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Report

## How Green Tea Protects Against Alzheimer's Disease

By Michael Downey

Green tea is well known for its defense against some of the most common and deadly diseases in America, including cardiovascular disease,<sup>1-3</sup> insulin resistance,<sup>4</sup> obesity,<sup>5-7</sup> autoimmune disorders,<sup>8,9</sup> and cancer.<sup>10-14</sup>

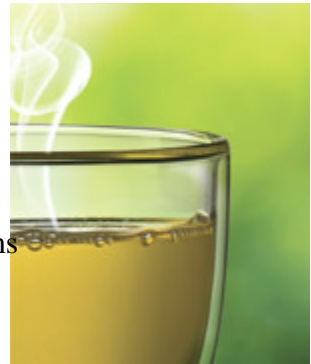
Recent developments have uncovered one of green tea's most exciting benefits discovered to date: its potential to prevent—and possibly reverse—the effects of Alzheimer's disease and other forms of dementia.<sup>15-19</sup>

Alzheimer's disease occurs as a result of your brain cells being impaired, and eventually killed. This is partially caused by the buildup of toxic protein fragments called *amyloid beta*.<sup>15,16</sup>

Green tea gets to the root of Alzheimer's disease by three distinct mechanisms: preventing the formation of amyloid plaques, breaking down existing plaques, and creating critical new neurons in the brain.

As a result, green tea consumption has now been associated with a **54%** reduction in the risk of developing cognitive decline.<sup>20</sup>

And now, in an exciting development, scientists have used *neuroimaging scanning* for the first time in a human clinical setting to demonstrate that **green tea extract** boosts activity in an area of the brain specifically used for working memory.<sup>19</sup>



## How Alzheimer's Disease Occurs



Alzheimer's disease is the **sixth** leading cause of death in America and the **fifth** leading cause of death in those 65 or older.<sup>21</sup> A shocking **one in three** seniors dies with Alzheimer's or another form of dementia.<sup>21</sup> Experts have recently predicted that the number of people living with dementia will nearly triple by 2050.<sup>22,23</sup>

Alzheimer's disease is a progressive, devastating, and eventually fatal neurodegenerative brain disorder.<sup>24,25</sup> It is caused when tightly bound protein sheets known as *amyloid* plaques slowly form in the brain. These plaques eventually create neuronal damage and loss. Then, deprived of their oxygen supply, brain cells begin to die.<sup>26</sup> Eventually, the result is memory and speech loss,<sup>27</sup> diminished motor skills,<sup>28</sup> and ultimately—death.<sup>29</sup>

Amyloids are a complex of stable misfolded proteins, and no current drug therapies have been able to halt or reverse their deadly impact on the central nervous system.<sup>30,31</sup> There are five drugs approved for Alzheimer's, but they only *partially* treat *some* of the symptoms and only *temporarily*—for about six to 12 months—and only for about *half* of the patients who take them.<sup>32</sup> That's not a promising track record for these expensive pharmaceutical drugs.<sup>33</sup>

Given this obvious void in either treating or preventing Alzheimer's, scientists have continued searching for natural interventions that would battle the disease at its root: by inhibiting the formation and accumulation of the *amyloid* plaques and blocking them from being toxic.

Scientists have found that green tea has three distinct actions that reduce neurodegeneration and protect against Alzheimer's by:

- **Preventing** formation of *amyloid* plaques that are characteristic of Alzheimer's disease,<sup>34</sup>
- **Breaking down** existing *amyloid* plaques by disrupting early-stage and late-stage aggregation processes,<sup>15</sup> and
- **Promoting** the production of **new neurons** (*neurogenesis*) in the adult hippocampus, the area of the brain responsible for converting memories from short-term to long-term.<sup>35</sup>

## Green Tea's Dramatic Impact On Neurodegeneration

**Green tea** (*Camellia sinensis*) contains *catechins*, which are naturally occurring, multifunctional compounds that have been found to have potent neuroprotective effects.<sup>36,37</sup> Specifically, the powerful green tea catechin *epigallocatechin-3-gallate* (EGCG) has been found to lessen cognitive impairments induced by psychological stress in rodent research,<sup>38</sup> which suggests its potential to be an effective protector of brain neurons.<sup>39</sup> EGCG has been shown to cross the blood-brain barrier in mammals.<sup>40,41</sup>

Laboratory investigations have revealed that—unlike other flavonoids—green tea compounds are able to **reduce** neurodegeneration.

