



Cognitive Vitality Reports[®] are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-indevelopment, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Green Tea

Evidence Summary

There are many health benefits associated with green tea, including lower risk of dementia, cardiovascular disease, cancer, all-cause mortality, and others. It is generally safe in moderation.

Neuroprotective Benefit: Meta-analyses have found that green tea intake is associated with lower risks of dementia and cognitive decline. The association between green tea intake and better cognitive health may depend on ethnicity and other factors.

Aging and related health concerns: Meta-analyses have reported that green tea intake is associated with lower risks of mortality, cardiovascular diseases, and many cancers. Green tea may also decrease body weight and improve lipid and metabolic profiles.

Safety: Multiple meta-analyses have concluded that green tea consumption at moderate amounts is safe with mild side effects, but it is worth paying attention to the source of the tea leaves, as those grown in areas of excessive pollution can have lead contamination.

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Availability: available	Dose : varies based on preparation	Compounds: caffeine, EGCG, L- theanine, arginine, and others
Half-life: 4-6 hours for caffeine, 2-6 hours for EGCG, ~1 hour for L-theanine	BBB : penetrant for caffeine, EGCG, and L-theanine	
Clinical trials : Numerous meta-analyses of randomized controlled trials examining the effects of green tea have included thousands of people.	Observational studies : Numerous meta-analyses of observational studies examining green tea consumption have included hundreds of thousands of people.	

What is it?

Green tea is made from dried leaves of *Camellia sinensis*, a perennial evergreen shrub. Green tea contains caffeine, catechins such as EGCG (antioxidants), and L-theanine (an amino acid derivative) (note: there are separate reports for caffeine, L-theanine, and EGCG). There are multiple types of green tea. Sencha, the most common type of green tea in Japan (and the US), is prepared by infusing the processed whole tea leaves in hot water. Gyokuro is a type of green tea that is produced from shading the tea leaves, increasing theanine and caffeine production while inhibiting catechin levels. Matcha is a type of green tea used in Japanese tea ceremony. The tea leaves are also shade-grown, to increase theanine and chlorophyll levels and to enhance flavor and color, then harvested and finely stone-ground. Matcha is consumed by adding hot water to the fine tea powder and mixing vigorously with a bamboo whisk. Matcha powder is also used as food coloring, for green tea ice cream, Japanese confectionary, and noodles.

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Neuroprotective Benefit: Meta-analyses have found that green tea intake is associated with lower risks of dementia and cognitive decline. The association between green tea intake and better cognitive health may depend on ethnicity and other factors.

Types of evidence:

- 3 meta-analyses of observational studies
- 3 double-blind randomized controlled trials, 2 on cognitive function and 1 on acute effects of green tea extract
- 6 observational studies on cognitive function and/or dementia
- 1 clinical study of Alzheimer's biomarkers
- 1 observational study on brain imaging metrics
- 1 review on tea and cognitive health in late life

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

In a 2025 meta-analysis of 18 observational studies including a total of 58,929 people without cognitive impairment at baseline, green tea consumption was inversely associated with cognitive impairment (OR=0.63, 95% CI, 0.54 to 0.73), with the greatest benefit observed in people aged 50-69 years (OR=0.52 for 50-59-year-olds, OR=0.65 for 60-69-year-olds)[1]. Of the 18 studies, 11 were cohort studies and 7 were cross-sectional studies. Subgroup analyses showed that green tea consumption was associated with lower risk of dementia (OR=0.75, 95% CI, 0.60 to 0.92), and lower risk of mild cognitive impairment (OR=0.64, 95% CI, 0.43 to 0.96). However, no significant association was found between green tea consumption and Alzheimer's disease (OR=0.57, 95% CI, 0.21 to 1.59). Lower risk of cognitive impairment was observed in Asian populations (OR=0.55 for Chinese, OR=0.74 for Japanese), but not in European populations. Both women (OR=0.51, 95% CI, 0.28 to 0.95) and men (OR=0.47, 95% CI, 0.28 to 0.80) had significantly lower risk of cognitive decline with green tea consumption. When comparing different levels of green tea consumption, no significant association with cognitive impairment was observed in the low consumption group (OR=0.70, 95% CI, 0.47 to 1.04), while a trend towards lower cognitive impairment risk was seen in the moderate consumption group (OR=0.73, 95% CI, 0.60 to 0.89) and high consumption groups (OR=0.63, 95% CI, 0.50 to 0.82). The authors noted that because of the observational nature of the included studies, they were not able to establish a causal relationship between green tea consumption and lower cognitive impairment. Green tea consumption is associated with other lifestyle factors that may affect cognitive function.

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A 2024 meta-analysis including 9 randomized controlled trials, 23 cohort studies, and 12 cross-sectional studies examined the effects of habitual tea drinking on dementia, mild cognitive impairment, and age-related cognitive decline [2]. A meta-analysis of randomized controlled trials found that habitual tea drinking decreased cognitive dysfunction, measured by the Mini-Mental State Examination (MMSE). A meta-analysis of cohort studies found that tea intake was significantly associated with a lower risk of adverse cognitive outcomes, with green tea (pooled RR=0.67; 95% CI, 0.59 to 0.76, p<0.01) and black tea (pooled RR=0.62; 95% CI, 0.53 to 0.73, p<0.01) significantly associated with a lower risk of adverse cognitive outcomes. A meta-analysis of cross-sectional studies found that habitual tea intake was associated with lower risk of cognitive decline in studies conducted in eastern countries (pooled OR=0.69, 95% CI, 0.60 to 0.79, p<0.01) and studies with high-quality scores (pooled OR=0.64, 95% CI, 0.54 to 0.76, p<0.01). Tea consumption was associated with a lower risk of dementia (pooled RR=0.45, 95% CI, 0.34 to 0.60, p<0.01) and mild cognitive impairment (pooled RR=0.69, 95% CI, 0.60 to 0.78, p<0.01). Intake of green tea (pooled RR=0.68, 95% CI, 0.58 to 0.79, p<0.01) and black tea (pooled RR=0.49, 95% CI, 0.37 to 0.64, p<0.01) were significantly associated with lower risks of adverse cognitive outcomes.

