Green tea, black tea and breast cancer risk: a meta-analysis of epidemiological studies

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Experimental studies have shown that tea and tea polyphenols have anti-carcinogenic properties against breast cancer. A number of epidemiologic studies, both case-control and cohort in design, have examined the possible association between tea intake and breast cancer development in humans. This meta-analysis included 13 papers which examined populations in eight countries and provided data on consumption of either green tea or black tea, or both in relation to breast cancer risk. Summary odds ratios (ORs) for highest versus non/lowest tea consumption level were calculated based on fixed and random effects models. Heterogeneity between studies was examined via the Q statistics. For green tea, the combined results from four studies indicated a reduced risk of breast cancer for highest versus non/lowest intake (OR = 0.78, 95% CI = 0.61–0.98). For black tea, conflicting results were observed in case-control versus cohort studies. The combined results from eight case-control studies showed a minor inverse association between black tea consumption and risk of breast cancer (OR = 0.91, 95% CI = 0.84–0.98). This inverse association was stronger in hospital-based (OR = 0.77, 95% CI = 0.50–1.19) than population-based case-control studies (OR = 0.94, 95% CI = 0.81–1.09). Five cohort studies demonstrated a modest increase in risk associated with black tea intake (OR = 1.15, 95% CI = 1.02–1.31). The results of this meta-analysis indicate a lower risk for breast cancer with green tea consumption. Available data suggest a possible late-stage, promotional effect of black tea on breast carcinogenesis.

Introduction

Tea is one of the most popular beverages consumed around the world, second only to water. Polyphenols are the naturally occurring compounds in fresh tea leaves and account for its pungency and unique flavor. The four primary polyphenols in fresh tea leaves are epigallocatechin gallate (EGCG), epigallocatechin, epicatechin gallate and epicatechin, with the most abundant being EGCG. These four catechins account for up to 30% of dry weight of the fresh tea leaves (1). Varying methods of processing the tea leaves after harvest lead to three major types of tea with different kinds and concentrations of polyphenols. To make green tea, fresh tea leaves are steamed or pan-dried at high temperature right after plucking, resulting in minimal oxidation of the naturally occurring catechins in the tea leaves. Alternatively, fresh tea leaves are rolled or crushed during the manufacture of black tea to encourage oxidation and polymerization of the polyphenols in a process commonly known as fermentation, resulting in the generation of other distinct polyphenols such as thearubigins and theaflavins. An intermediate stage of enzymatic oxidation yields Oolong tea. In general, the amounts of native polyphenols in green tea are ~30–40% weight of the water-extractable materials, as compared with 3–10% in black tea (2). About 78% of the tea production worldwide is black tea, which is the main tea beverage consumed in the US and Europe. Green tea, which is the main tea beverage in Japan and parts of China, accounts for ~20% of worldwide production, while the remaining 2% of tea production is Oolong tea which is consumed mainly in Southern China and Taiwan.

There has been extensive in vitro research regarding the possible cancer prevention mechanisms by green and black tea extracts and their polyphenols using human breast cancer cell lines. These studies suggested that multiple mechanisms are involved, including induction of apoptosis (3) and cell cycle arrest (4), down-regulation of telomerase (5), inhibition of vascular endothelial growth factor (6) and suppression of aromatase activity (7). Both green and black tea extracts also have demonstrated cancer preventive properties in carcinogen-induced or transplanted mammary tumors in experimental animal studies. Green tea extracts or catechins fed to rodents after administration of chemical carcinogens decreased the size and multiplicity of mammary tumors (8,9). Although less extensively studied, black tea extracts, given before carcinogen challenge, have been shown to reduce the tumor number, size and multiplicity in carcinogen-treated rats on a high fat diet (10,11).

Over the last three decades, a number of epidemiologic studies were conducted to investigate the association between tea consumption and breast cancer risk. This report presents results of a meta-analysis of all published data on this topic, including testing for homogeneity between studies, and computation of summary odds ratios for breast cancer in relation to green tea and black tea separately.

