Eur J Pharmacol, 606(1–3): 172–179.

[81] Kuhajda FP, 2000, Fatty-Acid Synthase and Human Cancer: New Perspectives on its Role in Tumor Biology. Nutrition, 16(3): 202–208.

[82] Yeh CW, Chen WJ, Chiang CT, et al., 2003, Suppression of Fatty Acid Synthase in MCF-7 Breast Cancer Cells by Tea and Tea Polyphenols: A Possible Mechanism for their Hypolipidemic Effects. Pharmacogenomics J, 3(5): 267–276.

[83] Wei R, Mao L, Xu P, et al., 2018, Suppressing Glucose Metabolism with Epigallocatechin-3-Gallate (EGCG) Reduces Breast Cancer Cell Growth in Preclinical Models. Food Funct, 9(11): 5682–5696.

[84] Xu P, Yan F, Zhao Y, et al., 2020, Green Tea Polyphenol EGCG Attenuates MDSCs-Mediated Immunosuppression through Canonical and Non-Canonical Pathways in a 4T1 Murine Breast Cancer Model. Nutrients, 12(4): 1042.

[85] Deb G, Thakur VS, Limaye AM, et al., 2015, Epigenetic Induction of Tissue Inhibitor of Matrix Metalloproteinase-3 by Green Tea Polyphenols in Breast Cancer Cells. Mol Carcinog, 54(6): 485–499.

[86] Sheng J, Shi W, Guo H, et al., 2019, The Inhibitory Effect of (-)-Epigallocatechin-3-Gallate on Breast Cancer Progression via Reducing SCUBE2 Methylation and DNMT Activity. Molecules, 24(16): 2899.

[87] Planas-Silva MD, Weinberg RA, 1997, The Restriction Point and Control of Cell Proliferation. Curr Opin Cell Biol, 9(6): 768–772.

[88] Liberto M, Cobrinik D, 2000, Growth Factor-Dependent Induction of p21(CIP1) by the Green Tea Polyphenol, Epigallocatechin Gallate. Cancer Lett, 154(2): 151–161.

[89] Vergote D, Cren-Olive C, Chopin V, et al., 2002, (-)-Epigallocatechin (EGC) of Green Tea Induces Apoptosis of Human Breast Cancer Cells but Not of Their Normal Counterparts. Breast Cancer Res Treat, 76(3): 195–201.

[90] Herbert BS, Wright WE, Shay JW, 2001, Telomerase and Breast Cancer. Breast Cancer Res, 3(3): 146–149.

[91] Mittal A, Pate MS, Wylie RC, et al., 2004, EGCG Down-Regulates Telomerase in Human Breast Carcinoma MCF-7 Cells, Leading to Suppression of Cell Viability and Induction of Apoptosis. Int J Oncol, 24(3): 703–710.

[92] Chen X, Li Y, Lin Q, et al., 2014, Tea Polyphenols Induced Apoptosis of Breast Cancer Cells by Suppressing the Expression of Survivin. Sci Rep, 4: 4416.

[93] Tang Y, Zhao DY, Elliott S, et al., 2007, Epigallocatechin-3 Gallate Induces Growth Inhibition and Apoptosis in Human Breast Cancer Cells Through Survivin Suppression. Int J Oncol, 31(4): 705–711.

[94] Lahiry L, Saha B, Chakraborty J, et al., 2008, Contribution of p53-Mediated Bax Transactivation in Theaflavin-Induced Mammary Epithelial Carcinoma Cell Apoptosis. Apoptosis, 13(6): 771–781.

[95] Li W, He N, Tian L, et al., 2016, Inhibitory Effects of Polyphenol-Enriched Extract from Ziyang Tea against Human Breast Cancer MCF-7 Cells through Reactive Oxygen Species-Dependent Mitochondria Molecular Mechanism. J Food

Drug Anal, 24(3): 527–538.

[96] Thomas P, Dong J, 2021, (-)-Epicatechin Acts as a Potent Agonist of the Membrane Androgen Receptor, ZIP9 (SLC39A9), to Promote Apoptosis of Breast and Prostate Cancer Cells. J Steroid Biochem Mol Biol, 211: 105906.

[97] Zhao Y, Ding ZG, Yan YJ, et al., 2024, Teadenol B as a Component of Microorganism-Fermented Tea Extract Inhibited Breast Cancers by Promoting Autophagy. Molecules, 29(4): 872.

[98] Hsuuw YD, Chan WH, 2007, Epigallocatechin Gallate Dose-Dependently Induces Apoptosis or Necrosis in Human MCF-7 Cells. Ann N Y Acad Sci, 1095: 428–440.

[99] Tian Y, Lei Y, Wang Y, et al., 2023, Mechanism of Multidrug Resistance to Chemotherapy Mediated by P-Glycoprotein (Review). Int J Oncol, 63(5): 119.

[100] Zhu A, Wang X, Guo Z, 2001, Study of Tea Polyphenol as a Reversal Agent for Carcinoma Cell Lines' Multidrug Resistance (Study of TP as a MDR Reversal Agent). Nucl Med Biol, 28(6): 735–740.

[101] Farabegoli F, Papi A, Orlandi M, 2011, (-)-Epigallocatechin-3-Gallate Down-Regulates EGFR, MMP-2, MMP-9 and EMMPRIN and Inhibits the Invasion of MCF-7 Tamoxifen-Resistant Cells. Biosci Rep, 31(2): 99–108.

[102] Sartippour MR, Pietras R, Marquez-Garban DC, et al., 2006, The Combination of Green Tea and Tamoxifen is Effective Against Breast Cancer. Carcinogenesis, 27(12): 2424–2433.

[103] Li Y, Yuan YY, Meeran SM, et al., 2010, Synergistic Epigenetic Reactivation of Estrogen Receptor-α (ERα) by Combined Green Tea Polyphenol and Histone Deacetylase Inhibitor in ERα-Negative Breast Cancer Cells. Mol Cancer, 9: 274.

[104] Tyagi T, Treas JN, Mahalingaiah PK, et al., 2015, Potentiation of Growth Inhibition and Epigenetic Modulation by Combination of Green Tea Polyphenol and 5-Aza-2'-Deoxycytidine in Human Breast Cancer Cells. Breast Cancer Res Treat, 149(3): 655–668.

[105] Li Y, Buckhaults P, Cui X, et al., 2016, Combinatorial Epigenetic Mechanisms and Efficacy of Early Breast Cancer Inhibition by Nutritive Botanicals. Epigenomics, 8(8): 1019–1037.

[106] Zhou Y, Tang J, Du Y, et al., 2016, The Green Tea Polyphenol EGCG Potentiates the Antiproliferative Activity of Sunitinib in Human Cancer Cells. Tumour Biol, 37(7): 8555–8566.