Review Article

L-Theanine: A Prospective Natural Medicine

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ABSTRACT

L-theanine, an important constituent of the tea, is consumed daily throughout the world and is said to greatly contribute to the umami taste of tea. The objective of this review is to summarize the currently available information of L- theanine with reference to health benefits. Relevant keywords like "Tea", "L-theanine" and "health benefits" were used for the extraction and subsequent analysis of the biomedical literature in the field. Two search engines, Google and Pubmed were used for that purpose. It is expected that the review update the basic features of L-theanine as well as, the current status pertaining to the role of the L-theanine in human health.

Keywords: Camellia sinensis, health benefits, L-theanine, Natural medicine, Tea.

INTRODUCTION

L-Theanine (γ-glutamylethylamide) is an unique, non-protein forming amino acid, present in tea (Camellia sinensis (L.) O. Kuntze)[1, 2]. It constitutes 1% to 2% of the total dry weight of tea leaves and about 50% of the total free amino acids[3]. Other than the tea plant it can be found in an inedible mushroom Xerocomus badius and in an Amazonian tree, Ilex guayusa[3-5]. Naturally L-theanine coexists with its 'D' isomeric form. However, the 'D' form constitutes only 1.85% of total theanine as evident from analyses of 17 types of tea[3]. After synthesis in the root of the tea plant, L-theanine accumulates in the leaves, where sunlight converts L-theanine to polyphenols[6]. Hence for preservation of L-theanine content, flavour and taste, some tea cultivators grow their plants away from direct sunlight exposure[6].

In 1949, Sakato discovered and isolated the glutamic acid analog, L-theanine, from green tea[7]. The theanine content of green tea has been believed to be higher than the oolong and black tea because during fermentation step (aerial oxidation), degradation of L-theanine to its two precursors, glutamic acid and ethylamine may take place[3]. However, a study by Neumann and Montag contradict the above findings and showed black tea contains more theanine than green tea[8]. Several studies suggest that L-theanine plays a pivotal role in the health promoting effect of tea[9]. Effects of L-theanine on mental stress, anxiety, cognition, neuronal health have been extensively studied. However, other avenues of research on 'L-theanine' are its infancy. Hence there is a growing need to identify the research gaps regarding therapeutic effects of L-theanine. Therefore, the main aim of the study is to summarize the medicinal values of the L-theanine and its basic characteristic features. This will not only update scientific readers for future research on L-theanine but also facilitate the promotion of L-theanine as herbal drug in global market.

Physiochemical Properties of L-theanine

Theanine is an analog to glutamate and glutamine. It is a non-protein forming amino acid. L-Theanine is commonly known as γ-glutamylethylamide or 5-N-ethyl-glutamine or 2-amino-4-(ethylcarbamoyl) butyric acid (IUPAC)[1]. L-theanine is responsible for umami taste of tea. It can enhance the umami intensity of sodium L-glutamate proportionally[10]. L-Theanine elicits an umami taste via T1R1 + T1R3 umami taste receptors[11]. Synergism between L-theanine and inosine 5'-monophosphate (IMP) for the umami taste was also observed[12]. Chemical formula of L-theanine is C7H14N2O3. The molecular weight of theanine is 174.2 g mol−1. The electron paramagnetic resonance (EPR) study of L-theanine at room temperature revealed -CH2ĊHCOOH radical as paramagnetic species that subsequently used to determine the hyperfine structure constant and 'g' value of L-theanine[13]. Raman spectral analysis of L-theanine showed characteristics Raman bands at 321, 900, 938, 1153, 1312, 1358 and 1647 cm (-1)[14]. It appears as a colourless needle shaped crystalline solid, having melting point of 214-216°C[15, 16]. L-Theanine is highly soluble in water (2.6 parts water at 0 deg C; soluble in 1.8 parts water at 100 deg C)[16, 17] but not soluble in ethanol, methanol, chloroform and ether[16, 17]. It is highly stable in acidic condition (pH= 3.0-6.6)[6]. No degradation of L-theanine was noted in beverages heated at 121 deg C for 5 min.[6]