Methods

Literature search strategy

To search for observational studies of tea consumption in relation to breast cancer risk, we conducted a literature search in MEDLINE database for all English-language papers published from January 1, 1966 to August 31, 2004. For outcome, we identified articles using medical-subject-heading term, ‘breast neoplasm’, or keywords, ‘breast cancer, breast tumor or mammary gland tumor.’ For exposure, we identified articles using medical-subject-heading terms, ‘tea, flavonoids or catechin’, or keywords, ‘green tea, black
For study design, we identified articles using medical-subject-heading terms or key words, ‘case–control studies’, retrospective studies’, ‘cohort studies’ or ‘prospective studies.’ Articles satisfying the exposure, outcome and study design criteria were pulled. In addition, all bibliographies of reviewed papers were screened for further relevant publications.

For inclusion into the meta-analysis, the identified articles have to provide information on (i) the number of breast cancer cases studied and (ii) the odds ratio (OR) or relative risk (RR), and its corresponding 95% confidence interval (CI), for highest versus non/lowest level of tea intake. In total, 20 papers (12–31) were identified and reviewed by two authors (Sun and Yuan). Nagano et al. (23) and Wu et al. (29) were excluded since these two data sets were merely subsets of Key et al. (16) and Wu et al. (30), respectively. Franceschi et al. (14) and La Vecchia et al. (17) were excluded since the two case–control data sets were subsequently combined in Tavani et al. (28). The reports by Ewertz et al. (12), Lawson et al. (18) and Stocks (26) were excluded due to insufficient information on ORs and 95% CIs. Thus, the meta-analysis of green tea and breast cancer included the following three papers: Key et al. (16), Suzuki et al. (27) and Wu et al. (30); the meta-analysis of black tea and breast cancer included the following 13 papers: Ewertz and Gill (13), Goldbohm et al. (15), Key et al. (16), Lubin et al. (19), Mannisto et al. (20), Mclaughlin et al. (21), Michels et al. (22), Rosenberg et al. (24), Schaier et al. (25), Suzuki et al. (27), Tavani et al. (28), Wu et al. (30) and Zheng et al. (31).

**Meta-analysis**

Study-specific ORs and 95% CIs for highest versus non/lowest tea consumption level were extracted for each paper. For all studies, the reported relative risk estimate was adjusted for age and race/ethnicity, if applicable. On the other hand, only some studies reported relative risk estimates that had taken into account the established menstrual and reproductive risk factors for breast cancer. Those studies were Goldbohm et al. (15), Mannisto et al. (20), Mclaughlin et al. (21), Michels et al. (22), Suzuki et al. (27), Tavani et al. (28), Wu et al. (30) and Zheng et al. (31). Lubin et al. (19) and Mannisto et al. (20) employed both hospital and population control groups. The results based on comparison with population controls were used in the meta-analysis. Mannisto et al. (20) reported pre- and post-menopause specific OR (95% CI) estimates separately. We calculated a single OR (95% CI) estimate for total subjects by means of a weighted average of pre-menopausal OR (95% CI) and post-menopausal OR (95% CI), with weights being the inverse of the respective subgroup variance. For cohort studies, the percentages of subjects in the highest and non/lowest consumption levels were calculated either as the proportions of the numbers of subjects in these two categories over the total number of study subjects (15,27,31), or as the proportions of person-years in these two categories over the total person-years (16,22). For case–control studies, the proportions (expressed in percentages) of control subjects in the highest and non/lowest consumption categories were stated. Statistical computing was performed using the STATA statistical software (College Station, TX).

We examined possible heterogeneity in results across studies using the Q statistic (32). We defined statistical significance as P < 0.10 rather than the conventional level of 0.05 because of the low power of this test (33). The null hypothesis that the studies are homogeneous would be rejected if P is <0.10. When we noted a significant heterogeneity among study results with respect to the black tea–breast cancer risk association, we stratified studies by design (cohort versus case–control) and found that results across studies with the same design were homogeneous. We used the fixed effect model to calculate the summary OR and its 95% CI across homogeneous studies. We used the random effect model to calculate the summary OR and its 95% CI across heterogeneous studies.

