

L-THEANINE:

A Versatile Nutrient

Green tea is a widely consumed beverage, especially in Asia where it has been consumed for hundreds of years. Numerous studies both in animals and humans have consistently supported the positive health benefits of green tea in various pathologies including cardiovascular, diabetes, cholesterol, cancer, bone health, inflammation, aging, as well as numerous neurological conditions like dementia, Parkinson's disease, Alzheimer's Disease, depression and so on.¹



How is it that many natural products can have such a diverse range of health benefits? Unlike pharmaceuticals that are produced with a "single molecule single disease" approach (the classic "magic bullet"), natural products differ in that many of them contain literally hundreds of active constituents. Some of these actives have been pharmacologically verified and studied, but many others remain to be uncovered and further researched. Green tea, like other natural health products such as curcumin from the turmeric root, pomegranate, ginger, garlic etc., contains many types of active molecules each with its own properties and mechanism of action.

One group of constituents commonly found in green tea are polyphenols, a broad category encompassing hundreds of different molecules, including catechins, tannins, lignans and other flavanoids as well as minerals, proteins and amino acids. The most well known active compound found in green tea is probably EGCG, or epigallocatechin gallate, a catechin with antioxidant and anti-cancer properties. However there are other widely studied compounds from green tea that have very different properties. One

of these compounds is the amino acid, L-theanine. L-theanine is unique in that unlike the 22 amino acids that are broadly classified into essential and non-essential and present in various products like whey soy and egg protein, it is mainly found in the tea plant where it comprises 1-2% of dry weight of the tea leaf. L-theanine is a typical amino acid with an amino (NH₂) and acid (COOH) groups and has a similar structure to the more widely present L-glutamine however its properties are quite unlike those of L-glutamine. In green tea L-theanine may represent up to 50% of total amino acids present.¹

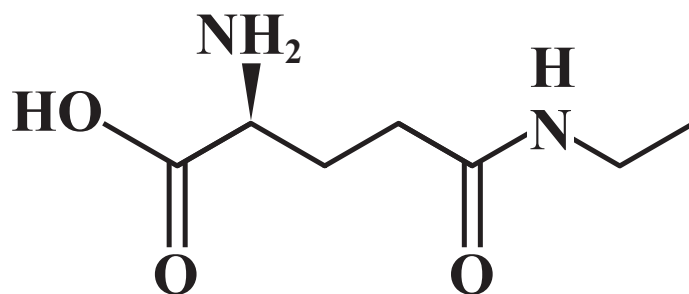


Figure 1. The molecular structure of L-Theanine

Pharmacological Properties of L-Theanine

Relaxation Effect

The human brain generates various types of weak electric pulses (brain waves) that are classified as alpha, beta, delta and theta waves. Each of these waves are associated with particular physiological activity e.g. theta waves are associated with drowsiness while alpha waves are associated with relaxation.

Repeated clinical trials have shown that L-theanine powerfully activates alpha waves and induces relaxation in test subjects.² Not only that, but these effects were very quick, occurring within 15-30 minutes following ingestion. Moreover, there was dose response effect, meaning the higher the dose used the stronger the effect. Typical doses used were between 50-200mg of L-theanine orally per day.² In addition, L-theanine is also thought to counteract the effects of caffeine possibly by inducing alpha waves and/or directly reducing caffeine levels at the receptor sites.³ This makes sense since caffeine is naturally present in the green tea and yet most people do not find that green tea induces the typical effects expected of a caffeine containing beverage. In fact, in Asia green tea is frequently used as a relaxant as well as during social events.



The quick acting action of L-theanine is important in that the nutrient must reach the brain rapidly to induce its relaxation effects. The brain is protected by the so called blood-brain-barrier, a membrane that prevents toxic and foreign compounds from entering the brain. L-theanine however, easily penetrates the blood-brain-barrier, allowing it to act directly on the brain.² An interesting aspect of L-theanine research has recently been reported in the *Journal of Veterinary Behavior* where one set of researchers reported that L-theanine significantly reduced anxiety related emotional disorders in cats, while another research group reported L-theanine as an effective treatment for phobias in dogs!^{4,5}

Blood Pressure Lowering Effect

Many peptides (group of amino acids joined together) have been shown to help lower blood pressure. Such peptides are present in milk, fish (bonito, mackerel), flaxseed, legumes and even green tea which undergoes fermentation with yeast or bacteria. The fermentation process breaks down the longer chain molecules into smaller ones that not only have their characteristic unique physiological properties but also are of sufficiently smaller size and therefore more absorbable (bioavailable) and thus more active.

L-theanine has been shown to lower blood pressure (both systolic and diastolic) in animals and humans. In animal studies rats that are prone to developing hypertension (spontaneously hypertensive), and which are considered a close model to the human disease,

were used. L-theanine was repeatedly found to lower blood pressure in these rats. Similarly, a recent 2009 human study showed that 200mg of L-theanine with a standardized green tea formulation significantly reduced blood pressure.⁶ The mechanism of action is thought to be due to the reduction of various neurotransmitters, particularly serotonin, both in the central nervous system (brain) and at the peripheral tissue (blood vessel) level.⁶

Improvement of Learning

Animal studies examining the effect of L-theanine on memory and learning have consistently shown that the amino acid has a positive effect on these factors.⁷ For example, the results of specific tests, such as the Operant and the Avoidance tests have shown that L-theanine improves the performance of the animals. For example, L-theanine improves the animal's ability to learn its way back through a maze, or to learn to avoid a negative stimulus, like a shock.⁷ Neurotransmitters like dopamine and serotonin are both linked to memory and learning.