Synthesis of L-theanine

L-theanine Biosynthesis in Tea Plant

In the tea seedling, L-theanine occurs in the cotyledons, shoots and roots. In mature tea plant, L-theanine synthesis occurs in roots[18]. Glutamic acid and ethylamine

are the immediate precursors of theanine[19]. Theanine synthase (TS) is the main enzyme of theanine biosynthesis pathway. Newly synthesized theanine relocates into the tender shoots through the xylem, where it either concentrates or theanine hydrolase (ThYD) split it down into glutamic acid and ethylamine[20]. Magnesium nutritional status plays a vital role in synthesis and mobility of theanine through xylem and phloem. It was observed that adequate supply of magnesium promoted the synthesis of theanine in roots and its accumulation in the young shoots of tea plants[21]. Theanine content increases within the 60 days of germination and decreases thereafter[22].

The enzymes responsible for L-theanine and its precursor's biosynthesis also include glutamine synthetase (GS), glutamate synthase (Fe-GOGAT), glutamate dehydrogenase (GDH), alanine transaminase (ALT), alanine decarboxylase (AIDA) and ThYD[23]. Most of these theanine biosynthetic pathway genes were found in http://www.biomedcentral.com/1471-2164/12/131 dataset, except for AIDA and ThYD, which are specific for tea plants only. Gene sequence of AIDA and ThYD are available at public database (http://www.ncbi.nlm.nih.gov/unigene)[23]. These gene sequences have been derived from EST sequence of *Camellia sinensis* cDNA clone[23]. The AIDA sequences were selected from the homologues of arginine decaboxylase (ADC) and S-adenosylmethionine decarboxylase (SAMDC), which have similar domains, to AIDA[24].

However, a study by Deng et al., 2012 revealed that theanine synthesis takes place both in root and shoot and theanine synthase accumulation is positively affected by salt treatment[22]. It was observed that the concentration of theanine and the total free amino acids were gradually increased in shoots, reached the maximum on the 8th day and subsequently declined, both in roots and shoots after salt treatment[25].

A study on seasonal variation of L-theanine content in Darjeeling black tea revealed that L-theanine concentration modulated with the season. L-Theanine concentration was highest in first flush and then gradually declined from first flush to second flush to third flush and then started to increase. From the study, it can be concluded that L-theanine synthesis is a function of temperature. With cold stress L-theanine started to increase and become highest during first flush[26].

Enzymatic Synthesis of L-theanine

L-Theanine can be obtained by chemical synthesis or isolation from tea. Chemical synthesis of theanine is a relatively complex multistep process whereas isolation of L-theanine from tea in high purity generally involves time-consuming, cost-ineffective, and complicated operational processes[27]. Hence, both the methods are not preferred in industry. Therefore, the biological production of L-theanine has recently attracted much attention[28].

Food grade L-glutamine and ethylamine, the two biosynthetic precursors of L-theanine in tea, were reacted in presence of the enzyme, bacterial glutaminase (source: *Pseudomonus nitroreducens* and *Bacillus amyloliquefaciens*) to produce L-theanine in the laboratory[3]. Shuai et al., 2010 reported an efficient enzymatic synthesis of theanine using gamma-glutamyltranspeptidase (GGT, EC 2.3.2.2) from a new *B. subtilis* strain SK11.004[29]. Another study using immobilized E. coli cells with GGT activity highlighted that enzyme activity was 1.2-fold higher when glutamic acid γ-methyl ester replaced glutamine as substrate[30].

Biochemistry and Pharmacokinetics

Chemical structure of L-theanine is comparable to the neurotransmitters glutamate and GABA; modification of one of the carboxylic ends of glutamic acid (further from the amine group) with another amine group followed by an ethyl group will produce L-theanine[13].

Due to its structural similarity with glutamic acid, L-theanine is known to block the binding of L-glutamic acid to glutamate receptors in the brain, and has been considered to cause anti-stress effects by inhibiting cortical neuron excitation[27].

L-theanine when ingested orally as a supplement or tea brew is quickly absorbed into the intestine[31]. Metabolism and toxicokinetic studies have revealed that the intestinal absorption of L-theanine is mediated by Na+ -coupled co-transporter in brush border membrane[32]. However, gut absorption of D-theanine was far less than L-theanine[33]. Recent studies on mammalian cell lines, e.g. T24, HepG2, COS1, 293A, Neuro2a and HuH7, revealed that L-theanine is transported mostly via the L transport pathway and its two isoforms LAT1 and LAT2[34]. Following absorption, L-theanine is quickly incorporated into the blood and attained its peak concentration in the blood between 30 min and 2 h after L-theanine administration in a rat model[35, 36].

