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## LifeExtension™

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### ALL ABOUT SUPPLEMENTS

#### Theanine

An Amino Acid from Tea Has Numerous Health-Protecting Effects By Dale Kiefer



Cultivated and used as a medicinal plant for thousands of years, tea is undoubtedly one of China's most important contributions to global civilization. Indeed, enjoying a carefully brewed cup of tea epitomizes civilized life in much of the world. Whether green tea brewed from fresh-picked leaves, or black and oolong teas made from the dried, fermented leaves of the perennial shrub *Camellia sinensis*, tea is second only to water as the world's most popular beverage.<sup>1</sup>

Although tea has been revered for its healthful properties since ancient times, only in recent decades have scientists seriously endeavored to unravel tea's chemical secrets. This research has confirmed what folk healers have long claimed: tea both calms and invigorates, while protecting against various ailments and even contributing to a longer, healthier life.

Tea contains a unique blend of chemicals with a variety of health-enhancing properties. Catechin polyphenols, for instance, are potent antioxidant and anti-inflammatory compounds.<sup>2</sup> The best known of these is epigallocatechin-3 gallate (EGCG), a chemical credited with benefits ranging from fighting cancer to promoting fat and weight loss.<sup>2-6</sup> Ingested or topically applied green tea polyphenols are even credited with protecting the skin from ultraviolet radiation-induced skin damage.<sup>2</sup>

In addition to EGCG, green tea contains other compounds with equally beneficial bioactive properties. One lesser known but no less important of these compounds is an amino acid called theanine.

#### CALMING PROPERTIES

Theanine is found almost exclusively in the leaves of *Camellia sinensis*, a relative rarity in the plant kingdom, where chemical redundancy is the norm.<sup>1</sup> Theanine accounts for up to 50% of the dry protein weight of green tea.<sup>7</sup> Of course, tea also contains caffeine, a familiar stimulant. Theanine is credited with counterbalancing caffeine's stimulating effect by inducing relaxation. The precise mechanism by which theanine produces this anxiety-reducing effect remains uncertain, though theanine is known to alter levels of two important mood-regulating neurotransmitters, dopamine and serotonin.<sup>8,9</sup>

Researchers in Australia recently compared theanine to alprazolam (Xanax®), a standard medication used to treat anxiety. They found that theanine tended to reduce anxiety during a relaxation phase of the study, while the drug had no such effect. Neither substance significantly reduced feelings of anxiousness during a phase of the experiment in which anxiety was induced experimentally.<sup>10</sup>

In an earlier study, scientists used brain-wave monitoring (electroencephalograph, or EEG) to determine the lowest dose at which caffeine stimulated laboratory rats. They then administered theanine directly into the rats' bloodstreams at a similar dose and noted that theanine counteracted caffeine's stimulatory effect on the brain.

Interestingly, when theanine was given by itself at smaller doses—at less than half the “calming” dose—it had a stimulatory effect. The researchers concluded that theanine may have two different effects, stimulating or relaxing, depending on the dose.<sup>11</sup>



### RELAXING EFFECTS

Theanine has also been shown to reduce high blood pressure, further evidence that it induces relaxation.<sup>9,12</sup> Japanese researchers, for instance, have demonstrated that theanine reduces blood pressure in a dose-dependent manner in rats serving as a model for human hypertension (elevated blood pressure). The larger the dose of theanine given the rats, the more dramatic was the reduction in their blood pressure. Intriguingly, when control rats with normal blood pressure were given the highest dose of theanine, they experienced no change in blood pressure. It appears that theanine has no effect of lowering blood pressure in normal individuals, but instead affects blood pressure only when a problem already exists.<sup>9,12</sup>

### CARDIOVASCULAR SUPPORT

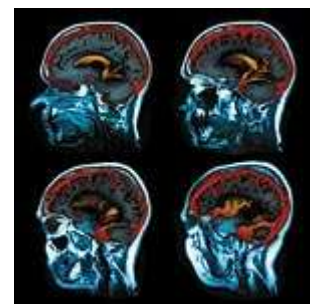
Theanine has also been shown to prevent lipid peroxidation of LDL (low-density lipoprotein), a protective effect that also undoubtedly contributes to tea’s reputation for promoting cardiovascular health. Peroxidation of lipids is thought to play a role in the development of degenerative conditions such as atherosclerosis.<sup>13</sup> Indeed, theanine appears to exert a variety of complementary, beneficial effects.

