

LE Magazine August 2007

## REPORT

### Quick Relief from Anxiety and Stress Without Tranquilizer Drugs

By Tiesha D. Johnson, RN, BSN



Daily stress and anxiety not only wreaks havoc with our sense of well-being, but also shortens our lives by contributing to heart disease, diabetes, and cognitive impairment.<sup>1-3</sup>

Drug companies offer medications to treat the symptoms of anxiety, but fears of addiction and side effects cause most health conscious people to avoid them.<sup>4,5</sup>

Fortunately, alternatives are available in the form of natural botanical extracts—one of which was shown to be as effective as a leading prescription medication.

Prescribed as a medicinal herb since ancient Greek times, lemon balm has long been known to relieve anxiety, promote sleep, and sooth agitation. Since this botanical extract cannot be patented, its beneficial effects have been completely ignored by pharmaceutical interests.

Animal studies of lemon balm have produced impressive results with regard to stress reduction. In one study, researchers gave low doses of a lemon balm extract to mice. They observed a decrease in anxiety-related behaviors when the animals were placed in an unfamiliar environment.<sup>6</sup> In the same study, higher doses of the lemon balm extract produced analgesic (pain-relieving) effects. Most dramatically, lemon balm extracts induced sleep in mice that had been given tiny (non-sleep-inducing) doses of traditional sedative medications.

A very recent study of herbs used in traditional Lebanese medicine as sedatives demonstrated that lemon balm extracts had the ability to bind to receptors that trigger relaxation and reduce anxiety in the brain.<sup>7</sup>

#### HUMAN STUDIES CONFIRM LEMON BALM'S BENEFITS

A large amount of published data has emerged on the benefits of lemon balm for alleviating anxiety and mood disorders in humans. In the past five years alone, the powerful relaxing effects of lemon balm extracts have been documented by scientists around the world. These studies confirm what herbal practitioners have long known—that lemon balm in combination with other herbal agents is effective in addressing conditions related to stress and anxiety.<sup>8,9</sup>

In 2004, a study documented the effectiveness of a lozenge containing lemon balm along with several other herbal preparations known to reduce anxiety. In a placebo-controlled, double-blind trial, 16 volunteers used the active lozenge or a placebo twice, two hours apart. Brain wave tracings were recorded both before and at various time intervals after the use of the lozenges. When the subjects used the active lozenges, they demonstrated marked increases in the alpha wave activities that are associated with relaxation. Interestingly, there were also increases in the brain wave activity associated with attention, suggesting that the combined herbal preparation helped subjects cope with psychological and emotional stress—without loss of cognitive function.<sup>10</sup>



Lemon Balm (*Melissa officinalis*)

In another 2004 study, lemon balm was examined for its effect on laboratory-induced stress in humans.<sup>11</sup> In this case, 18 healthy volunteers took a single dose of lemon balm extract (300 mg or 600 mg) or a placebo. Their mood was assessed before the dose and one hour after, via a standardized stress-simulation test. Subjects' cognitive performance was also measured. The higher (600 mg) dose ameliorated the stress induced by the test, and produced significantly improved self-ratings of calmness and alertness. Even the lower (300 mg) dose produced a significant increase in the speed at which the subjects could do math problems, without any reduction in accuracy.

- In today's high-pressure environment, stress is ubiquitous. Poorly managed stress contributes not only to anxiety, but also to insomnia and impaired concentration.
- Many of the medicines that are commonly used to relieve stress and promote sleep can produce unwanted side effects, ranging from sedation to memory problems.
- Scientists have uncovered two natural remedies that safely relieve the effects of stress while promoting focused calm.
- Derived from green tea, theanine helps support a sense of relaxation, while maintaining the ability to think clearly.
- Studies show that lemon balm extract is effective in relieving anxiousness and insomnia. Further, lemon balm helps boost cognitive performance and the ability to learn and retain information.
- Theanine and lemon balm hold promise in helping preserve cognitive function with age, and perhaps even warding off Alzheimer's disease.
- Together, theanine and lemon balm offer an antidote to the stresses of modern day life. By promoting focused calm, these two natural agents can help you stay relaxed yet razor-sharp, while ensuring a peaceful night's rest.