Van der Pijl et al., 2010 reported that L-theanine plasma concentration reached its highest value within 32 min to 50 min after oral ingestion, and its half-life ranged from 58 min to 74 min in humans[31].

Similar kinetics study of L-theanine uptake in healthy participants revealed that maximum plasma concentration of L-theanine occurred 0.8 h after intake of 100 mg via capsules (24.3±5.7 µmol/L) and tea (26.5±5.2 µmol/L), respectively[37]. L-theanine crosses the blood-brain barrier via the large neutral amino acid (leucine-preferring) transport system and increase both serotonin and dopamine production in brain[35]. The mechanism of dopamine release caused by theanine is clearly distinct from glutamate transporter blockers or glutamic acid[38]. It was hypothesized that L-theanine may cease excitatory neurotransmission and results inhibitory neurotransmission via glycine receptors[38]. It was found that L-theanine can bind with three receptor AMPA,

kainate, and NMDA glycine but 80- 30,000-fold less than that of L-glutamic acid[39].

Hydrolysis of L-theanine to ethyl amine and glutamic acid occurs in kidney by phosphate independent glutaminase[36,40]. Subsequently, metabolites concentration increased in the blood and thereafter excreted by urine[36, 37]. However, D-theanine eliminated with minimal metabolism[41].

Health Benefits of L-theanine

Effect on brain

L-Theanine is one of the known substances that can easily cross the blood brain barrier. L-Theanine has been studied for its potential strength to relieve mental and physical stress, improve cognition, and boost mood and cognitive performance in a synergistic manner with caffeine. It acts on brain by altering the levels of GABA, serotonin and dopamine as well as increase the alpha-brain wave activity indicates a relaxed state. It was also observed that combining L-theanine in combination with caffeine, at levels and ratios equivalent to one to two cups of tea, eliminated the vasoconstrictive effect and behavioural effects of caffeine[42].

Stress/ Anxiety Relief/ Alleviate Hypertension

Recently, black as well as, other types of tea are believed to provide relaxation. The substance that is responsible for a sense of relaxation is L-theanine[6]. L-Theanine promotes relaxation without drowsiness. Unlike conventional sleeping pills, L-theanine is not a sedative but induce good quality of sleep through anxiolysis[43].

It was found that intake of 200 mg of L-theanine generated alpha-brain waves in female volunteers aged from 18 to 22 years and a subjective sense of relaxation[6,44, 45]. Nobre et al., 2008 showed that, at the dose of ~50 mg L-theanine significantly increases the activity of alpha frequency band, which indicates that L-theanine relaxes the mind[46].

Lu et al., 2004 compared the effect of L-theanine with a standard anti-anxiety drug, alprazolam under a relaxed and experimentally induced anxiety condition in humans and reported that under experimentally induced anticipatory anxiety neither L-theanine nor alprazolam had any anxiolytic effect as measured by behavioural measures of anxiety. However, L-theanine showed some relaxing effect under resting condition[47]. Heese et al., 2009 proposed that L-theanine does not produce anxiolysis by modulation of GABA receptor[48]; however, in combination with midazolam, L-theanine modulates the central nervous system (CNS) by decreasing fine and basic motor movements and increasing anxiolysis[48]. Park et al., 2011 suggested that combination of green tea extract and L-theanine (LGNC-07) have beneficial effects on cognition in animal model[49]. Yin et al., 2011 worked on antidepressant-like effects of L-theanine in the forced swim and tail suspension tests in mice and suggested that L-theanine possessed an antidepressant-like effect in mice, which may be mediated by the central monoaminergic neurotransmitter system[50].

Improvement in Alertness and Learning Ability

Dimpfel et al., 2007 reported that decaffeinated green tea has stimulation effect due to presence of L-theanine and theogallin[51]. Owen et al., 2008 suggested that L-theanine in combination with caffeine play a beneficial role for improving performance on cognitively demanding tasks like word recognition, rapid visual information processing, critical flicker fusion threshold and attention switching[52].