Japanese researchers experimented on rats with elevated lipid and triglyceride levels caused by liver tumors. After adding powdered green tea and theanine to the rats’ diet, the scientists concluded that theanine was at least partially responsible for suppressing tumors and lowering cholesterol and triglyceride levels. While the blood lipid changes may have resulted solely from the decrease in tumor mass, the scientists speculated that both tea and theanine exert anti-cancer as well as lipid-lowering effects.<sup>14</sup>

That explanation appears to be supported by the findings of another study, which determined that theanine plus green tea catechins, such as EGCG, reduced triglyceride levels in the serum and livers of laboratory mice. The mice also experienced a significant reduction in serum fatty acids while ingesting theanine and tea catechins, and lost significant body fat as well.<sup>6</sup>

### DEMONSTRATED NEUROPROTECTION

Theanine has been demonstrated to cross the blood-brain barrier.<sup>8</sup> In an epidemiological study of nearly 6,000 women living in Japan, those who consumed five or more cups of green tea a day were significantly less likely than non-tea drinkers to suffer stroke. In a follow-up to the study, researchers determined that women who routinely drank little or no green tea were more than twice as likely as heavy tea drinkers to suffer stroke or cerebral hemorrhage.<sup>15</sup>



Subsequent experiments have confirmed that theanine protects the brain from damage during ischemia, a condition in which the brain temporarily receives too little oxygen due to reduced blood flow, which may result from stroke.<sup>16</sup> A recent Japanese study showed that theanine significantly protects the brain after an ischemic incident occurs. Using a rodent model of cerebral artery blockage, researchers injected theanine immediately before or immediately before and three hours after blood flow to an area of the rodents’ brains was interrupted. Theanine significantly decreased the amount of tissue damaged by the temporary lack of blood. The scientists concluded that theanine provided direct nerve cell protection and

suggested that theanine “may be clinically useful for preventing cerebral infarction.”<sup>17</sup>

Efforts to explain this neuroprotective effect have focused on theanine’s close chemical similarity to an important neurotransmitter, glutamic acid (glutamate). Glutamate plays an important role in memory and learning. It is released by nerve cells into the extracellular space, where it normally elicits a desired response and is subsequently taken up by neurons for recycling. Interruptions in blood supply, as in stroke, interfere with this ability to recycle glutamate. Excess glutamate is released and builds up in the extracellular spaces, where it sets off a chemical chain reaction that results in neuronal death. Theanine is believed to compete with glutamate to bind with glutamate receptors, thus reducing glutamate toxicity.<sup>18-20</sup>

### ENHANCING CHEMOTHERAPY

The multifunctional molecule theanine has been shown to have anti-cancer effects, by making cancer-killing drugs more efficient while reducing toxicity to normal cells.<sup>21-25</sup> When co-administered with three common chemotherapeutic agents—doxorubicin, idarubicin, and pirarubicin—theanine prevents cancerous cells from ejecting the drugs after the drugs have entered the tumor cells. The result is increased chemotherapy effectiveness and decreased toxicity to healthy tissues.<sup>21-25</sup>

### PRIMING IMMUNITY

Proponents of tea consumption have long believed that tea enhances immunity. In a report published in 2003 in the *Proceedings of the National Academy of Sciences*, Harvard researchers provided scientific evidence to support this claim. According to the scientists, tea acts to prime the immune system to recognize bacterial, fungal, and parasitic invaders. It accomplishes this amazing feat, they revealed, by acting as a sort of natural vaccine that “teaches” immune system cells to recognize certain markers that are commonly present on the surfaces of tumor cells and invading pathogenic organisms.<sup>7</sup>



Tea contains antigens—structures known as nonpeptide alkylamines—that are capable of eliciting an immune system response. These alkylamines prime immune system T cells to produce memory and non-memory cytokines.<sup>26</sup> Cytokines are a broad category of immune system proteins that coordinate interactions between T cells and antibodies, while amplifying immune reactivity. Theanine is a precursor to ethylamine, an alkylamine found in brewed tea.