Results of the meta-analysis may be biased if the probability of a study being published is dependent on its results. In other words, studies with strong positive findings may be more likely to be published. In an attempt to detect publication or related bias, we first visually explored asymmetry in funnel plots, i.e. plots of effect estimates against their estimated precision (34). In the absence of publication bias, the funnel plots should be symmetrical with estimates from larger studies in the center, flanked equally on either side by the less precise estimates. The funnel plots would be skewed (i.e. asymmetrical) in the presence of publication bias. We then formally tested the degree of asymmetry of the funnel plot using Egger’s un-weighted regression asymmetry test (35). We considered the funnel plot to be asymmetrical if the intercept of the regression line deviated from zero with a P-value of <0.10. We should note that these tests for asymmetry possess relatively low power to detect real publication bias when the number of individual studies included in the meta-analysis is small (<25), which is the case in the current review.

### Green tea

Four studies were included in the meta-analysis on green tea consumption and breast cancer risk, consisting of three cohort studies from Japan (16,27) [results from two separate cohort studies were reported in ref. (27)] and one population-based case–control study from Los Angeles (30). Table I and Figure 1 present the relative risk or odds ratio for each of the studies along with their summary OR.

**Table I. Green tea consumption and breast cancer risk**

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Design</th>
<th>Study period</th>
<th>Population</th>
<th>No. of cases/</th>
<th>No. of exposure levels</th>
<th>Lowest exposure level</th>
<th>Highest exposure level</th>
<th>Percent in lowest, highest exposure levels</th>
<th>RR (95% CI) for highest versus lowest exposure level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suzuki 2004a</td>
<td>Cohort</td>
<td>1984–1992</td>
<td>Japan</td>
<td>103/1430</td>
<td>4</td>
<td>&lt;1 cup/day</td>
<td>≥5 cups/day</td>
<td>18%, 43%</td>
<td>1.17 (0.67–2.05)</td>
</tr>
<tr>
<td>Suzuki 2004b</td>
<td>Cohort</td>
<td>1990–1997</td>
<td>Japan</td>
<td>119/2047</td>
<td>4</td>
<td>&lt;1 cup/day</td>
<td>≥5 cups/day</td>
<td>29%, 26%</td>
<td>0.61 (0.36–1.06)</td>
</tr>
<tr>
<td>Key 1999</td>
<td>Cohort</td>
<td>1969–1993</td>
<td>Japan</td>
<td>405/54325</td>
<td>3</td>
<td>≤1 cup/day</td>
<td>≥5 cups/day</td>
<td>13%, 28%</td>
<td>0.86 (0.62–1.21)</td>
</tr>
<tr>
<td><strong>Summary OR; cohort studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.85 (0.66–1.09)</td>
</tr>
<tr>
<td>Population-based case–control (PCC) study</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu 2003 (30)</td>
<td>PCC</td>
<td>1995–1998</td>
<td>USA</td>
<td>501/593</td>
<td>3</td>
<td>Non-drinkers</td>
<td>&gt;85.7 ml/day</td>
<td>22%, 10%</td>
<td>0.47 (0.26–0.85)</td>
</tr>
<tr>
<td><strong>Summary OR; all studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.78 (0.61–0.98)</td>
</tr>
</tbody>
</table>

Test for homogeneity among all studies: Q = 5.95 based on 3 degrees of freedom P = 0.11. Summary OR was based on fixed effect models.

Test for homogeneity among all cohort studies: Q = 2.71 based on 2 degrees of freedom P = 0.26. Summary OR was based on fixed effect models.