Haskell et al., 2008 also proposed the combination of caffeine (150 mg) and L-theanine (250 mg) led to faster simple reaction time, faster numeric working memory reaction time and improved sentence verification accuracy[53].

Kelly et al., 2008 found that an increase in hit rate and target discriminability (d') for the combined treatment of L-theanine (100 mg) and caffeine (50 mg) relative to placebo, and an increase in d' but not hit rate for caffeine alone (50 mg) whereas no effects were detected for L-theanine alone[54]. The randomized, placebo controlled, double-blind cross-over study by Einother et al., 2010 showed that L-theanine and caffeine significantly improved attention on switch task but not inter-sensory attention or subjective alertness[55].

In a recent study by Lyon et al., 2011, in a randomized double-blind, placebo-controlled clinical trial, showed that 400mg of daily consumption of L-theanine for 6 weeks is safe and effective in enhancing the higher sleep percentage, sleep efficiency scores and a non-significant trend for less activity during sleep in boys diagnosed with ADHD in compared to placebo group[56].

Jang et al., 2012 reported that L-theanine can inhibit the excitatory effects of caffeine like sleep disturbances in rats[57]. Low dose of L-theanine can partially reverse caffeine induced reduction in slow wake sleep, however effect of L-theanine on caffeine induced insomnia do not appear to increase dose dependently.

Protection of Neuronal Health

L-Theanine can boost brain serotonine, dopamine, GABA level and has affinities for AMPA kainate and NMDA receptors. Nathan et al., 2006 suggested that L-theanine may be a possible neuroprotective and cognitive intensifying agent[58].

L-Theanine shows it neuroprotective activity by interacting with GABA (A)-receptor[59]. It was observed that Bicuculline, a GABA (A)-receptor antagonist can inhibit the neuroprotective effect of theanine whereas 3-mercaptopropionic acid, a glutamate decarboxylase inhibitor has no effect on L-theanine mediated neuroprotective effect. L-Theanine can prevent memory impairment induced by repeated cerebral ischemia in rats[60]. Moreover, L-theanine inhibited the neuronal cell death in the hippocampal CA1 field significantly as well as

protects neurotoxin-induced Parkinson Disease like ailments. L-Theanine (500µM) reduced both dieldrin and rotenone induced DNA fragmentation and programmed cell death in cultured human dopaminergic cell line, SH-SY5Y. It partially prevented both rotenone and dieldrin-induced heme oxygenase-1 (HO-1) up-regulation as well as it attenuated the down-regulation of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF)[61]. L-theanine at the dose 2 and 4 mg/ kg reduce amyloid β (Aβ) (amino acid range: 1-42) levels and accompanying amyloid β peptide (amino acid range: 1-42) induced neural cell death in cortex and hippocampus of mice brain. Moreover, it has positive effects on memory, may be mediated by suppression of ERK/p38 (Extracellular Signal-Regulated kinase/ p38) and NF- kappa ß as well as reduction of macromolecular oxidative damage[62]. It can protect the APP (Swedish mutation) transgenic SH-SY5Y cell against glutamate induced excitotoxicity via inhibition of NMDA receptor pathway[63]. Hence, it may be helpful in the prevention and treatment of Alzheimer Disease. However, these are all cell culture or animal studies. clinical trials are highly needed.

L-theanine relieves positive, activation and anxiety symptoms in Schizophrenia and schizoaffective disorder patients[64]. Miodownik et al., 2011 showed that circulating BDNF and cortisol-to-DHEAS*100 molar ratio may be involved in the positive clinical outcomes of L-theanine[65]. Wakabayashi et al., 2011 reported that L-theanine possibly has antidepressant like effect along with antipsychotic effect and it employs its effects, at least part, through induction of BDNF in the hippocampus and the competitive action of L-theanine on N-methyl-D-aspartate (NMDA) receptor.[66] Ota et.al., 2015 have shown that l-theanine is effective in ameliorating positive symptoms and sleep quality in schizophrenia by stabilising the glutamatergic concentration in the brain, which is a possible mechanism underlying the therapeutic effect[67] .