In a 2023 meta-analysis of 7 prospective cohort studies including a total of 410,951 participants, green or black tea consumption was associated with a lower risk of all-cause dementia (RR=0.71, 95% CI, 0.57 to 0.88, p<0.01)[3]. Greater degree of lowering of all-cause dementia was seen in people with less physical activity, older age, APOE4 carriers, and smokers. Subgroup analysis also found that tea intake is associated with a lower risk of Alzheimer's disease (RR=0.88, 95% CI, 0.79 to 0.99, p=0.024) and vascular dementia (RR=0.75, 95% CI, 0.66 to 0.85, p<0.001).

Several randomized controlled trials have evaluated the effects of green tea extracts on cognitive functions. In a double-blind randomized controlled trial in 91 patients with mild cognitive impairment, the combination of green tea extract and L-theanine (1680 mg of LGNC-07, including 240 mg of L-theanine but no caffeine) for 16 weeks resulted in significant improvements in memory and attention, particularly in patients who had relatively severe baseline impairment (MMSE scores of 21-23)[4]. Brain theta waves were increased in the temporal, frontal, parietal, and occipital cortex after 3 hours, suggestive of cognitive alertness. A double-blind randomized controlled trial examining the acute effects of a drink containing 27.5 g of green tea extract reported that the extract increased brain connectivity and that the magnitude of that effect correlated with improvement in working memory task performance [5]. In a double-blind randomized controlled trial of 99 older adults with subjective cognitive decline or mild cognitive impairment, 2 grams of matcha daily (containing 170 mg of catechins and 48 mg of theanine) for 12 months significantly improved the social acuity score (p=0.028), as

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evaluated by the perception of facial emotions [6]. There was also a trend toward improvement in sleep quality (measured by change from baseline on the Pittsburgh Sleep Quality Index scores) with the matcha intervention compared to placebo (p=0.088). However, the primary outcomes, Montreal Cognitive Assessment (MoCA) or Alzheimer's Disease Cooperative Study Activity of Daily Living (ADCS-ADL) scores showed no significant changes with the matcha intervention compared to placebo. There were also no significant differences between matcha and placebo groups for reaction time, complex attention, cognitive flexibility, executive function, simple attention, ADCS-MCI-ADL, MMSE, ADAS-J cog, or Repeatable Battery for Assessment of Neuropsychological Status (RBANS).

Two prospective studies have reported that greater green tea consumption is associated with lower risk of incident dementia [7; 8]. In the larger study (13,645 Japanese people over 65 years old), the hazard ratio for 5 or more cups/day was 0.73 (95% CI, 0.61-0.87) [8]. The smaller study (723 Japanese people over 60 years old) showed that compared with individuals who did not consume green tea at all, the incidence of overall cognitive decline (dementia or MCI) was 0.32 (95% CI: 0.16-0.64) among individuals who consumed green tea every day and 0.47 (95% CI: 0.25-0.86) among those who consumed green tea 1-6 days per week [7]. While positive effects of green tea drinking may be attributable to the benefits of social interactions and leisurely activities with peers [9], in the latter study they did not find an association between coffee or black tea consumption and incidence of dementia or MCI. (But other studies have shown protection with coffee intake—please see the report on coffee for details).

In a population-based longitudinal cohort study in Chinese people aged 80-115 years old, tea drinking was associated with higher verbal fluency at baseline and throughout the follow-up period (up to 7 years) [10]. Thus, regular tea drinking is associated with better cognitive function at old age. In a cross-sectional study, low green tea consumption was associated with a higher prevalence of cognitive impairment in older Japanese people [11].

In a population-based cohort study in 1,115 Japanese people aged 44-66 years old at baseline who were followed for 20 years, people who consumed 2-3 cups of green tea daily had a significantly lower risk of cognitive decline (OR=0.56, 95% CI, 0.35 to 0.91) after adjusting for potential confounders [12]. However, consumption of 4 or more cups of green tea was not associated with lower risk of cognitive decline. In subgroup analyses, 2-3 cups of green tea daily was associated with a 62% lower risk of cognitive decline (OR=0.38, 95% CI, 0.19 to 0.76).

In a cross-sectional community-based observational study of 5,440 Chinese people with polyvascular abnormalities, habitual (OR=0.47, 95% CI, 0.33 to 0.68, p<0.001) and high frequency tea consumption

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(p<0.001) were associated with a lower risk of cognitive impairment, after adjusting for age, sex, level of education, hs-CRP, smoking, alcohol consumption, hypertension, diabetes, dyslipidemia, BMI, physical activity, and salt intake [13]. The risk of cognitive impairment (measured by MMSE) was lower with green tea consumption (OR=0.36, 95% CI, 0.22 to 0.61, p<0.001) than other types (OR=0.59, 95% CI 0.38 to 0.91, p=0.017). Tea intake for 1-3 times/week (OR=0.45, 95% CI, 0.21 to 0.94, p<0.001) and \geq 4 times/week (OR=0.47, 95% CI, 0.31 to 0.73, p<0.001) showed statistically significant associations with lower risk of cognitive impairment. Similar results were seen when MoCA was used as a cognitive outcome.

