Anxiolytic effects of oral administration of L-Theanine: a revision

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Abstract:
L-theanine is a non-protein amino acid, derived from L-glutamic acid, commonly found in the plant Camellia sinensis and contains bioactive substances, vitamins, minerals and antioxidants. This amino acid can be obtained by chemical synthesis or tea isolation. It was commercially developed due to its promising effects of promoting relaxation and feeling of well-being. In oral administration, L-theanine is absorbed through the intestinal tract and, soon a large amount in the blood flows to the brain through the blood-brain barrier. Theanine (C7H14N2O3) is metabolised in the kidneys to glutamic acid and ethylamine. Its main targets are glutamate, gamma-aminobutyric acid (GABA), dopamine and serotonin, impacting to a certain extent on neurochemical levels. According to studies, after 15 minutes of oral administration of 200mg, brain activity is influenced by the stimulation of alpha wave production. This form of administration can help anxious people to concentrate in their daily tasks and the continuous intake can increase brain levels of dopamine and GABA, explaining the feeling of relaxation. The action of L-theanine also suggests that it may cause a modulation of the effects of caffeine and thereby lower cortisol levels. This review intends to analyze the effects of L-theanine and its interaction with the central nervous system, relating it to anxiolytic effects and decrease of stress levels, in order to confirm a pattern of change between physiological indices after ingestion.

Keywords: Theanine; anxiety; Camellia sinensis; tea.
1. Introduction
The plant *Camellia sinensis*, which is part of the composition of green tea, is composed of polyphenols belonging to the catechins (MANCINI et al., 2017). Studies have shown that its main compounds have antioxidant effects, acting against several environmental and chemical toxins (RAMESHRAD et al., 2016). L-theanine (C\(_7\)H\(_{14}\)N\(_2\)O\(_3\)) is a non-protein amino acid, the most important one found in green tea, having various therapeutic and pharmacological effects. It is the main component responsible for the flavor and taste of tea (MU et al., 2015). L-theanine is synthesized at the root of the plant *Camellia sinensis*, from glutamic acid and ethylamine, before being transported to the leaves (NATHAN et al., 2006), being structurally similar to glutamic acid, which is one of the excitatory neurotransmitters of the central nervous system. It can be obtained from chemical synthesis or tea isolation. Isolation has a high cost and time consuming processing to obtain a maximum degree of purity (MU et al., 2015), thus being a less used method. Neurochemical studies *in vivo*, suggests that L-theanine increases the levels of serotonin, dopamine and GABA (NATHAN et al., 2006).

2. Results and Discussion
In some studies, it has been observed that L-theanine increases both serotonin and GABA levels, and since both neurotransmitters play an important role in anxiety disorders, it is possible that L-theanine may cause anxiolytic effects (NATHAN et al., 2006). Another study reported an increase in aminobutyric acid (GABA) concentrations after the administration of L-theanine in mice. In the same study, the convulsive effect of caffeine was inhibited by L-theanine, suggesting a possible anticonvulsive action related to GABA (NATHAN et al., 2006). It was observed that, even though green tea has a high caffeine content, it is able to produce a calming effect (BORZELLECA et al., 2006), therefore being able to relate L-theanine with anxiolytic properties seen in different studies, since it is able to modulate the stimulating effect of caffeine in green tea. The administration of 200mg of L-theanine stimulates the production of alpha waves when administered in resting participants, causing a sensation of relaxation without drowsiness (HASKELL et al., 2007). Anxiety states and stress perception had their levels reduced after administration of L-theanine, compared to placebo (HASKELL et al., 2007). L-theanine can also influence neurotransmitter function in the central nervous system 30 minutes after oral administration (KIMURA et al., 2007).

Figure 1. *Camellia sinensis* plant

Figure 2. Chemical structure of L-theanine (N-ethyl-L-glutamine)

3. Materials and Methods
A bibliographic review was made from articles available on the platforms: ScienceDirect, Oxford Academic Journals, Taylor and Francis Online, Springer Link and PubMed. The articles selected
were from the years 2006, 2007, 2015 and 2017. Searched with the following keywords: theanine, l-theanine, anxiety, green tea, Camellia sinensis and cognitive effects of l-theanine. The selection of articles was carried out focusing on the therapeutic effects of L-theanine, its anxiolytic properties and effects on the reduction of stress levels.

4. Conclusions
The chemical behaviors of neurotransmitters affects the emotional and physiological states of humans, so they can also be influenced by L-theanine due to its effects on the central nervous system. No side effects have been reported in animal and human studies, ensuring the safety of L-theanine use, as well as the use of the Camellia sinensis plant as tea. Administration may benefit people in anxiety states or in stressful situations regulating their neurochemical levels by influencing neurotransmitters. There is still a need for further studies on anxiolytic effects within different parameters.

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Conflicts of Interest
The authors declare no conflict of interest.

References and Notes
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