### **CLINICAL STUDY SHOWS EFFECTS AGAINST ANXIETY, INSOMNIA**

A recent clinical trial highlighted the powerful stress-relieving benefits of lemon balm. In a double-blind, placebo-controlled trial, 20 volunteers suffering from anxiety and sleep disturbances received 300 mg of a specialized lemon balm extract twice daily (in the morning and evening). After 15 days of treatment, the participants who received lemon balm reported a 49% reduction in their state of anxiety, a 72% reduction in anxiety-associated symptoms, and a 39% decrease in insomnia. In contrast, individuals receiving placebo did not experience significant changes in anxiety or insomnia. These important findings show that lemon balm helps modulate the effects of stress on the body and mind to improve quality of life. Impressively, the benefits are clearly evident approximately two weeks after beginning treatment. While the individuals using lemon balm experienced less difficulty sleeping, it is important to note that the lemon balm extract did not produce unwanted daytime drowsiness. This suggests that lemon balm helped restore sleep by offsetting the effects of stress and anxiety.<sup>12</sup>

### **ENHANCING ATTENTION AND COGNITION**

An elegant and dramatic study published in 2002 demonstrated just how effective lemon balm can be in modulating both attention and cognitive performance.<sup>13</sup> Single doses of lemon balm extract at 300, 600, and 900 mg, or matching placebo, were given to 20 healthy volunteers at one-week intervals, and their cognitive performance was assessed using standardized tests. The results were compelling—the subjects all showed sustained improvement in their accuracy of attention after the 600 mg dose, as well as reductions in memory problems. Subjects also rated their calmness as higher, even shortly after the lowest dose of lemon balm.

The same researchers soon published another study demonstrating further benefits of lemon balm extracts.<sup>14</sup> In this study, 20 healthy volunteers took single doses of lemon balm (600, 1000, and 1600 mg) or placebo at one-week intervals. Cognitive performance was measured before and at one, three, and six hours following the dose. Subjects experienced markedly improved memory and increased calmness at every time-interval

following the highest dose; lower doses produced less dramatic improvements. Further, the scientists used a laboratory model to show that lemon balm binds with cholinergic receptors in human brain tissue of the occipital cortex. Since activity at these receptors is altered in age-related cognitive decline and Alzheimer's disease, lemon balm extract could offer benefits for individuals experiencing memory loss related to these conditions.

There's now exciting data to support lemon balm as a cognition-enhancing agent in age-related cognitive decline.<sup>9,15,16</sup> Since people suffering from cognitive decline frequently have significant agitation, stress, and anxiety, these benefits may offer hope for those who suffer agitation and anxiety related to progressive dementia.

### **RECOMMENDED BY EUROPEAN BOTANICAL SCIENTISTS**

Lemon balm has a long history of additional uses, which include alleviating conditions such as gas and bloating, vomiting, earache, headache, toothache, and sleeplessness. In fact, lemon balm's unique properties have led to its being recommended by the European Scientific Cooperative on Phytotherapy for tension, restlessness, and irritability.<sup>16,17</sup>

## THE CALMING AND NEUROPROTECTIVE EFFECTS OF THEANINE

Another powerful stress reliever is green-tea-derived theanine. When swallowed, theanine is readily absorbed and easily crosses the "blood-brain barrier," allowing it to quickly reach brain cells.<sup>18-20</sup> Like some other components of tea, theanine has tremendous potential as a cellular protectant.<sup>21</sup> Studies in animals and humans demonstrate theanine's ability to help promote relaxation, boost cognitive function, and support brain health.<sup>21,22</sup>



Numerous studies in animals have shown the diverse and beneficial effects that theanine produces in the nervous system. In one study where rats were supplemented with theanine, the animals experienced increased levels of the neurotransmitter serotonin.<sup>20</sup> Boosting serotonin is the mechanism by which many of the leading antidepressant pharmaceuticals work on the brain. Thus, theanine worked in a similar fashion as an antidepressant medication. Other research has highlighted further calming properties of theanine. In another study, theanine decreased the release of excitatory (stimulating) neurotransmitters, while increasing the release of inhibitory (calming) neurotransmitters.<sup>19</sup> The result was a more relaxed state of being.

Even more promising, theanine's effects go beyond promoting relaxation to protecting the delicate nervous system against numerous potential dangers. When researchers injected mice with theanine three hours after a surgically-induced stroke, the size of the damaged area of brain was significantly decreased, as compared with untreated animals. Furthermore, vital brain functions such as blood flow were preserved in the theanine-treated animals.<sup>22</sup> This led the scientists to propose that theanine may be useful in stroke prevention. In another study, theanine helped reduce brain cell death due to stroke in gerbils.<sup>23</sup>

In findings with special relevance for Alzheimer's disease, scientists found that theanine helped protect brain cells against toxicity caused by glutamate, an excitatory neurotransmitter.<sup>24,25</sup> Glutamate toxicity has been linked with the nervous system damage that occurs in Alzheimer's disease, suggesting that theanine could help protect against this devastating neurological disease.<sup>26</sup>

## HUMAN STUDIES CONFIRM THEANINE'S EFFICACY

Building on these exciting animal studies, scientists have conducted a number of well-executed and scientifically sound human trials of theanine. These studies have focused chiefly on theanine's effects on stress, anxiety, and cognitive function.