In an observational study of 8,766 Japanese community-dwelling older adults without dementia, higher green tea consumption was associated with lower cerebral white matter lesion volume, measured by MRI [14]. White matter lesions are associated with cerebral small vessel disease. The association remained unchanged after adjusting for age, sex, research site, educational levels, presence of ApoE4, hypertension, BMI, serum LDL- and HDL-cholesterol levels, regular exercise, and smoking and drinking habits. Cerebral white matter lesion volumes were 3% lower (95% CI, 0.94 to 0.99) and 6% lower (95% CI, 0.90 to 0.98) with daily green tea consumption levels of 600 ml (approximately 3 glasses) and 1500 ml (approximately 7-8 glasses), respectively, as compared to a consumption level of 200 ml. A significant relationship between higher green tea consumption and lower white matter lesions was observed in people without depression, whereas no significant relationship was found in people with depression. There were no associations between green tea consumption and hippocampal or total brain volume. The authors speculate that the association between green tea on reducing blood pressure, which is a risk factor for white matter lesions.

It is unclear whether benefits of life-long green tea consumption can be mimicked by late-in-life changes in tea drinking. Also, observational studies cannot tease apart the benefits of green tea with the benefits of avoiding alternatives to tea/coffee, such as sodas and other sugared beverages.

Human research to suggest benefits to patients with dementia:

No studies have been published on the effects of green tea in patients with dementia.

In a biomarker study of 722 cognitively intact people from the Chinese Alzheimer's Biomarker and LifestylE (CABLE) database, frequent green tea consumption was associated with a lower level of

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cerebral spinal fluid (CSF) total tau (p=0.41) but not with the levels of CSF A β 42 or CSF p-tau181 [15]. There were no interaction effects of green tea consumption with APOE4 or sex.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Green tea contains several compounds that may be neuroprotective, including caffeine, L-theanine, and green tea catechins (e.g., EGCG). Mechanisms of action for caffeine, EGCG, and L-theanine are discussed in the individual reports.

Green tea and its polyphenols have numerous potential neuroprotective effects, including antioxidant and iron-chelating activity, anti-inflammatory actions (by reducing pro-inflammatory cytokines, microglial activation, and TLR4/NFkB pathway), anti-amyloid/tau effects (by inhibiting aggregation, tau hyperphosphorylation, etc.), and effects on neurotransmitter homeostasis [2]. Green tea catechins act as cholinesterase inhibitors and may enhance acetylcholine levels [16].

APOE4 interactions:

In a 2023 meta-analysis of 7 prospective cohort studies that reported that green or black tea consumption was associated with a lower risk of all-cause dementia (RR=0.71, 95% CI, 0.57 to 0.88, p<0.01), a greater degree of risk lowering was seen in APOE4 carriers than non-carriers [3].

Other studies have examined the interactions between ApoE status and caffeine intake [17], which have produced inconclusive results. A pilot randomized crossover trial has shown that drinking 6 mugs of black tea daily was associated with some beneficial effects on factors associated with cardiovascular disease risk (triacylglycerol, blood coagulation factors) in E2 carriers but not in people with E3/E4 or E4/E4 genotype [18].

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Aging and related health concerns: Meta-analyses have reported that green tea intake is associated with lower risks of mortality, cardiovascular diseases, and many cancers. Green tea may also decrease body weight and improve lipid and metabolic profiles.

Types of evidence:

- 4 Cochrane meta-analyses
- 26 meta-analyses on age-related conditions
- 1 longitudinal study on mortality
- 1 European cohort study on diabetes incidence
- Numerous reviews

Mortality: DECREASED

Two meta-analyses of 18 and 22 prospective studies (each with over 800,000 total subjects) reported that tea consumption is associated with lower mortality [19; 20]. High green tea consumption specifically was associated with lower all-cause mortality (RR=0.80, 95% CI, 0.68-0.93) and cardiovascular disease mortality (RR=0.67, 95% CI, 0.46-0.96) compared to the lowest consumption [19]. The dose-response analysis indicated that for every additional cup of green tea/day, all-cause mortality and cardiovascular disease mortality was decreased by 4% and 5%, respectively.

In a 2020 Cochrane meta-analysis of 8 observational studies including a total of 504,366 participants, no association between green tea consumption and cancer-related mortality was found (RR=0.99, 95% CI, 0.91 to 1.07)[21].

Cardiovascular diseases: DECREASED

A 2016 meta-analysis of 8 observational studies and 1 randomized controlled trial reported benefits of green tea consumption [22]. Those who drank 1-3 cups of green tea per day had a reduced risk of myocardial infarction (OR=0.81, 95% CI: 0.67-0.98) and stroke (OR=0.64, 95% CI: 0.47-0.86) compared to those who drank less than 1 cup/day. People who drank 4 cups or more per day had an even greater reduction of risk of myocardial infarction (OR=0.68, 95% CI: 0.56-0.84).