Test for homogeneity between study designs (cohort versus case–control): Q = 3.26 based on 1 degree of freedom P = 0.07.
There was no significant heterogeneity among the study results ($P = 0.11$). Overall summary OR showed an $\approx 20\%$ statistically significant reduction in risk of breast cancer associated with high intake of green tea (summary OR $= 0.78$, 95% CI $= 0.61–0.98$). The risk reduction was stronger among Asian women in Los Angeles, California (OR $= 0.47$, 95% CI $= 0.26–0.85$) than among native Japanese in Japan (summary OR for cohort studies $= 0.85$, 95% CI $= 0.66–1.09$). There was no indication of publication bias from either visualization of the funnel plot or the Egger’s test (intercept $= 0.19$, $P = 0.83$) (Figure 2).

![Begg's funnel plot with pseudo 95% confidence limits](image)

**Fig. 2.** Funnel plot of green tea consumption and breast cancer risk.

### Table II. Black tea consumption and breast cancer risk

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Design</th>
<th>Study period</th>
<th>Population</th>
<th>No. of cases/ no. of non-cases</th>
<th>No. of levels</th>
<th>Lowest/ highest exposure level</th>
<th>Percent in lowest, highest levels</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suzuki 2004 (27)</td>
<td>Cohort</td>
<td>1984–1997</td>
<td>Japan</td>
<td>222/34782</td>
<td>3</td>
<td>Never/Daily</td>
<td>NA</td>
<td>1.44 (0.77–2.69)</td>
</tr>
<tr>
<td>Michels 2002 (22)</td>
<td>Cohort</td>
<td>1987–1997</td>
<td>Sweden</td>
<td>1271/57765</td>
<td>5</td>
<td>$\leq 1$ cup/week/4 cups/day</td>
<td>32%, 8%</td>
<td>1.13 (0.91–1.40)</td>
</tr>
<tr>
<td>Key 1999 (16)</td>
<td>Cohort</td>
<td>1969–1993</td>
<td>Japan</td>
<td>342/3432</td>
<td>3</td>
<td>$\leq 1$ cup/week/5 cups/day</td>
<td>62%, 15%</td>
<td>1.10 (0.82–1.48)</td>
</tr>
<tr>
<td>Goldbohm 1996 (15)</td>
<td>Cohort</td>
<td>1986–1990</td>
<td>The Netherland</td>
<td>507/1376</td>
<td>6</td>
<td>$&lt; 1$ cup/day/5 cups/day</td>
<td>11%, 19%</td>
<td>1.31 (0.86–1.99)</td>
</tr>
<tr>
<td>Zheng 1996 (31)</td>
<td>Cohort</td>
<td>1986–1993</td>
<td>USA</td>
<td>1015/10056</td>
<td>4</td>
<td>Never/monthly/2 cups/day</td>
<td>58%, 9%</td>
<td>1.14 (0.92–1.41)</td>
</tr>
<tr>
<td><strong>Summary OR:</strong> all cohort studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.15 (1.02–1.31)</td>
</tr>
<tr>
<td><strong>Summary OR:</strong> cohort studies excluding the two Japanese studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.15 (1.00–1.33)</td>
</tr>
</tbody>
</table>