# REPORT

## Quick Relief from Anxiety and Stress Without Tranquilizer Drugs

By Tiesha D. Johnson, RN, BSN

### THEANINE VS. XANAX®: COMPARISON OF EFFECTS

One of the most compelling studies on theanine was published in 2004. In a double-blind, head-to-head comparison study, investigators compared theanine with alprazolam (Xanax®), a commonly prescribed anxiolytic (anti-anxiety) drug.<sup>27</sup> Each of 16 healthy human volunteers took either 1 mg alprazolam, 200 mg theanine, or a placebo on separate occasions; thus, all participants were tested with all three treatments. Following each dose, the researchers obtained behavioral measures of anxiety in all participants, both before and after an experimentally-created state of anxiety.



The results were nothing short of remarkable. Theanine, but not alprazolam or the placebo, induced relaxing effects that were evident at the initial measurement of whether a person felt tranquil versus troubled. This study is even more impressive when the dose of alprazolam is taken into consideration. One milligram is a substantial dose of this medication—generally, most people use just 0.25 to 0.5 mg of alprazolam as a bedtime sleep aid. Theanine's superior performance to a potentially habit-forming medication is truly stunning good news.<sup>27</sup>

#### THE TROUBLE WITH BENZODIAZEPINES

The most widely used class of anxiety-relieving drugs is the benzodiazepines. This class of drugs includes diazepam (Valium®) and alprazolam (Xanax®).

While these drugs are highly effective in calming anxiety, they may also be habit-forming—a factor that dramatically limits their usefulness and possibly their long-term safety.<sup>28,29</sup> Many of the benzodiazepines also cause significant memory impairment, a highly undesirable effect.<sup>4,5</sup>

The dramatic effects of theanine have been further explored in several studies published just this year. A group of Japanese researchers studied the effects of theanine on psychological and physiological stress responses in humans.<sup>3</sup> The researchers assigned a mental arithmetic task to each of 12 participants on four separate occasions, inducing so-called “math anxiety.” On one occasion, the subjects took theanine at the beginning of the test, on another they took the supplement halfway through, on a third they took a placebo that was identical to the supplement, and on a fourth they took nothing at all.

Astonishingly, even this extremely short-term use of theanine had remarkable effects on manifestations of anxiety. Subjects using theanine experienced a reduction in heart rate in response to the math testing, compared with those receiving placebo. Analysis of heart-rate variability suggested that theanine modulated activation of the sympathetic nervous

system, the part of the nervous system that produces the “fight-or-flight” response. Because the sympathetic nervous system stimulates the release of adrenalin and triggers the first steps in the stress response that eventually leads to elevated stress hormone levels, keeping this system in check may help avert the deleterious long-term health consequences of stress.<sup>3</sup>

### THEANINE SUPPORTS COGNITIVE FUNCTION

A growing body of research suggests that theanine may be a powerful tool in boosting cognitive function. Theanine may work via several mechanisms of action to help keep the mind sharp.<sup>30</sup>

A 2007 report on theanine provides a detailed look at exactly how theanine works to improve cognition. New York-based researchers affiliated with the US Air Force were interested in “mapping” exactly where theanine produces effects in the brain.<sup>31</sup> Previously, scientists have noted that when a person concentrates attention on a task, an electroencephalogram (EEG) study will show increased brain waves in the “alpha” region of the EEG spectrum.<sup>32,33</sup> The Air Force investigators sought to determine whether theanine might cause changes in the important alpha region of the EEG during tasks that involve selective focus, indicating enhanced ability to perform attention-requiring tasks.<sup>31</sup>

While study subjects performed a standard task requiring focused attention, the researchers gathered data from EEG electrodes. As expected, the subjects showed significant increases in their alpha brain wave activity while concentrating on the tasks. When the subjects took theanine



prior to the task, they showed a surprising decrease in alpha wave background activity, but a prominent increase in the important alpha activity related to the attention-requiring tasks.<sup>31</sup> This critical result suggests that theanine has important and specific effects on the brain circuits involved in focusing attention on critical tasks.

An innovative Japanese study corroborates theanine's ability to support essential brain function. Study participants who chewed gum containing 200 mg of theanine displayed significant increases in brain wave activity associated with focus and attention, as compared with individuals who chewed gum that did not contain theanine.<sup>34</sup> This study suggests that theanine has the ability to promote attention to vital tasks, while minimizing interference from distracting outside stimuli—a finding that may have a wealth of important applications. These potential applications of theanine include enhancing concentration and performance in stressful situations, and potentially helping manage conditions such as attention-deficit disorder.

