



## EGCG

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Green tea, white tea, and black tea are made from dried leaves of *Camellia sinensis*, a perennial evergreen shrub. Up to 40% of the dry weight of tea leaves is accounted for by antioxidants called catechins; epigallocatechin gallate (EGCG) is the most abundant catechin found in green tea. EGCG could theoretically promote brain health, but no studies have evaluated whether it can protect from cognitive decline or dementia. EGCG supplements are considered safe for most people, but high doses may affect liver function.

### EVIDENCE AND POTENTIAL BENEFIT FOR BRAIN HEALTH

#### Rated 2/4 based on 2/4 evidence

Long-term studies are lacking and no studies have evaluated whether EGCG may slow cognitive decline or prevent dementia. Short-term studies show minor benefits at best.

Randomized controlled trials: No human studies have evaluated whether EGCG can protect from cognitive decline. Some positive effects of EGCG on cognitive function have been observed in people with Down syndrome, though the doses used were very low compared to other clinical studies [1; 2]. In a pilot study of 29 patients with Down syndrome, EGCG (9 mg/day) for 3 months significantly improved episodic memory [2]. The EGCG-treated group showed a higher percentage of correct answers in visual memory recognition compared to placebo and a trend for a benefit with EGCG was observed for working memory and psychomotor speed. In a phase 2 double-blind randomized controlled trial (RCT) of 84 people with Down syndrome, EGCG (9 mg/day) treatment combined with cognitive training for 6 months was associated with significantly higher scores in visual recognition memory, inhibitory control, and adaptive behavior compared to the group receiving placebo with cognitive training [1]. However, this protective effect was evident in only 3 out of 24 cognitive tests and no significant differences were seen in measures of social skills or quality of life. Phase 3 trials will be needed to assess and confirm long-term efficacy of EGCG and cognitive training in this population.

Effects of acute EGCG treatment have also been examined in healthy adults. In one double-blind RCT of 31 healthy adults, EGCG treatment significantly increased calmness and reduced stress, and EGCG treatment was associated with a significant overall increase in alpha, beta, and theta activities [3], which are associated with relaxation, arousal/focused attention, and quiet wakefulness, respectively [4]. These results are consistent with anecdotal accounts that green tea is relaxing and alerting. In another double-blind RCT in healthy adults, administration of 135 mg EGCG resulted in reduced cerebral blood flow in



the frontal cortex compared to placebo, but no significant differences were observed for cognitive performance or mood measures [5].

Biology: Preclinical studies have found a wide range of actions of EGCG, including chelating metals, reducing inflammation, scavenging free radicals, improving mitochondrial function, and preventing death of brain cells [6]. *In vitro* and *in silico* studies have also shown that green tea polyphenols inhibit acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) [7; 8].

In Alzheimer's disease mouse models, EGCG treatment (10-50 mg/kg/day) resulted in many benefits: improved cognitive function [9; 10], improved psychomotor coordination [11], reduction of both soluble and insoluble A $\beta$  levels in the cortex and hippocampus [10], reduction of phospho-tau [10], improved AChE activity [9], and improved measures of oxidative stress (glutathione peroxidase activity, nitric oxide metabolites, and reactive oxygen species) [9].

In a mouse model of accelerated aging (SAMP8), EGCG treatment (5-15 mg/kg/day) for 60 days rescued cognitive decline and reduced A $\beta$  accumulation [12]. In a rat model of chronic unpredictable mild stress, EGCG treatment (25 mg/kg/day, i.p.) significantly improved memory performance, attenuated pathological abnormalities in the hippocampus, reduced A $\beta$  levels, and restored autophagic flux [13].

The four major tea catechins are EGCG, epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC). In young rats that were treated for 26 weeks with polyphenon E, a mixture of these four catechins (63% EGCG, 11% EC, 6% EGC, and 6% ECG, dissolved in water), cognitive benefits were observed [14]. Polyphenon E-treated rats had improved reference and working memory. They also had lower plasma concentration of lipid peroxides, decreased reactive oxygen species in the hippocampus, and greater plasma ferric-reducing power compared to controls.