### Population-based case–control (PCC) studies

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Design</th>
<th>Study period</th>
<th>Population</th>
<th>No. of cases/ no. of non-cases</th>
<th>No. of levels</th>
<th>Lowest/ highest exposure level</th>
<th>Percent in lowest, highest levels</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu 2003 (30)</td>
<td>PCC</td>
<td>1995–1998</td>
<td>USA</td>
<td>501/593</td>
<td>3</td>
<td>Non-drinkers/50+, 21%</td>
<td>21%, 7%</td>
<td>0.81 (0.49–1.34)</td>
</tr>
<tr>
<td>Mannisto 1999 (20)</td>
<td>PCC</td>
<td>1990–1995</td>
<td>Finland</td>
<td>310/454</td>
<td>5</td>
<td>$&gt; 150$ g/day/20%, 20%</td>
<td>20%, 20%</td>
<td>0.89 (0.50–1.57)</td>
</tr>
<tr>
<td>McLaughlin 1992 (21)</td>
<td>PCC</td>
<td>1982–1984</td>
<td>USA</td>
<td>1617/1617</td>
<td>2</td>
<td>Never/Ever/21%, 79%</td>
<td>21%, 79%</td>
<td>0.97 (0.81–1.16)</td>
</tr>
<tr>
<td>Ewertz 1990 (13)</td>
<td>PCC</td>
<td>1983–1984</td>
<td>Denmark</td>
<td>1474/1322</td>
<td>5</td>
<td>5 cups/day/17%, 7%</td>
<td>17%, 7%</td>
<td>0.99 (0.69–1.42)</td>
</tr>
<tr>
<td>Scharier 1987 (25)</td>
<td>PCC</td>
<td>1973–1980</td>
<td>USA</td>
<td>1510/1882</td>
<td>6</td>
<td>5 cups/day/33%, 0.6%</td>
<td>33%, 0.6%</td>
<td>0.60 (0.20–1.90)</td>
</tr>
<tr>
<td>Lubin 1985 (19)</td>
<td>PCC</td>
<td>1975–1979</td>
<td>Israel</td>
<td>804/804</td>
<td>4</td>
<td>4 cups/day/28%, 10%</td>
<td>28%, 10%</td>
<td>0.80 (0.40–1.80)</td>
</tr>
<tr>
<td><strong>Summary OR:</strong> PCC studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td>0.94 (0.81–1.09)</td>
</tr>
</tbody>
</table>

### Hospital-based case–control (HCC) studies

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Design</th>
<th>Study period</th>
<th>Population</th>
<th>No. of cases/ no. of non-cases</th>
<th>No. of levels</th>
<th>Lowest/ highest exposure level</th>
<th>Percent in lowest, highest levels</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tavani 1998 (28)</td>
<td>HCC</td>
<td>1983–1994</td>
<td>Italy</td>
<td>5882/5399</td>
<td>2</td>
<td>$\geq 1$ cup/day/21%</td>
<td>21%, 79%</td>
<td>0.94 (0.85–1.03)</td>
</tr>
<tr>
<td>Rosenberg 1985 (24)</td>
<td>HCC</td>
<td>1975–1982</td>
<td>USA</td>
<td>2645/1476</td>
<td>4</td>
<td>5 cups/day/55%, 6%</td>
<td>55%, 6%</td>
<td>0.60 (0.50–0.90)</td>
</tr>
<tr>
<td><strong>Summary OR:</strong> HCC studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.77 (0.50–1.19)</td>
</tr>
<tr>
<td><strong>Summary OR:</strong> all case–control studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.81 (0.84–0.98)</td>
</tr>
<tr>
<td><strong>Summary OR:</strong> all studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.98 (0.88–1.09)</td>
</tr>
</tbody>
</table>

Test for heterogeneity among all studies: $Q = 20.54$ based on 12 degrees of freedom $P = 0.06$. Summary OR was based on random effect model.
Test for heterogeneity among all cohort studies: $Q = 0.98$ based on 4 degrees of freedom $P = 0.91$. Summary OR was based on fixed effect model.
Test for heterogeneity among all case–control studies: $Q = 9.70$ based on 7 degrees of freedom $P = 0.21$. Summary OR was based on fixed effect model.
Test for heterogeneity between study designs (cohort and case–control): $Q = 9.75$ based on 1 degrees of freedom $P = 0.002$.

**Black tea**

Thirteen studies, including five cohort studies (15,16,22,27,31) and eight case–control studies (13,19–21,24,25,28,30), were included in the meta-analysis on black tea consumption and breast cancer risk. Two cohort studies were conducted in Europe (15,22), one in the US (31) and the remaining two in Japan (16,27). Three case–control studies were conducted in Europe (13,20,28), four in the US (21,24,25,30) and one in the Middle East (19).