In a 2023 meta-analysis of 7 prospective cohort studies from China and Japan, green tea consumption was associated with a lower risk of coronary heart disease, with a relative risk of 0.89 (95% CI, 0.83 to 0.96) for 1 cup (300 mL)/day, 0.84 (95% CI, 0.77 to 0.93) for 2 cups/day, 0.85 (95% CI, 0.77 to 0.92) for 3

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cups/day, 0.88 (95% CI, 0.81 to 0.96) for 4 cups/day, and 0.92 (95% CI, 0.82 to 1.04) for 5 cups/day compared to non-consumers [23]. In this meta-analysis, there were 9,211 coronary heart disease cases and 772,922 participants.

In a 2023 meta-analysis of 5 prospective cohort studies from Japan and China, the highest green tea consumption was associated with a 26% lower risk of stroke (RR=0.74; 95% CI, 0.66 to 0.83)[24]. Compared with non-consumers, the relative risks of stroke across levels of green tea consumption were 0.91 (95% CI, 0.89 to 0.94) for 150 ml/day, 0.84 (95% CI, 0.80 to 0.89) for 300 ml/day, 0.79 (95% CI, 0.74 to 0.84) for 500 ml/day, 0.77 (95% CI, 0.72 to 0.82) for 900 ml/day, and 0.84 (95% CI, 0.77 to 0.91) for 1500 ml/day.

Cholesterol and triglycerides: IMPROVED

In a 2023 meta-analysis of up to 55 randomized controlled trials, green tea extract supplementation for 2-48 weeks significantly reduced total cholesterol (weighted mean difference [WMD]=-7.62; 95% Cl, - 10.51 to -4.73; p<0.001) and LDL-cholesterol (WMD=-5.80; 95% Cl, -8.30 to -3.30; p<0.001), and significantly increased HDL-cholesterol (WMD=1.85; 95% Cl, 0.87 to 2.84; p=0.010)[25]. No significant effects were seen for triglycerides, though in subgroup analyses, significant reductions in triglycerides with green tea extract intervention were seen when both men and women were included in the study, when the duration of the intervention was longer than 12 weeks, when the dosage was less than 1000 mg/day, the baseline BMI was between 25-29.9 kg/m2, and when the baseline triglyceride levels were higher than 200 mg/dl. Randomized controlled trials included in the meta-analysis enrolled healthy people (29 studies) as well as people with type 2 diabetes (15 studies), liver disorders (3 studies), hypercholesterolemia (2 studies), overweight/obesity (3 studies), polycystic ovarian syndrome (2 studies), and others. Clinical trials were run in different countries including Australia, US, Iran, Brazil, UK, China, Spain, Japan, Taiwan, Lithuania, Poland, Netherlands, Finland, Pakistan, and Mexico.

A 2024 meta-analysis of 15 randomized controlled trials including a total of 1,818 overweight and obese women, green tea supplementation for 1-12 months significantly reduced total cholesterol (WMD=-4.45 mg/dl; 95% Cl, -6.63 to -2.27; p<0.001) and LDL-cholesterol (WMD=-4.49 mg/dl; 95% Cl, -7.50 to -1.47; p=0.003), but did not significantly affect HDL-cholesterol [26]. Randomized controlled trials included in the meta-analysis enrolled women with prediabetes, menopause, obesity, metabolic syndrome, polycystic ovary syndrome, breast cancer, or healthy women. A significant reduction in total cholesterol was seen in overweight/obese women (WMD=-4.45 mg/dl; 95% Cl, -6.63 to -2.27; p<0.001), in postmenopausal women (WMD=-8.71 mg/dL; 95% Cl, -11.44 to -5.98; p<0.001) and when the baseline

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value was ≥200 mg/dL (WMD=-4.78 mg/dL; 95% CI, -7.06 to -2.51; p<0.001) versus <200 mg/dL (WMD=-4.41 mg/dL; 95% CI, -17.33 to 8.50; p=0.50). A greater reduction in LDL-cholesterol was seen in postmenopausal women (WMD=-9.35 mg/dL; 95% CI, -12.40 to -6.30; p<0.001) compared to other subgroups. Whole green tea supplementation significantly decreased total cholesterol (WMD=-4.26 mg/dl; 95% CI, -8.28 to -0.24; p=0.03) and LDL-cholesterol (WMD=-5.73 mg/dl; 95% CI, -8.82 to -2.63; p<0.001) but total cholesterol or LDL-cholesterol was not significantly decreased with decaffeinated green tea. A significant reduction in triglyceride levels was observed when the baseline value was ≥150 mg/dL (WMD=-24.45 mg/dL; 95% CI, -40.63 to -8.26; p=0.003) or in overweight women (BMI: 25-29.99 kg/m2)(WMD=-5.88 mg/dl; 95% CI, -10.76 to -0.99; p=0.01), but not in obese women.

A 2013 meta-analysis of randomized controlled trials in healthy adults or those at high risk of cardiovascular disease reported that green tea produced statistically significant reductions in total cholesterol by 23.9 mg/dL (95% CI, -29.7 to -17.8)[27]. A 2016 meta-analysis of mostly observational studies reported that people who drank over 10 cups of green tea per day had lower LDL-cholesterol compared to those who drank fewer than 3 cups/day [22].

Blood pressure: DECREASED

Three meta-analyses based on 10, 13, and 25 RCTs showed that consumption of green tea significantly reduced systolic blood pressure by 1.98-2.36 mmHg and diastolic blood pressure by 1.70-1.92 mmHg [28; 29; 30]. These effects are typically seen after long-term intervention (12+ weeks).