In human experiments, subjects consumed either tea (containing caffeine and a known amount of theanine) or coffee, which also contains caffeine but not theanine. Blood tests showed that tea drinkers, but not coffee drinkers, saw increased production of an important disease-fighting cytokine by their T cells.<sup>7</sup> When pathogens invade, their surfaces often bristle with alkylamines similar to those found in tea.<sup>26</sup> T cells that have been primed by prior exposure to theanine are better equipped to promptly recognize and neutralize the microbial threat.<sup>7</sup> The Harvard researchers concluded, “These data provide evidence that dietary intake of tea . . . containing alkylamine antigens or their precursors [for example, theanine] may prime human [gamma] [delta] T cells that then can provide natural resistance to microbial infections and perhaps tumors.”<sup>7</sup>

### CONCLUSION

Theanine is clearly one of nature’s remarkably beneficial compounds. While it is possible to ingest enough green tea daily to consume therapeutic doses of theanine, it may be more convenient to reap the benefits of this natural health enhancer by taking supplemental theanine in capsule form.

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## REPORT

### Theanine

#### Natural Support for Sleep, Mood, and Weight

By Terri Mitchell



Back when Europe was stone huts and the Mayans were playing soccer, the Chinese were drinking tea. Tea goes back at least 5,000 years as medicine and more than 1,000 years as a simple beverage. Made from the leaves of a bush related to flowering camellia, tea has had a starring role in major features such as the American Revolution and Zen Buddhism. The Japanese regard tea so highly that they've created a ceremony for it, and a separate little tea house in which to serve it.

The tea ceremony is remarkable in that it dramatizes tea's physical effects on the human body. Tea causes changes in body chemistry that rejuvenate, relax, enhance the ability to think, and change mood.<sup>1-6</sup> The biochemical changes provoked by tea are scientifically supported, and they're not due to caffeine.<sup>6</sup>

Among the latest discoveries about tea is that it can prevent depression and lower blood pressure.<sup>7,8</sup> Both green and black teas have beneficial health effects, the main difference being that black tea is oxidized. That would seem to destroy tea's bioactivity, but it does not. Black tea continues to prove itself in scientific studies. Researchers with the US Department of Agriculture, for example, recently reported that five cups of black tea a day can lower potentially harmful low-density lipoprotein (LDL) and total cholesterol in people with mildly elevated cholesterol.<sup>9</sup>

Black tea has benefits, but green tea has undergone more investigation, especially in Japan, where it's the most popular beverage. Many new reports have come out about green tea's amino acid, theanine, since Life Extension introduced it. The only other known source of this unique amino acid is a mushroom.<sup>10</sup> Discovered in 1949, yet just now undergoing substantial research, theanine occupies a place on the shelf quite different from that of other dietary supplements. It has to do with the tea ceremony.

#### BALANCING SLEEP/WAKE

Millions of Americans will have trouble sleeping tonight. They won't be able to fall asleep, won't be able to stay asleep, or won't feel like they slept. The primary reason is stress, followed by illness, inactivity, medications, and bad sleep environment. The net effect is a lot of grouchy, depressed, and accident-prone people.<sup>11</sup> Most won't see a doctor, even though insomnia can lead to depression, traffic accidents, and a pink slip. Instead, most people will reach for America's favorite drug: caffeine.

Every day, millions of people take caffeine in one form or another. It's not only in coffee, it's in fruity sodas, over-the-counter drugs, and diet elixirs. "Energy drinks" and espresso are popular caffeine fixes with megadoses of caffeine. Caffeine keeps Americans alert during the day, but it has a price. It can stay in the body for about 10 hours. That's if you have a fully functioning liver. If you drink alcohol or take cimetidine (Tagamet®) and other drugs, it will stick around even longer.<sup>12,13</sup> That means the cappuccino you had at three in the afternoon is still around at midnight.



To relax at night, Americans don't have many choices except prescription sleeping pills. But these drugs don't work for everyone, and have undesirable side effects. Better solutions are needed.

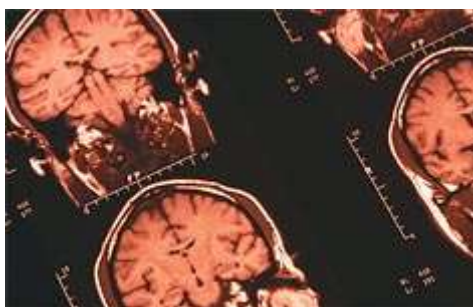
### TEA CEREMONY IN A CAPSULE

Relaxation, rejuvenation, focus. The tea ceremony energizes without draining, calms without putting to sleep, and motivates without causing a jagged edge. Although tea can have as much or more caffeine than some coffees, it doesn't have the same "speedy" effect.<sup>14,15</sup> The reason is its secret ingredient, L-theanine. Research shows that L-theanine neutralizes the speedy, jagged, bad effects of caffeine without reducing its mind-energizing, fat-burning features.<sup>16,17</sup>