When the catechins in green tea were scientifically tested in a wide array of cellular models of neurological diseases, they exhibited dramatic iron-chelating, free-radical-scavenging, and anti-inflammatory activities.<sup>42</sup> They were also neuroprotective in models of both Alzheimer's and Parkinson's disease.<sup>43</sup>

Further investigation of these promising compounds showed that they enhanced gene modulating and cell-signaling activities,<sup>42</sup> favorably increased detoxifying enzymes and antioxidant enzymes,<sup>44,45</sup> and protected DNA against oxidative damage.<sup>46</sup>

## Combating The Underlying Factors Of Alzheimer's

Green tea compounds have demonstrated additional actions on the factors involved in the development of Alzheimer's disease.

Studies on brain hippocampal cells of rats showed that green tea extract inhibited the formation of amyloid-beta *fibrils*, or fine fibers. This was a crucial finding because these amyloid fibrils are implicated in neuron death<sup>41</sup> and Alzheimer's-related cognitive symptoms.<sup>47</sup>

Amyloid-beta fragments (fibrils) require copper, iron, or zinc to aggregate into stable plaques.<sup>48,49</sup> A **2013** study in the *Proceedings of the National Academy of Sciences* found that EGCG interfered with pathways involved in the binding of copper and zinc to amyloid-beta fragments, thus preventing the formation of larger, stable amyloid plaques.<sup>15</sup>

A **2010** study, documented in the *Proceedings of the National Academy of Sciences*, determined that the way EGCG stops the accumulation of amyloid-beta is by transforming amyloid fibrils into shapes that are stable and not toxic to cells.<sup>16,50</sup> Sticky and toxic amyloid aggregates of varying shapes adhere to neurons by attaching themselves to misfolded proteins called *prions* on the cells' surfaces. The study found that EGCG changed the shapes of these amyloid fibrils so they could no

longer bind to the prions.<sup>16</sup>

Once research determined the effect green tea had on the underlying factors involved in the process of developing Alzheimer's disease, scientists set out to determine if green tea compounds would block actual neurodegeneration in experimental animals and—more importantly—in healthy humans.

#### WHAT YOU NEED TO KNOW

### Green Tea Extract Battles Alzheimer's Disease

- Amyloid-beta accumulates in the brain and occupies, and often kills, nerve cells—resulting in **Alzheimer's** disease, the **sixth** leading cause of death in the US.
- A growing body of compelling evidence demonstrates that **green tea extract** greatly reduces the risk of Alzheimer's and other forms of dementia.
- Researchers found that the potent green tea compound **EGCG** prevents amyloid plaque buildup, breaks down existing amyloid plaques, and triggers production of *new neurons* in the adult hippocampus.
- In an exciting breakthrough, scientists have used MRI scanning in a human clinical setting to watch in real time the immediate boost in working-memory activity that green tea extract produces—confirming the potent neuroprotection of green tea molecules.



### Green Tea Improves Age-Related Memory Problems

Amyloid-beta plaques affect rodent brains similarly to human brains in that the accumulation of amyloid-beta quickly leads to the development of Alzheimer's-like memory problems.<sup>51,52</sup> This makes them especially valuable in Alzheimer's research.