In a 2023 meta-analysis of 28 randomized controlled trial arms, green tea extract supplementation for 2-48 weeks significantly reduced diastolic blood pressure (WMD=-0.87; 95% CI, -1.45 to -0.29; p=0.003) [25]. Subgroup analyses indicated that a significant decrease in diastolic blood pressure was observed if the duration of intervention was \leq 12 weeks, the dosage of supplementation was less than 1,000 mg/day, baseline values of diastolic blood pressure were more than 80 mmHg, and the baseline value of BMI was \geq 30 kg/m2.

Type 2 diabetes mellitus: IMPROVED BIOMARKERS, DECREASED RISK

In a 2024 meta-analysis of 15 randomized controlled trials in people with type 2 diabetes, green tea intervention significantly improved fasting blood glucose (standardized mean difference [SMD]=-0.41; 95% Cl, -0.67 to -0.19; p=0.001), glycated hemoglobin (HbA1c, used for diagnosing prediabetes and diabetes; SMD=-0.68; 95% Cl, -1.15 to 0.21; p=0.004) and insulin resistance index (SMD=-0.70; 95% Cl, -

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1.18 to -0.22; p=0.005) compared to the control group [31]. Of the 15 randomized controlled trials, 5 were in Iran, 4 in China, 2 in Japan, 2 in Brazil, 1 in Mexico, and 1 in Sweden.

In a 2023 meta-analysis of up to 55 randomized controlled trials, green tea extract supplementation for 2-48 weeks significantly reduced fasting blood glucose (WMD=-1.67; 95% CI, -2.58 to -0.75; p<0.001) and HbA1c (WMD=-0.15; 95% CI, -0.26 to -0.04; p=0.008) but had no effects on fasting insulin or HOMA-IR (index for insulin resistance)[25]. In subgroup analyses, significant reductions in fasting blood glucose with green tea extract supplementation were observed when the baseline BMI was between 25-29.9 kg/m2, when studies included women only or men and women, when the duration of the intervention was longer than 12 weeks, when the dosage was less than 1000 mg/day, and when baseline fasting blood sugar levels were less than 100 mg/dl. Subgroup analyses found that green tea extract supplementation was ≥1,000 mg/d, baseline values of HbA1c were less than 6.5%, male or both genders were involved, and the baseline value of BMI was ≥30 kg/m2.

A 2013 meta-analysis of 17 RCTs (total of 1133 subjects) reported that green tea extracts (tea catechins, EGCG, polyphenols, or tea extract) was associated with decreased fasting glucose and glycated hemoglobin [32]. Glucose was decreased by -0.09 mmol/L (95% CI: -0.15, -0.03 mmol/L) and HbA1c concentration was decreased by 0.30% (95% CI, -0.37 to -0.22%). No significant effects on fasting insulin concentrations were observed. In a smaller meta-analysis of 7 RCTs in people at risk of type 2 diabetes, green tea consumption did not significantly decrease levels of fasting glucose, fasting insulin, HbA1c, and HOMA-IR [33].

While not on green tea specifically, 1 meta-analysis and 1 large cohort study showed that tea consumption is associated with a reduced risk of type 2 diabetes [34; 35]. The meta-analysis including 16 cohorts (total of 545,517 subjects) showed that for every 2 additional cups/day of tea consumption, there was a 4.6% lower risk of type 2 diabetes (95% CI, 0.9-8.1%)[35]. The large case cohort study was carried out in Europe and included 340,234 subjects across 8 European countries [34]. In this study too, tea consumption was associated with a lower incidence of type 2 diabetes. The hazard ratio was 0.84 (95%CI, 0.71-1.00) when subjects who drank 4 or more cups/day were compared with non-drinkers.

Body weight: DECREASED IN OVERWEIGHT/OBESE

A Cochrane meta-analysis based on 14 RCTs in overweight or obese adults reported that green tea consumption for at least 12 weeks was associated with weight loss, but the magnitude of change was

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small and not likely to be clinically important [36]. Green tea had no effect on the maintenance of weight loss.

In a 2024 dose-response meta-analysis of randomized controlled trials in adults, green tea extract supplementation (varied between 60 to 3000 mg/day) for 2-48 weeks significantly reduced body mass (WMD=-0.64 kg, 95% Cl, -0.97 to -0.30, p<0.001), BMI (WMD=-0.16; 95 % Cl, -0.25 to 0.07; p<0.001), and body fat % (WMD=-0.62%, 95% Cl, -1.02 to -0.23, p=0.002) based on 38, 46, and 19 randomized controlled trials [37]. Included randomized controlled trials enrolled people who were healthy or with type 2 diabetes, obesity, and other conditions. Green tea extract supplementation did not significantly alter waist circumference or fat mass. A meta-analysis of 19 randomized controlled trials found that green tea extract supplementation (varied between 60 to 3000 mg/day) for 2-48 weeks significantly increased levels of adiponectin (lower levels are associated with obesity)(WMD=0.62 μ g/ml; 95 % Cl, 0.09 to 1.14; p=0.020), especially at higher dosages of ≥ 1000 mg/day in people who were overweight and older than 50 years old. Green tea extract supplementation did not significantly alter other obesity-related hormones, leptin and ghrelin.