Cancer Prevention

Plentiful *in-vitro* and *in-vivo* animal studies have investigated the anti-cancer activity of L-theanine. L-theanine has been accounted for augmenting the antitumor activity by inhibiting the efflux of anticancer drugs from cancer cells and help to decrease the size of tumours[68-72]. In another study, theanine almost doubled the effect of doxorubicin DOX) in Erlich ascites carcinoma, while increasing the drug's concentration in tumor cells threefold[69]. L-theanine and glutamate transporter inhibitors enhance the anti-tumor efficacy of the chemotherapeutic agents like doxorubicin (DOX) via increasing the concentration of DOX in tumor of M5076 ovarian sarcoma-bearing mice through inhibition of the glutamate transporter via the GS-X pump[72]. On the other hand, L-theanine can protect normal cells from adverse effects of DOX. The fate of L-theanine in normal and cancer cells is depend on variance of glutamate receptors expression in normal and tumor cells. In tumor cells L-Theanine do binds the glutamate receptor whereas in normal cells it is metabolized to glutamate which increased the efflux of DOX from the normal cells[72].

Friedman et al., 2007 showed that theanine treatment was found to induce cell death in four cancer cell lines i.e. breast (MCF-7), colon (HT-29), hepatoma (liver) (HepG2), and prostate (PC-3)[73]. Percival et al., 2008 reported that L-theanine enhances γδ T cell proliferation and interferon – γ secretion which play an active role against tumour cells and thereby may be used in cancer prevention[74]. Liu et al., 2009 showed that L-theanine inhibited the in vivo and ex vivo growth of human non-small cell lung cancer A549 and leukaemia K562 cell lines in dose and time dependent manner[75].

Hepatoprotective Effects

Lee et al., 2008 reported that among the green tea constituents, (-) epigallocatechingallate (EGCG) attenuated the ethanol cytotoxicity effectively, by inhibiting Gamma-glutamate transferase (GGT) activity which may provide a novel strategy for attenuating ethanol induced liver damage[76], whereas L-theanine and caffeine had no effects.

A recent study by Li et al., 2012 contradict the above result and showed that L-theanine significantly inhibited the ethanol induced LO2 cell (hepatocyte) apoptosis by attenuating the ethanol-induced increase of ALT, AST, TG and MDA in mice as well as by augmenting the hepatocyte antioxidant status by inducing the activities of SOD, AT, GR and increased the level of GSH[77]. Overall it indicates that L-theanine prevents alcoholic liver injury through enhancing the antioxidant capacity of hepatocyte. In the same year, Jiang et al. showed that L-theanine can protects the CCl4 induced liver injury by inhibiting metabolic activation of CCl4, inducing the activation of cellular antioxidant status, and decrease the serum level of TNFα and IL-1β as well as down regulate the expression of COX2 and i-NOS in liver[78].

Effect on Immune System

Evidence suggests that tea can help strengthen our ability to fight diseases. L-theanine may play a role to enhance the immune system because one of the metabolites of L-theanine, ethyl amine (non-peptide antigen) activates an immune system element called the gamma-delta T cell. Kamath et al., 2003 showed that, the non-peptide antigen in tea beverage primed human peripheral gamma-delta T cells, to mediate a memory response on exposure of ethyl amine, in-vitro and in-vivo for memory and non-memory antibacterial cytokine responses which facilitate an explanation for health benefits of tea[79]. Percival et al., 2008 suggested that L-theanine may play a role in cancer prevention by enhancing the gamma delta subtype of T cell[80].

It was found that, co-administration of L-theanine (80 mg/kg) and L-cystine (200 mg/kg) enhanced antigen-specific immunoglobulin G (IgG) production, partly

through amplification of glutathione (GSH) levels and T-helper cell (Th2)-mediated responses[81]. A study carried out by Miyagawa et al., 2008 showed that co-administration of L-cystine and L-theanine before vaccination intensified the immune response by means of enhancing antigen specific anti dinitrophenyl (DNP) IgM and IgG antibody to influenza vaccine in elderly people with low serum total protein or haemoglobin[82]. It was further supported by Takagi et al., 2009 and showed that combined administration of (L)-cystine and (L)-theanine for 14 days before primary immunization enhanced significantly the serum antigen-specific IgM and IgG levels in 24-month-old mice and protects against influenza virus infection in aged mice[83]. Kurihara et al., 2010 reported oral administration of cystine and theanine (490mg) tablets twice daily useful for prevention of common cold 84 which supports the previous work of Bukowski et al., 2007[85].