Scientists administered EGCG into a group of mice with simulated aging to determine its effect on age-related memory loss.<sup>53</sup> For this study, researchers divided healthy male and female mice into four groups: The first group received *D-galactose* (a type of sugar that causes accelerated aging,<sup>54</sup> but no EGCG); the second and third groups received *D-galactose* plus two different doses of EGCG; the fourth group received a placebo.<sup>53</sup>

As expected, the group injected with *D-galactose*—but not with EGCG—showed learning and memory impairment in a water maze test, compared to non-aged controls. This was not surprising considering similar impairment occurs in aging humans and Alzheimer's patients. In this aging-induced group, researchers also observed decreased activities of two powerful antioxidants, *total superoxide dismutase (T-SOD)* and *glutathione peroxidase (GSH-Px)*. And in the hippocampus, they noted increased levels of *malondialdehyde (MDA)*, a dangerous marker for oxidative stress. Cell death, or apoptosis, was also increased.<sup>53</sup>

The two groups that were injected with both *D-galactose* and EGCG showed almost the opposite response of the *D-galactose*-only group. These groups experienced marked improvement in memory and learning deficits, elevated T-SOD and GSH-Px activities, decreased MDA contents in the hippocampus, and reduced cell apoptosis. The researchers concluded: “*The results suggest that EGCG has potent neuroprotective effects on aging mice.*”<sup>53</sup>

Although tea comes in many varieties, evidence suggests that the healthiest choice may be green tea, due to its high concentration of powerful polyphenols.

Beneficial polyphenols make up roughly **30 to 40%** of green tea, as opposed to only **3 to 10%** of black tea. The polyphenols in tea are classified as *catechins*, and of the eight catechins in green tea, *epigallocatechin-3-gallate*, or EGCG, is the most active.<sup>60</sup>



Green tea catechins scavenge oxygen-free radicals, restoring cells to health and reducing inflammation. Because inflammation underlies so many age-related afflictions, green tea may have a myriad of applications in preventing disease.<sup>61,62</sup>

Findings from animal studies suggest that green tea polyphenols promote the repair of damaged DNA. Since DNA damage can lead to cancer, green tea may play an important role in preventing cancer.<sup>63</sup>

The EGCG in green tea has been shown to produce *apoptosis* (cell death) in experimental prostate cancer, inhibit the growth of squamous cell carcinomas of the head and neck, inhibit the production and limit the invasion of experimentally induced breast cancers, reduce the incidence of carcinogen-induced lung cancers, and sensitize melanoma cells to growth inhibition by other agents.<sup>10-14,64</sup>

Green tea is also well-known to provide substantial defense against an array of diseases, including cardiovascular,<sup>1-3</sup> insulin resistance,<sup>4</sup> obesity,<sup>5-7</sup> and autoimmune.<sup>8,9</sup>

High-quality extracts are available that provide green tea compounds standardized to **45%** EGCG and **98%** polyphenols so individuals can derive the maximum benefit from green tea without having to drink numerous cups of tea each day.

## Green Tea Gets To The Root Of Alzheimer's

This finding indicated that EGCG provides neurons with strong protection against the cognitive and memory impairments associated with aging. Scientists next wanted to determine if these effects occurred as a result of inhibiting the accumulation of *amyloid* plaques.

So in late **2013**, researchers in China reporting in the journal *Molecular Neurobiology*, conducted a similar experiment—this time focusing specifically on the effects of EGCG on amyloid.<sup>55</sup>

In order to test this, investigators administered EGCG daily to age-matched, male and female APP/PS1 mice.<sup>55</sup> (APP/PS1 transgenic mice are those that are genetically inclined to increased expression of *amyloid precursor protein* and amyloid-beta. They imitate the physical and behavioral changes of Alzheimer's disease and have early-onset Alzheimer's, and to a more intense degree, amyloid plaque buildup.)