In a 2024 dose-response meta-analysis of 15 randomized controlled trials of overweight and obese women, green tea supplementation (in the forms of green tea extract capsules/tablets or drinking green tea) for 2 weeks to 5 months significantly decreased body weight (weighted MD [WMD]=-1.23 kg; 95% Cl, -2.13 to -0.33; p=0.007), BMI (WMD=-0.47 kg/m2; 95% Cl, -0.87 to -0.07; p=0.020) and waist circumference (WMD=-3.46 cm; 95% Cl, -6.75 to -0.16; p=0.040)[38]. Subgroup analyses showed that green tea supplementation lowered body weight with doses ≥1000 mg/day (WMD=-1.38 kg) and with interventions that lasted ≥8 weeks (WMD=-1.24 kg). A subgroup analysis based on the type of green tea found a significant decrease in body weight with green tea (WMD=-2.06 kg, p=0.001) compared to green tea extract (WMD=-0.87 kg) and green tea drink (WMD=-1.13 kg). The randomized controlled trials included in the meta-analysis were conducted in Brazil, Malaysia, Iran, US, Taiwan, China, and the Netherlands.

A 2024 meta-analysis of 15 randomized controlled trials including a total of 1,818 overweight and obese women, green tea supplementation for 1-12 months significantly decreased body weight when the intervention lasted <12 weeks (WMD=-5.89 mg/dl; 95% Cl, -9.92 to -1.86, p=0.004) and in overweight (but not obese) women (BMI: 25-29.99 kg/m2; WMD=-6.55 mg/dl; 95% Cl, -8.97 to -4.12; p<0.001)[26].

Liver cancer: DECREASED

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Based on a 2011 meta-analysis of 8 observational studies, green tea consumption was associated with a moderately lower risk of primary liver cancer (RR=0.79, 95% CI, 0.68-0.93) [39].

In a 2024 meta-analysis of 4 cohort studies with a total of 169,599 subjects who were cancer-free at baseline, green tea consumption was associated with a significantly lower risk of developing liver cancer (OR=0.85; 95% CI, 0.74 to 0.97, p= 0.02) compared to non-consumption [40]. There was also a significant association of green tea intake with lower liver enzymes including alanine aminotransferase (MD=-0.65; 95% CI, -0.92 to -0.38, p< 0.001) and aspartate aminotransferase (MD=-0.77; 95% CI, -1.40 to -0.14, p= 0.02; both based on 4 studies) compared to no green tea intake.

In a 2023 meta-analysis of 18 observational studies including a total of 1,481,647 participants, green tea intake was associated with a lower risk of hepatocellular carcinoma (RR=0.80; 95% CI, 0.67 to 0.95)[41]. Lower risk of hepatocellular carcinoma with green tea intake was observed for both cohort (RR=0.89; 95% CI, 0.77 to 1.03) and case-control studies (RR=0.55; 95% CI, 0.25 to 1.20). Subgroup analysis found that green tea intake was significantly associated with lower hepatocellular carcinoma at \geq 4 cups/day (RR=0.79; 95% CI, 0.64 to 0.96).

In a 2020 Cochrane meta-analysis of observational studies, a slightly lower risk of liver cancer was observed with green tea intake (RR=0.88, 95% CI, 0.68 to 1.14)[21].

Breast cancer: DECREASED

Several meta-analyses have linked green tea consumption with decreased incidence of breast cancer and its recurrence. In a meta-analysis of four studies, high green tea consumption was associated with a reduced risk of breast cancer compared to non/lowest green tea consumption (OR = 0.78, 95% CI, 0.61-0.98)[42]. Another meta-analysis showed that breast cancer incidence was lower with increased green tea consumption (more than 3 cups/day) in case-control studies (RR=0.81, 95% CI, 0.75-0.88) but failed to find an association in cohort studies [43]. The same meta-analysis reported that high green tea consumption was associated with lower breast cancer recurrence (RR=0.73, 95% CI, 0.56-0.96). A third meta-analysis also reported that the highest level of green tea consumption was associated with a significantly lower risk of breast cancer recurrence in early stage (stages I and II) cancers (RR=0.56. 95% CI, 0.38-0.83) [44]. But this meta-analysis did not find a significant effect of green tea consumption on breast cancer incidence (RR=0.89, p=0.28).

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In a 2020 Cochrane meta-analysis of observational studies, higher green tea intake was associated with a lower breast cancer risk (RR=0.88, 95% CI, 0.75 to 1.02), though findings varied depending on study designs [21]. Five cohort studies found no association between green tea intake and risk of breast cancer, but 4 population-based case-control studies and 5 hospital-based case-control studies found greater green tea intake associated with lower breast cancer risk.

In a 2020 dose-response meta-analysis of 16 observational studies, higher amounts and longer durations of green tea drinking was associated with lower breast cancer risk [45]. Drinking 1, 2, 3, 5, and 7 cups of green tea per day were associated with 3%, 6%, 8%, 13%, and 18% lower risk of breast cancer, respectively.

Black tea appears to not be as protective, despite coming from the same plant as green tea. Conflicting results were observed in case-control (OR = 0.91, 95% CI, 0.84-0.98) versus cohort studies (OR = 1.15, 95% CI = 1.02-1.31), with the latter showing a modest increase in breast cancer risk with black tea consumption [42]. A different meta-analysis showed that black tea consumption is not associated with the risk of breast cancer [46].

Lung cancer: DECREASED

In a meta-analysis of 22 observational studies (12 studies on green tea, 14 on black tea), there was a borderline significant association between highest green tea consumption and lower risk of lung cancer (RR=0.78, 95% CI, 0.61-1.00) [47]. An increase in green tea consumption by 2 cups/day was associated with an 18% lower risk of developing lung cancer (RR=0.82, 95% CI, 0.71-0.96). For black tea, no statistically significant association was observed (highest versus non/lowest, RR=0.86, 95% CI=0.70-1.05).