Prevention of Vascular Diseases

Vascular disease is a pathological state of large and medium sized muscular arteries and is activated by endothelial cell dysfunction. It is a form of cardiovascular disease primarily affecting the blood vessels. Epidemiological and clinical studies in recent years have shown that regular green or black tea consumption significantly reduces the risk of cardiovascular diseases[86], including ischemic stroke. Recent studies are continuously highlighting the beneficial effect of L-theanine, one of the potent bioactive components, on vascular health.

Hypertension and increased blood pressure are closely related. It was found that L-theanine administration showed a considerable reduction in blood pressure in spontaneously hypertensive rats. More importantly, L-theanine has an inhibitory effect on caffeine induced blood pressure increase. Hence, L-theanine might be placed in antihypertensive treatment regimens[87].

It was found that L-theanine has protective effect on cerebral ischemia-reperfusion injury[88-89]. Siamwala et al., 2013 have shown that L-theanine promoted activation of ERK/eNOS signalling pathway in vitro in human endothelial cell line that results enhanced NO production and thereby vasodilatation in the artery[90].

Effects on Obesity

Obesity is a medical disorder in which excess body fat has accumulated to the extent (BMI ≥ 30 (feet/pounds)) that it may have an adverse effect on health 91. A mechanistic study by Zheng et al., 2004 on the anti-obesity effect of three major green tea components e.g. catechins, caffeine, and L-theanine, showed that combined dosage of L-theanine and caffeine were responsible for the suppressive effect of green tea powder on body weight increase and fat accumulation in mice model[92]. Zhang et al., 2002 showed that L-theanine can reduce cholesterol levels in both humans and gerbils thereby it may prevent obesity and improve heart health. Another study also found that theanine prevents cholesterol peroxidation 93. It was also observed that the food intake tended to decrease in the mice given L-theanine. However, L-theanine did not augment the anti-obesity action of caffeine and/or catechins[92].

Effect on Gastric Ulcer

It was observed that L-Theanine can heal gastric ulcer on experimental mice model at a dose of 10 mg/kg b.w for 3 days (once daily) by nullifying adverse oxidative effect of indomethacin through improved synthesis of PGE2 by modulation of cyclo-oxygenase-1 and 2 [COX-1 and COX-2] expression, Th1/Th2 cytokine balance, and restoration of cellular antioxidant status at the gastric ulcer margin. However, it made the ulcerated condition worst at a higher dose (40 mg/kg b.w.)[94].

Effect on Human Embryonic Stem Cells (hESCs)

Human embryonic stem cells (hESCs) have the potential to differentiate into all cell types in the body and hold immense promise for regenerative medicine; however, large-scale expansion of undifferentiated hESCs remains a major challenge 95. However, Desbordes et al., 2008 have shown that L-theanine can promote the short-term self-renewal of hESCs like other three compounds viz. sinomenine (SNM), gatifloxacin (GTFX) and flurbiprofen (FBP) using high throughput assay[96].

Side Effects and Toxicity

Borzelleca et al., 2006 conducted a study to evaluate the side effects and toxicity of L-theanine (Suntheanine) where L-theanine was added to diet at various concentration to provide target doses of 0, 1500, 3000 or 4000 mg/kg body wt/day to male and female Crl: CD (SD)GS BR rats for 13 weeks[97]. However, no consistent, statistically significant treatment-related adverse effects on behaviour, morbidity, mortality, body weight, food consumption and efficiency, clinical chemistry, haematology, urinalysis, or gross pathology, organ weights or histopathology, were found out[97]. The no-observed-adverse-effect-level (NOAEL) was found to be 4000 mg/kg bw/day. It is not mutagenic or carcinogenic in animals or bacteria[98].

In 1964 the Japanese Ministry of Health and Welfare endorsed the use of L-theanine as a food additive for universal consumption. In the US it is also sold as a dietary supplement, and according to FDA L-theanine can be considered as 'Generally Recognized As Safe' (GRAS) (FDA reference) and nontoxic compound. Based on L-theanine's high LD50 (5 g/kg) and the history of extensive consumption of L-theanine in green tea by a significant number of consumers over longer periods of time, no dietary exposure limits were recommended[6]. However, external addition of isolated theanine to beverages has been objected by the German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR) (http://en.wikipedia.org/wiki/Theanine).

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