L-theanine's effect on the brain can be visualized on an EEG. Brain waves are actually smoothed out—but not flattened out—by supplemental L-theanine.<sup>16</sup> The body is relaxed, the mind is calmed, but no drowsiness occurs.<sup>5</sup> This is exactly the type of relaxation prescribed by sleep therapists. The person seeking help will be asked to listen to music or engage in a similarly relaxing activity immediately before retiring. Studies show that pre-sleep relaxation is very effective against insomnia, even in tough cases.<sup>18-20</sup>

Falling asleep is one thing; staying asleep and getting quality sleep is another. Researchers in Japan gave volunteers 200 mg of L-theanine daily and recorded their sleep patterns on devices worn around their wrists. The L-theanine didn't cause the subjects to sleep longer, but it did cause them to sleep better. It was documented that sleep quality, recovery from exhaustion, and refreshed feelings were all enhanced by L-theanine. Those taking L-theanine felt like they slept longer than they actually did.<sup>21</sup> This is good news for people who don't get enough sleep, or those who want to sleep less and do more.

One of the other effects of the tea ceremony is that it leaves people in a better mood. Knowing that L-theanine can cross the blood-brain barrier and positively affect brain chemistry, scientists investigated its mood-modulating effects. The results of those studies have led to L-theanine being patented as a mood enhancer.<sup>22</sup> How it works is not completely understood, but one thing researchers have discovered is that L-theanine changes levels of amino acids affecting serotonin and other neurotransmitters in the brain.<sup>5</sup>



### BALANCING BRAIN CHEMISTRY

Memory impairment is frequently associated with old age or Alzheimer's disease, but there are other causes. Stress and depression, for example, cause memory loss. Although usually thought of as mere psychological states, stress and depression cause physical changes in body chemistry. The brain is notably affected.

Stress hormones known as glucocorticoids are activated by both stress and depression. In turn, they cause imbalances in brain chemistry that interfere with mood and memory.<sup>23-26</sup> The effect is biochemical. Glucocorticoids disrupt serotonin, dopamine, norepinephrine,

and other brain chemicals.<sup>27,28</sup> These “neurotransmitters” are the target of prescription antidepressants such as Prozac® and Wellbutrin®. And it has been shown that glucocorticoids can interfere with the ability of Prozac® and other drugs to work.<sup>29</sup> Worse still, glucocorticoids can cause the brain to shrink.<sup>30,31</sup> Counteracting glucocorticoids is extremely important.

Drugs that block glucocorticoids have been proposed as a treatment for depression, and strangely enough, people have been treated successfully with ketoconazole (Nizoral®), an antifungal drug with the side effect of suppressing glucocorticoids.<sup>32,33</sup> Theanine also suppresses glucocorticoids, and it is one of the few dietary supplements that crosses the blood-brain barrier.

Theanine’s connection to the suppression of glucocorticoids is through glutamate. Researchers have discovered that this natural component of brain chemistry, which is not traditionally associated with depression, in fact plays a major role.<sup>34</sup> In people who are depressed, glutamate levels are out of balance.<sup>35</sup> Preliminary studies show that blocking certain signals in the brain activated by glutamate may be as effective as prescription antidepressants.<sup>36,37</sup> L-theanine may act as a glutamate antagonist.<sup>38</sup> Researchers believe that glutamate receptor antagonists may offset the harmful effects of high glucocorticoid levels and offer neuroprotective effects against both acute and chronic neurodegenerative diseases.<sup>39</sup>

Glutamate-activated signals not only affect mood, they affect memory and learning.<sup>40</sup> Memory and learning are similar biochemical processes in the brain. If an animal can’t remember, it can’t learn. Stroke, Alzheimer’s disease, and alcohol all cause memory loss involving disruptions in glutamate-related signals that inhibit the storage and retrieval of memories.<sup>41-44</sup>

If theanine is present in the body at the time stroke occurs, the damaged area will be significantly reduced.<sup>45</sup> This is supported by a Chinese study of 14,000 people, which found that drinking tea slashes the risk of stroke by 40%.<sup>46</sup> Maintaining healthy levels of L-theanine and other tea-related compounds in the body may thus help prevent memory loss and stroke-induced damage to brain tissue.