In a 2020 Cochrane meta-analysis of 16 observational studies, green tea intake was associated with a lower lung cancer risk (RR=0.88, 95% CI, 0.76 to 1.02); however, findings were inconsistent across study designs [21]. Five cohort studies found no association between green tea intake and lung cancer risk (RR=1.02), while population-based case-control studies (RR=0.73, 95% CI, 0.61 to 0.87) and hospital-based case-control studies (RR=0.90, 95% CI, 0.69 to 1.17) found higher green tea intake associated with lower lung cancer risk.

Stomach cancer: DECREASED

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In a 2020 Cochrane meta-analysis of 20 observational studies, green tea intake was associated with a significantly lower stomach cancer risk (RR=0.86, 95% CI, 0.74 to 1.01)[21]. Subgroup analysis of 8 population-based case-control studies showed a lower stomach cancer risk in people who had the highest green tea intake (RR=0.74; 95% CI, 0.53 to 1.02).

Colorectal cancer: DECREASED

In a 2020 Cochrane meta-analysis of observational studies, the highest green tea intake was associated with a significantly lower risk of colorectal cancer (RR=0.84, 95% CI, 0.74 to 0.96) compared to the lowest green tea intake, though findings were inconsistent across study designs [21]. The relative risks of colorectal cancer with green tea intake from cohort studies, population-based case-control studies, and hospital-based case-control studies were 1.00, 0.74, and 0.53, respectively.

Pancreatic cancer: DECREASED

In a 2020 Cochrane meta-analysis of 20 observational studies, the highest green tea intake was associated with a significantly lower pancreatic cancer risk (RR=0.88, 95% CI, 0.70 to 1.10) compared to the lowest green tea intake, though findings were inconsistent across studies [21].

Endometrial Cancer: DECREASED

A meta-analysis of 7 observational studies showed that tea consumption is associated with a lower risk of endometrial cancer (RR for ever-drinkers vs non/lowest drinkers was 0.85, 95% CI, 0.77-0.94) [48]. An increase in tea intake by 2 cups/day was associated with a 25% lower risk of endometrial cancer. The protective association was more evident for green tea compared to black tea.

In a 2020 Cochrane meta-analysis of observational studies, higher green tea intake was associated with a lower endometrial cancer risk (RR=0.69, 95% CI, 0.57 to 0.83)[21].

Prostate cancer: DECREASED

In a large meta-analysis of various cancers, observational studies with higher methodological quality and 1 RCT suggested that men consuming higher quantities of green tea or green tea extracts have a lower risk of prostate cancer (RR ranged from 0.24-0.99)[49].

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In a 2020 Cochrane meta-analysis of 3 randomized controlled trials in people with high risk of prostate cancer (high-grade prostatic intraepithelial neoplasia), treatment with green tea extract significantly reduced risk of prostate cancer (RR=0.50, 95% Cl, 0.18 to 1.36)[21]. In the Cochrane meta-analysis of observational studies, the highest green tea intake (RR=0.73; 95% Cl, 0.56 to 0.94) was significantly associated with a lower risk of prostate cancer compared to the lowest intake of green tea. A significant association between the highest green tea intake and lower prostate cancer risk was observed in population-based studies (RR=0.59, 95% Cl, 0.40 to 0.87) and for hospital-based studies (RR=0.50, 95% Cl, 0.39 to 0.63).

Ovarian cancer: DECREASED

In a 2020 Cochrane meta-analysis of 5 population-based case-control studies, the highest green tea intake was associated with a 36% lower ovarian cancer risk compared to the lowest green tea intake (RR=0.64, 95% CI, 0.45 to 0.90)[21].

Oxidative stress: DECREASED

In a 2024 meta-analysis of 10 randomized controlled trials, green tea extract supplementation (varied between 60 to 3000 mg/day) for 2-48 weeks significantly reduced an oxidative stress marker, malondialdehyde (MDA; WMD=-0.32 µmol/l; 95% CI, -0.46 to -0.19; p<0.001)[37]. Subgroup analysis showed that green tea extract supplementation significantly reduced MDA when doses were <1000 mg/day, doses were ≥ 1000 mg/day, in studies that enrolled women, in short-term studies under 12 weeks, and in people younger than 50 years old. A meta-analysis of 11 randomized controlled trials showed that green tea extract supplementation significantly increased total antioxidant capacity (TAC; WMD=0.10 mmol/l; 95% CI, 0.06 to 0.15, p<0.001). TAC was significantly increased in studies that enrolled men, short-term studies of under 12 weeks, and in people younger than 50 years old.

Inflammation: MIXED

In a 2024 meta-analysis of randomized controlled trials in people with metabolic syndrome and related disorders, green tea supplementation (green tea extract, green tea leaf powder, or EGCG) for 4 to 16 weeks significantly decreased TNF- α levels (-0.4293 pg/mL; 95% CI, -0.7821 to -0.0764; p=0.0171) but did not affect CRP and IL-6 levels [50]. Subgroup analysis showed that green tea supplementation in studies lasting \leq 8 weeks significantly increased levels of CRP.

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Safety: Multiple meta-analyses have concluded that green tea consumption at moderate amounts is safe with mild side effects, but it is worth paying attention to the source of the tea leaves, as those grown in areas of excessive pollution can have lead contamination.