As in the previous study, behavioral tests demonstrated that EGCG treatment had improved learning and memory impairment in the APP/PS1 mice, reduced the death of brain neurons, and significantly reduced hippocampal neurodegeneration after four weeks. However, this time scientists determined that EGCG also dramatically reduced the levels of *amyloid precursor protein* and reduced the buildup of *amyloid-beta plaques* in the hippocampus.<sup>55</sup>

Together, these impressive findings answered the question as to whether EGCG can block the accumulation of amyloid-beta plaques and other factors associated with the development of Alzheimer's disease symptoms.

But Chinese researchers posed another extremely tantalizing question: If EGCG can prevent changes associated with the

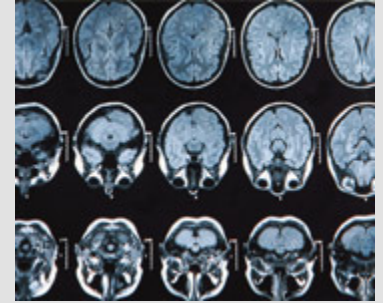
death of hippocampal neurons in the development of Alzheimer's, could it also trigger the production of new hippocampal neurons—in effect *reversing* the effects of this disease?

Shockingly, the answer is yes.

#### HOW GREEN TEA PROTECTS THE BRAIN

EGCG is the most potent neuroprotective compound in green tea, as well as its most abundant polyphenol.<sup>60</sup>

Initially, researchers wondered if green tea's beneficial effects on the brain occurred as a result of its antioxidant activity.<sup>65</sup> Although free-radical quenching may indeed play a part, a wealth of studies finally determined that EGCG's antioxidant activity could *not* fully explain its broad and powerful neuroprotective effects.<sup>66</sup>



Scientists now realize that EGCG's neuroprotection works through multiple higher-level mechanisms. Through a significant number of *in vitro* studies, it appears that EGCG protects the brain via at least nine mechanisms:

1. **It interferes with the assembly of amyloid-beta proteins.**<sup>67</sup>
2. **It inhibits the formation of amyloid-beta fibrils**, halting their aggregation to plaques.<sup>41</sup>
3. **It prevents the proper binding of copper and zinc**, which is required for the creation of stable amyloid-beta plaques.<sup>15</sup>
4. **It changes the shape of amyloid fibrils**, preventing them from binding to neuronal prions<sup>16</sup> and transforming them into shapes that are not toxic to neurons.<sup>68</sup>
5. **It inhibits the toxicity to neurons** that would otherwise be induced by hydrogen peroxide<sup>69</sup> and amyloid-beta.<sup>34,69-72</sup>
6. **It prevents mitochondrial dysfunction**, usually induced by amyloid-beta in brain cells.<sup>73</sup>
7. **It normalizes responses of brain cells** to an excitatory neurotransmitter (NMDA).<sup>74</sup>
8. **It down-regulates pro-apoptotic genes.**<sup>66</sup>
9. **It up-regulates kinase enzymes**, such as protein kinase C.<sup>72</sup>

## Reverse The Effects Of Alzheimer's Disease

The production of new adult neurons, a process called *neurogenesis*, is the key feature of brain plasticity, which is critical to brain function as we age.<sup>17</sup>

Producing new adult neurons in the hippocampus (the part of the brain that converts information from short-term to long-term memory<sup>56</sup>) may serve as a new treatment strategy for early stage Alzheimer's or other forms of dementia.<sup>57</sup> That's why scientists focused their attention on the effects of EGCG on neurogenesis in this specific area of the mouse brain.<sup>17</sup>

Amazingly, both the *in vitro* and *in vivo* results of this study showed that EGCG boosts the production of *neural progenitor cells*, which are brain cells that can transform into various types of neural cells.<sup>17,58</sup>

In order to determine if this increased brain-cell production would result in a direct boost in memory or spatial learning, the researchers gave one group of lab mice EGCG from green tea, while the other group was given a placebo containing no

EGCG. The mice were subsequently trained for seven days to find a hidden platform.