### **BALANCING THE LIVER: ALCOHOL**

Another part of the body that responds positively to theanine is the liver. Research from Japan shows that theanine is a powerful antidote to the effects of alcohol. If theanine is given to mice before or after they drink alcohol, it significantly lowers blood levels of alcohol.<sup>47</sup> It works by modulating alcohol chemistry.

Alcohol is converted to a toxic chemical known as acetaldehyde, which is similar to formaldehyde and more toxic than alcohol itself. Theanine accelerates the break-down of acetaldehyde and blocks toxic radicals.<sup>47</sup> The remarkable powers of theanine to intercept free radicals was demonstrated in the same study. It not only blocked radicals caused by alcohol, it suppressed levels to below normal for five hours.

One reason theanine is able to reverse damage caused by alcohol is that it restores the liver’s all-purpose antioxidant and detoxifier known as glutathione. Drinking alcohol causes significant suppression of this critical factor. If the suppression is infrequent, the liver bounces back; if suppression is chronic, however, the liver can’t overcome the stress. It breaks down and the effects are felt throughout the body. Theanine helps counteract the alcohol-induced loss of glutathione.<sup>47</sup>

Glutathione is not only something people who drink alcohol have to worry about, it’s something that oncologists have to worry about. Depletion of glutathione in vital organs like the heart is a major cause of chemotherapy toxicity. Because of it, some drugs that could otherwise be useful in treating certain types of cancers can’t be used. Researchers looking into the possibility of adding theanine to chemotherapy have found that it counteracts drug-induced losses of glutathione in vital organs like the heart, but not in tumors.<sup>48</sup> In fact, it blocks tumors from getting glutathione, thus enabling some types of chemotherapeutic drugs to work better.<sup>49</sup> By enhancing glutathione where it’s beneficial and reducing it

where it's not, theanine again shows its propensity to restore balance.

### BALANCING FAT AND MUSCLE

If there's one place people want to restore balance, it's in the area of body fat. As everyone knows, when fat loss is the goal, calorie expenditure is the game plan. One of the differences in people who are overweight and those who are not is that overweight people sit about two hours longer every day.<sup>50</sup> Clearly, inactivity causes imbalance in the system, yet the mere thought of exercising makes some people tired. Motivation is lacking, and they might as well try to climb Mt. Everest as do a round on the stair climber.



But what if they really did have to climb Mt. Everest? Researchers in the United Kingdom made a surprising discovery in a study of mountain climbers. Hot tea, they found out, does wonders for fatigue and vigor (as in let's get up and go!).<sup>51</sup> Finnish researchers made a similar discovery when questioning people about depression. None of the subjects who drank five or more cups of tea a day was depressed, whereas those drinking no tea had the highest rate of depression.<sup>7</sup> Neither research team attributed the motivational effects of tea to caffeine. Caffeine is effective for a different aspect of weight loss: speeding up metabolism. But 100 milligrams of caffeine only increases the resting metabolic rate 3-4%.<sup>52</sup> Upping the dose can leave a person tired and shaky. So, caffeine by itself isn't the answer to weight loss. Enter green tea.

Researchers know that green tea extract promotes thermogenesis above and beyond its caffeine content.<sup>53</sup> They have been aware for several years that compounds in green tea increase caffeine's calorie-burning effects. What those compounds are was a mystery until Japanese researchers decided to look into it in 2004. They divided green tea into its various components and investigated how catechins, theanine, caffeine, and green tea powder itself affect weight gain in female mice.<sup>54</sup> They found that all the components suppressed weight gain. Green tea powder, catechins, and theanine also reduced triglyceride levels. The researchers concluded that not only can caffeine help prevent weight gain and fat accumulation, but theanine can, too. It's not known whether the same results occur in humans.

In Japan, you will more likely find theanine in your beverage than caffeine. The Japanese value the rejuvenating, mind-clearing qualities of theanine. It's not surprising that something that restores balance is very popular in a culture where restoring balance is the foundation of medicine. Westerners would do well to take note of this gift from the East.

Theanine is unique in a sea of supplements that promise much but deliver little. It's one of the few supplements that crosses the blood-brain barrier. Research to date indicates that theanine is very useful for restoring balance to systems neglected by people who are on the go. It helps counteract the stimulating effects of caffeine, but complements caffeine's positive aspects such as fat burning. It relaxes and rejuvenates. It reduces alcohol levels in the bloodstream and supports liver health. It restores mood and motivation, increases thermogenesis, and protects the brain. Supplemental theanine thus helps recreate the calming and centering effects of a tea ceremony in a convenient and accessible form.

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