It is thought that L-theanine's effect on learning and memory is achieved by raising dopamine levels and reducing serotonin levels.^{3,7} For this reason, L-theanine supplement foods and beverages are quite popular with the children in Japan that wish to improve their memory and learning skills!

Depression

Many risk factors are recognized as contributors to the depression. Stress is a particularly well established factor that can cause depression. Inflammation is also associated with depression as evidenced by the raised levels of inflammatory proteins like C-reactive protein (CRP) in individuals suffering from depression. Several animal studies have suggested that L-theanine has a

tranquilizing effect on the brain. Human clinical studies have confirmed these animal findings and have shown that L-theanine can effectively lower stress levels in human participants under acute stress.^{8,9}

Furthermore, a study conducted in Japan in 2010 found a strong correlation between green tea intake and depression.⁸ In other words, the higher the intake of green tea, the lower the incidence of depression. This study was impressive in that it was fairly large (over 1000 patients), included seniors (over the age of 70 years) and that many of the confounding factors that can influence the study, such as age, sex, disease status, inflammation, body mass index, folic acid intake etc. were carefully adjusted for. The study also showed a dose response relationship, with a lower incidence of depression being associated with higher daily consumption of green tea.⁸

Another much larger study also from Japan analyzed over 42,000 individuals aged over 40 years. Again, this study confirmed a strong correlation between green tea consumption and improved mental health. The authors suggested that catechins and L-theanine were probably the reason for the activity of the green tea.⁹

Immune Enhancement

Green tea and its various constituents have been shown to exert a powerful effect on the immune system. L-theanine has been shown to stimulate various important immune system cells, including macrophages, neutrophils and natural killer cells, as well as the production of cytokines, the chemical messengers that help the various immune cells to communicate and co-ordinate their actions.^{10,11}

A recent double blind placebo controlled study has shown that a standardized and proprietary L-theanine with green tea extract reduced the occurrence of colds and respiratory tract infections.¹⁰ The authors attributed this protective effect to raised levels of gamma delta T cells. These are highly specialized immune cells that are considered the first line of defense against infection. Moreover, these cells also produce gamma interferon, a powerful antimicrobial compound. Supplementation with L-theanine has also been shown to raise cellular glutathione levels. Glutathione is a powerful antioxidant that the body produces to protect its cells against free radical damage and against dangerous toxins.^{10,11,12}

Various animal studies have pointed to the fact that L-theanine can also exert potent anti cancer effects.^{12,13} Such effects included increasing apoptosis or "cellular

suicide" by damaged cells, preventing cellular proliferation or multiplication of cancer cells and immune system enhancement. Furthermore, L-theanine has been found to work synergistically with radiation and chemotherapy to reduce unwanted side effects as well as to improve the cancer killing effects of drugs like doxorubicin.^{13,14}

Other Physiological Effects

L-theanine is such a versatile molecule that research continually uncovers new and exciting applications. Many of these studies are double blind placebo controlled human studies, the gold standard for evaluating unbiased pharmacological efficacy. Several studies have assessed L-theanine's immune stimulation in athletes undergoing endurance and high intensity exercise. Athletes are particularly prone to reduced immune function in large part due to the excessive formation of free radicals. These reactive oxygen species are known to cause multiple pathologies including damage to the blood vessels which ultimately leads to atherosclerosis (hardening of the arteries), oxidation of LDL cholesterol, high blood pressure, cancer, cataracts and so on. L-theanine on its own and in conjunction with another amino acid, cysteine, has been shown to quench free radicals in a powerful manner.^{15,16}



Another exciting area of L-theanine research is in the protection of nerve cell (neuron) health.^{17,18} Damage to these cells is responsible for degenerative diseases such as Alzheimer's disease (due to the formation of beta amyloid plaque and tendrils) and Parkinson's disease (resulting from the destruction of dopamine producing cells in the substantia nigra in the brain).

Conclusion

L-theanine is a safe and versatile nutrient naturally found in green tea. There is much research on this exciting nutrient and many publications. Much of the work has been done in Japan where the ingredient was first isolated in the 1940s and is widely used in foods, candy, beverages etc. Taiyo International in Japan has studied this and other green tea constituents very actively and has conducted extensive research to assess the safety, proper dose and applications of this exciting nutrient, in addition to working towards gaining a better understanding of its mechanisms of action. Taiyo alone has several dozen patents ranging from anxiety inhibition, promotion of sleep, treatment of premenstrual symptoms, anti-obesity, smoking as well as the suppression of behaviour problems in pets!. The brand name under which most of the research has been done is Suntheanine™, the world's most widely studied L-theanine.

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