There was statistically significant heterogeneity in results across the 13 studies ($P = 0.06$). The summary OR based on all studies indicated no association between black tea consumption and breast cancer risk (summary OR $= 0.98$; 95% CI $= 0.88–1.09$) (Table II and Figure 3). There was no indication of publication bias from either visualization of the funnel plot or the Egger’s test (intercept $= -0.03$, $P = 0.71$) (Figure 4).

Although the results across all studies were heterogeneous, results from either cohort studies alone ($P = 0.91$) or case–control studies alone ($P = 0.21$) did not reject the homogeneity hypothesis. The summary OR from all cohort studies showed a modest increase (summary OR $= 1.15$, 95% CI $= 1.02–1.31$) while the summary OR from all case–control studies showed a modest decrease in risk of breast cancer (summary OR $= 0.91$, 95% CI $= 0.84–0.98$) associated with high black tea intake.

There was a statistically significant difference in the summary OR from the cohort studies and the one calculated from the case–control studies. Exclusion of the two cohort studies from Japan, where black tea consumption is rare, did not materially change the cohort study summary OR (summary OR $= 1.15$, 95% CI $= 1.00–1.33$). When we separated the population-based case–control studies from their hospital-based...
counterparts, we noted a stronger association from hospital-based (summary OR = 0.77, 95% CI = 0.50–1.19) than population-based studies (summary OR = 0.94, 95% CI = 0.81–1.09). Since menstrual (such as age at menarche, menopausal status) and reproductive (such as parity, age at first birth) factors are established major risk factors for breast cancer, we separated the case–control studies by whether any menstrual/reproductive risk factors were adjusted for in the statistical analysis. We noted a stronger association in the four studies (13,19,24,25) that did not adjust for any menstrual or reproductive risk factors (summary OR = 0.73, 95% CI = 0.59–0.91) compared with the four studies (20,21,28,30) that did (summary OR = 0.94, 95% CI = 0.87–1.02).

Discussion

This meta-analysis evaluated the association between green tea and black tea consumption and breast cancer risk based on all published epidemiological studies. There is suggestion that green tea but not black tea consumption is related to a decreased risk of breast cancer. Although we failed to observe any publication bias visually or in formal statistical testing, we would caution that the number of published studies on this topic is too small for the results to be conclusive.

Overall, there is no evidence of heterogeneity among the four studies (16,27,30) on green tea and breast cancer risk. In addition, there is no evidence of heterogeneity across the three cohort studies whose summary result indicates a modest breast cancer risk reduction associated with high green tea intake (summary OR = 0.85, 95% CI = 0.66–1.09). Although Key et al. (17) examined tea intake in a specialized cohort, majority of subjects were atomic bomb survivors of Hiroshima and Nagasaki, Japan, there is no evidence that these subjects’ unique experience in August 1945 could have a confounding effect on the observed green tea-breast cancer association noted in that study. Patterns of green tea intake were comparable between the three Japanese cohorts (16,27) (see Table I).

However, the single case–control study by Wu et al. [The Los Angeles Asian Breast Cancer Study, ref. (30)] showed a considerably stronger green tea–breast cancer association relative to the overall cohort study result, and the test for homogeneity between study design (cohort versus case–control) reached borderline statistical significance (P = 0.07). There are some important differences between the cohort studies in Japan and the Los Angeles Asian Breast Cancer Study. The Japanese cohort studies suffer from a relative lack of unexposed subjects. In Japan, where green tea drinking is pervasive, only 2% of the population are non-drinkers of green tea (23). In contrast, 22% of the controls in Wu et al. were either non-drinkers or occasional (<1 cup/month) drinkers of green tea (30). In the Japanese studies, only intake frequency was asked while Wu et al. assessed both frequency and usual amounts drunk each time. Wu et al. also reported that the beneficial effect of green tea on breast cancer risk was primarily observed among women with low soy intake (30) and soy intake was high in Japan (36). Thus, differences in the prevalence and range of exposure to green tea and other dietary cofactors may explain, at least partly, the disparate findings between the study among Asians in Los Angeles (30) and those among natives of Japan (16,27).