Doses used in rodent studies are comparable to those used in human clinical studies after accounting for differences in body surface area [15]. While a pharmacokinetic study in healthy volunteers has shown that a single dose of EGCG (up to 1600 mg) can result in micromolar plasma concentration (130-1392 ng/ml), remaining questions include the extent of blood-brain-barrier permeability and the optimal doses of EGCG for possible neuroprotection in humans.



### For Dementia Patients

No studies have tested whether EGCG alone is beneficial to patients with dementia. While some benefits have been observed in preclinical studies of Alzheimer's disease, including improved cognitive function [9; 10] and reduction of pathological markers of Alzheimer's [10], these effects have not been confirmed in people with dementia.

### SAFETY

#### Rated 3/4

In a systematic review, randomized controlled trials (RCTs) were found that examined the effects of relatively high doses of green tea extracts (containing 800–1600 mg of EGCG or 500 mg of green tea polyphenol). A few cases of liver enzyme elevation were reported, but most of these cases were mild and there were no serious liver-related adverse events [16]. Based on these analyses, liver-related adverse events with green tea extracts are expected to be rare. In a large double-blind RCT of 1075 postmenopausal women, 843 mg of EGCG taken daily for 1 year was associated with a higher incidence of liver enzyme (alanine aminotransferase; ALT) elevation, and 1.3% of women experienced ALT-related serious adverse events [17]. In a smaller double-blind RCT of 83 obese women, EGCG treatment (300 mg/day) for 12 weeks did not cause any adverse effects on liver function biomarkers [18]. Liver-related adverse events may be more common at higher doses. Another common side effect of EGCG supplementation is nausea [17; 19].

**Drug interactions:** Three drugs are known to interact with green tea, but the interactions are judged to be minor and minimally clinically significant ([drugs.com](https://www.drugs.com)). 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 ([drugs.com](https://www.drugs.com)).

### HOW TO USE

Very wide ranges of doses, from 9 to 1200 mg per day, have been used in clinical trials examining the effects of EGCG on cognitive function, cholesterol levels, blood pressure, and insulin resistance. Many studies using 300–400 mg/day [3; 18; 20]. One third-party company offers a [top 10 list of green tea supplements](#), based on label accuracy, purity, contaminants (lead and arsenic), and safety.

EGCG is also abundant in green and white tea. Black tea contains much lower levels of EGCG (~20 mg) as it is converted during the oxidation process to thearubigin, a different type of polyphenol [20]. Sencha, the most common type of green tea in Japan, contains 40–60 mg of caffeine, 8–25 mg of L-theanine, and 25–200 mg of EGCG per 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) [21], along with vitamins A, B-complex, C, E, K, and trace minerals.

It has been reported that EGCG bioavailability may be improved with cool and dry storage, fasting conditions, albumin, soft water, vitamin C, fish oil, and piperine [22], but we have not evaluated the evidence behind these claims. Factors that theoretically may decrease bioavailability include: air contact oxidation, gastrointestinal inactivation, calcium, magnesium, metals, catechol-O-methyltransferase (COMT; an enzyme that degrades dopamine, norepinephrine, and epinephrine) polymorphisms, sulfation, and glucuronidation.

### WHAT'S THE FUTURE?

A clinical trial is testing whether a brain health supplement (BBG-1001) that contains green tea extract, turmeric, fish oil, and vitamin D can slow cognitive decline in people with mild cognitive impairment ([NCT02741804](https://clinicaltrials.gov/ct2/show/study/NCT02741804)). This study is scheduled to be completed in May 2019. This study has not started recruiting participants yet.

Unanswered questions include the extent of blood-brain-barrier permeability and the optimal dose of EGCG, as well as more trials testing whether EGCG can influence brain health and cognition.

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