The mice that were administered EGCG found the hidden platform substantially faster—indicating that EGCG’s ability to enhance the production of *new* adult neurons had directly boosted learning and memory by improving object recognition and spatial memory.<sup>17</sup>

What’s remarkable is that EGCG promotes the production of new neurons in the same area of the brain in which neurons are killed during the development of Alzheimer’s disease!

This study offers an exciting look into the potential to not only prevent—but *reverse* —the effects of Alzheimer’s disease in the brain.

However, the real challenge was whether this effective green tea compound would deliver the same preventive effect to healthy humans.

Continued on [Page 2](#) of 2

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### Live Images Reveal Immediate Memory Enhancement



Data about the consumption of black, oolong, or green tea and cognitive function was obtained and examined for over 1,000 Japanese subjects age 70 or over during a period of four months. Analysis of the data revealed that consumption of 2 or more cups per day of green tea reduced the odds of cognitive impairment by **54%**, whereas those that consumed equal amounts of black or oolong tea had an odds reduction of only **13%**.<sup>20</sup>

However, this was a cross-sectional study that did not provide hard scientific evidence of effectiveness. To achieve more definitive results, scientists use double-blind, placebo-controlled studies. Unfortunately, it is extremely difficult to conduct intervention studies that would continually monitor human volunteers for adherence and allow for the time required to sufficiently establish, through memory tests, whether green tea enhances memory and recall.

But in a recent study published in the *European Journal of Clinical Nutrition*, scientists performed the first neuroimaging study allowing them to see the real-time effects of green tea extract inside the human brain’s working-memory area!<sup>19</sup>

On four separate occasions, with a one-week interval between sessions, healthy volunteers between 21 and 28 years old consumed either a placebo drink, a **250 mL**, or a **500 mL** combination drink containing green tea extract. The researchers used a feeding tube to rule out taste as a factor.

After consuming the drink, the subjects then performed a memory-stimulating task while researchers simultaneously monitored their brain function using functional magnetic resonance imaging, or fMRI, to zero-in on the working-memory region.

Thanks to this imaging technique, rather than relying on possibly imperceptible differences in performance on a brief

memory test following a single dose or even a week of supplementation—scientists could watch the volunteers’ working memories in action on a second-by-second basis.

Compared to placebo, the beverages containing green tea extract significantly **boosted** activity in the *dorsolateral prefrontal cortex*—the area of the brain used for working-memory processing.<sup>19,59</sup> This small region allows the brain to simultaneously store and process information, and it facilitates complex cognitive tasks, such as language comprehension, reasoning, and learning.

Activity in this memory area was increased even further by the higher dose drink.<sup>19</sup> This dose-related response backs up the cause-and-effect connection between green tea and improved memory processing.

Not only did this finding confirm green tea extract’s immediate and significant enhancement of working-memory activity, the researchers noted that it also established for the first time the effectiveness of neuroimaging in observing green tea’s instant impact on the human brain.<sup>19</sup>

Taken together, all of these findings indicate green tea extract’s marked protection of brain neurons by inhibiting the formation of *amyloid-beta fibrils* and other processes associated with Alzheimer’s disease and, possibly, by triggering the production of new brain **neurons**.

## Summary

*Amyloid-beta plaques* slowly form in the brain and interfere with nerve cells, often killing them. The tragic result too often is Alzheimer’s disease—the sixth leading cause of American deaths.

Accumulating evidence demonstrates that **green tea extract** may reduce the risk of Alzheimer’s disease and other forms of cognitive decline by **54%**.

Studies show that the powerful green tea compound **EGCG** prevents formation of amyloid plaques, breaks down existing amyloid plaques, and promotes production of new neurons in the adult hippocampus.

In an exciting development, scientists used MRI scanning for the first time in a human clinical setting to watch the immediate boost in **working-memory activity** that green tea extract produces—illustrating in real-time the potent neuroprotection of green tea compounds.

If you have any questions on the scientific content of this article, please call a **Life Extension**<sup>®</sup> Health Advisor at 1-866-864-3027.

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