Types of evidence:

- 4 Cochrane meta-analyses
- 1 meta-analysis analyzing the link between hot tea drinking and esophageal cancer
- 3 case studies on excessive tea drinking and skeletal fluorosis
- Several articles on tea leaf contamination from soil and pollution

Meta-analyses: There are 3 Cochrane meta-analyses that have included analysis of the safety profile of green tea. A Cochrane meta-analysis based on 14 RCTs in overweight or obese adults (total of 703 subjects) reported that side effects from green tea consumption were mild and none of the serious adverse events observed were related to the intervention [36]. In another Cochrane meta-analysis based on 11 RCTs in healthy adults and those at high risk of cardiovascular disease (total of 821 subjects), side effects were mild and no significant differences in adverse events were observed between green tea and placebo groups [27]. In another Cochrane meta-analysis based mostly on observational studies (27 case-control studies, 23 cohort studies, and 1 RCT) that included a total of over 1.6 million subjects, green tea was judged to be safe at moderate and regular amounts (3 to 5 cups per day, up to 1200 ml/d) [49].

A 2020 Cochrane meta-analysis reported that treatment with green tea extract resulted in some adverse effects including gastrointestinal issues, elevation of liver enzymes, and more rarely, insomnia, raised blood pressure, and skin/subcutaneous reactions [21].

Drug interactions: Three drugs are known to interact with green tea, but the interactions are judged to be minor and minimally clinically significant (<u>drugs.com</u>). The three drugs are warfarin (also known as Coumadin[™] and Jantoven[™]), anisindione (or Miradon[™]), and dicumarol. Caffeine in green tea can also interact with some drugs (<u>drugs.com</u>).

Lead: Tea leaves can absorb lead from the soil, and according to the ConsumerLab.com analysis, tea from Lipton and Bigelow contained up to 2.5 μ g of lead per serving, compared to no measurable amounts from Teavana tea, which sources tea leaves from Japan [51]. Green tea from areas with excessive pollution may contain higher amounts of lead [52]. While lead is not thought to readily seep

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into the fluid from steeping, lead contamination is a concern if you are drinking matcha, as the whole tea leaves are consumed.

Fluoride: Fluoride is known to prevent dental cavities and tap water is fluoridated in many areas of the US. While tea is safe when consumed in moderate amounts, long-term and excessive amounts of tea consumption can cause bone problems from fluoride in tea leaves. A case study reported that a 47 year-old woman who consumed a pitcher of tea made from 100 to 150 tea bags (estimated fluoride levels, > 20 mg/d) every day for 17 years developed skeletal fluorosis [53]. Several other case studies have also reported skeletal fluorosis in people who consumed gallons of tea daily for several decades [54; 55].

Esophageal cancer: In a 2022 meta-analysis of 12 case-control studies, hot tea drinking (not necessarily green tea) was significantly associated with the risk of esophageal cancer (pooled OR=2.04; 95% Cl< 1.78 to 2.31)[56]. The authors note that heat stress can damage the barrier function of esophageal mucosa, which may increase the risk of gastric acid reflux that in turn damages the esophagus. One caveat of this meta-analysis is that most studies did not include objective measures of tea temperature. It is also worth adding that green tea is typically brewed at ~80°C (and even lower temperatures for some forms of green tea such as gyokuro), which is lower temperature than black tea (typically with boiling water at 100°C).

In a 2021 dose-response meta-analysis that specifically examined the relationship between green tea intake and risk of esophageal cancer, there was no significant association between green tea intake and risk for esophageal cancer (OR=1.00, 95% CI, 0.95 to 1.04)[57]. In this meta-analysis, 14 observational studies were included, with 5057 total cases of esophageal cancer and 493,332 participants. Of the 14 studies, 11 were in East Asia, 1 was in Europe, 1 was in Iran, and 1 was in India.

Sources and dosing:

There are multiple types of green tea. Sencha, the most common type of green tea in Japan, contains 40~60 mg of caffeine, 8~25 mg of L-theanine, and 25~60 mg of EGCG in a cup (200 mL). Gyokuro, a type of green tea that is produced from shading the tea leaves, contains 240 mg of caffeine, 85 mg of L-theanine, and 86 mg of EGCG per cup. Matcha is powdered Japanese green tea often used in Japanese tea ceremony and contains 25 mg of caffeine, 36 mg of L-theanine, and 17-109 mg of EGCG per serving (80 ml) [58], along with vitamins A, B-complex, C, E, K, and trace minerals. No clinical studies have compared these different types of green tea for long-term heath associations. In observational studies,

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high green tea consumption has often been defined as those who consumed over 7 cups of tea in Asia and over 2 cups of tea in the US [48].

Research underway:

There are numerous clinical trials ongoing that are testing the effects of green tea in various conditions, such as cardiovascular diseases, metabolic diseases, gingival disease, various cancers, glaucoma, and others (<u>ClinicalTrials.gov</u>).

The PENSA study, which is part of the World Wide FINGERS Initiative, is testing if a multimodal lifestyle intervention combined with EGCG (<u>BarcelonaBeta.org</u>).

Search terms:

Pubmed, Google: Green tea

+ cognitive, + memory, + dementia, + meta-analysis, + systematic review, + ApoE4, + cancer, + cardiovascular, + diabetes, + safety

Clinicaltrials.gov: Green tea, EGCG, L-theanine, matcha

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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact <u>INFO@alzdiscovery.org</u>. To view our official ratings, visit <u>Cognitive Vitality's Rating page</u>.

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