In contrast to green tea, there is no overall protective effect of black tea on breast cancer risk. Interestingly, all five cohort studies (15,16,22,27,31) reported increased risk, with
a statistically significant summary OR of 1.15. The summary OR did not change materially after exclusion of the two Japanese studies (16,27), where black tea intake is relatively rare and thus raising doubts on a causal interpretation of the observed positive black tea–breast cancer association. All three US/Europe-based cohort studies assessed tea intake at the time of baseline interview. The follow-up periods of these three cohort studies ranged from 4 to 10 years. Recently, we noted higher levels of circulating estrogens in black tea drinkers than in non-tea drinkers, while estrogen levels were lower in green tea drinkers than in non-tea drinkers (37). It is well established in experimental studies that estrogen is a strong promoter of mammary carcinogenesis [reviewed in (38)]. Hence, we speculate that the overall cohort findings are compatible with the notion of black tea intake having a late-stage, promotional effect on breast cancer, possibly via its effect on circulating estrogen levels. The summary OR for breast cancer associated with high consumption of back tea based on case
control studies was 0.91 (95% CI = 0.84–0.98). However, we noted a weaker association in population-based studies (summary OR = 0.94, 95% CI = 0.81–1.09) versus hospital-based studies (summary OR = 0.77, 95% CI = 0.50–1.19). We also noted a weaker association in studies adjusted for major menstrual/reproductive risk factors for breast cancer (summary OR = 0.94, 95% CI = 0.87–1.02) than those which made no attempt to adjust for any menstrual/reproductive risk factors for breast cancer. Therefore, we conclude that the overall evidence do not support black tea drinking as having a protective effect on breast cancer.

There has been extensive research into the possible anti-carcinogenic mechanisms of tea and its polyphenols, and many of these mechanistic studies relate specifically to the catechins. In experimental studies involving breast cancer cell lines, EGCG, the major catechin in green tea, has been shown to suppress cell viability and induce apoptosis by down-regulation of telomerase (5), and to inhibit angiogenesis by reducing expression of vascular endothelial growth factor in a dose-dependent manner (6). Epigallocatechin, another major catechin in green tea, has also strong effects in inducing apoptosis and inhibiting growth of breast cancer cells in vitro (3). Green tea catechins can increase hepatic glucuronidation of estrone and estradiol in animal studies (39) and have been shown to inhibit human placental aromatase, an enzyme which converts androstenedione to estrone (40). Hence, if the beneficial effect of tea on breast cancer risk comes mainly from the tea catechins, an explanation for the relative lack of risk reduction associated with black tea drinking can be due to the much lower level of catechins in black tea compared with green tea (up to 10-fold difference in catechin contents) (2). Compared with green tea, black tea has been shown to be a less potent inhibitor of tumor progression in a mouse model of a hormone-dependent human breast tumor (41). In addition, as mentioned previously, levels of circulating estrogens were higher in Singapore Chinese women who drank black tea regularly relative to their non-tea drinking counterparts, while lower levels of circulating estrogens were found among regular green tea drinkers compared with non-tea drinkers (37). Furthermore, in a study of Caucasian women in The Netherlands, serum levels of prolactin, another female hormone implicated in breast carcinogenesis, has been shown to correlate positively with black tea consumption (42).

In summary, the current epidemiologic literature supports the hypothesis that green tea protects against breast cancer. Given the relative paucity of human data, prospective cohort studies with a wide range of green tea exposure and longer duration of follow-up are needed to affirm the protective effect of green tea on human breast cancer development. Current epidemiological data do not support a role for black tea in protection against breast cancer in humans. Cohort studies with longer duration of follow-up are needed to elucidate the effect of black tea on different stages of breast cancer development. Since genetic and lifestyle/dietary cofactors may influence the effect of green/black tea on breast carcinogenesis (29,30,43), future studies should address the possible interaction effects between tea and other dietary/genetic cofactors.

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References


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