Growing evidence suggests a potential role for theanine in averting the most dreaded cause of memory loss—Alzheimer's disease. Recent data have shown that theanine—along with other phytochemicals derived from green tea—promotes the activity of an enzyme that breaks down the harmful beta-amyloid protein, which is commonly found in the brains of Alzheimer's patients.<sup>35</sup> This promising preliminary study suggests that theanine could offer crucial protection against the brain changes that precede Alzheimer's disease.

## **OTHER BENEFITS OF THEANINE**

While theanine has received the most attention for its anxiety- and stress-relieving effects, this versatile natural agent is also attracting attention for its many other potential benefits.

Theanine may offer important support for healthy blood pressure levels. When scientists administered theanine to laboratory rats prone to high blood pressure, the animals displayed a significant drop in blood pressure. Notably, theanine did not cause any changes in rats with normal blood pressure. These findings suggest that theanine may benefit those with elevated blood pressure, while maintaining blood pressure levels that are already within a healthy range.<sup>36</sup>

Theanine may have further applications in promoting healthy weight management. When researchers studied body weight changes in laboratory mice in response to supplementation with the green tea constituents catechins, theanine, and caffeine, they found remarkable effects.<sup>37</sup> The green tea-derived supplements notably modulated the tendency to gain weight and abdominal fat. In addition, the theanine-containing supplements reduced serum fatty acids. The researchers concluded that caffeine and theanine together “were responsible for the suppressive effect of green tea powder on body weight gain and fat accumulation.”

Theanine may find important use as an adjuvant cancer therapy. Scientists now know that theanine enhances the activity of certain chemotherapy drugs, while minimizing their destructive effects on healthy tissues. Theanine can increase the concentration of the drug doxorubicin (Adriamycin®) in tumors by suppressing a transport system that tumor cells normally use to rid themselves of the drug. Theanine also reduces tumor cell content of antioxidants that could reduce the drug's destructive action on the cancer cells.<sup>38,39</sup> While highly promising, further investigation is needed to fully evaluate the interaction between theanine and various cancer therapies.

Together, these findings suggest a host of new areas for exploration of theanine's life-enhancing properties.

## **SAFETY AND DOSAGE**

Theanine is used in daily dosages ranging from 100-400 mg. There are no known adverse reactions associated with theanine. Pregnant women and nursing mothers should avoid theanine supplements until more is known about its effects. Theanine may enhance the anti-tumor effects of doxorubicin and idarubicin. The use of theanine supplements with cancer chemotherapeutic agents should only be conducted under medical supervision.<sup>18</sup>

The suggested dose of lemon balm is 300 mg, once or twice daily. Lemon balm may be used in the morning to address daytime anxiety, or may be used in the evening to support relaxation and sleep. There are no known contraindications to using lemon balm.<sup>16</sup>

## **COMPLEMENTARY BENEFITS OF THEANINE AND LEMON BALM**

Both green tea and lemon balm have centuries-old reputations as beneficial therapies for anxiety, stress, and impaired cognition. Together, these soothing natural agents hold promise in restoring the relaxed focus and mental clarity that are so easily eroded by the stressors of modern life. Further, these plant-derived remedies may even help stave off the cognitive decline associated with aging.

## References

---

1. Sridhar GR. Psychiatric co-morbidity & diabetes. *Indian J Med Res.* 2007 Mar;125(3):311-20.
2. Csaba BM. Anxiety as an independent cardiovascular risk. *Neuropsychopharmacol Hung.* 2006 Mar;8(1):5-11.
3. Kimura K, Ozeki M, Juneja LR, Ohira H. L-Theanine reduces psychological and physiological stress responses. *Biol Psychol.* 2007 Jan;74(1):39-45.
4. Beracochea D. Anterograde and retrograde effects of benzodiazepines on memory. *ScientificWorldJournal.* 2006;6:1460-5.
5. Savic MM, Obradovic DI, Ugresic ND, Bokonjic DR. Memory effects of benzodiazepines: memory stages and types versus binding-site subtypes. *Neural Plast.* 2005;12(4):289-98.
6. Soulmani R, Fleurentin J, Mortier F, et al. Neurotropic action of the hydroalcoholic extract of *Melissa officinalis* in the mouse. *Planta Med.* 1991 Apr;57(2):105-9.
7. Salah SM, Jager AK. Screening of traditionally used Lebanese herbs for neurological activities. *J Ethnopharmacol.* 2005 Feb 10;97(1):145-9.
8. Gyllenhaal C, Merritt SL, Peterson SD, Block KI, Gochenour T. Efficacy and safety of herbal stimulants and sedatives in sleep disorders. *Sleep Med Rev.* 2000 Jun;4(3):229-51.
9. Kennedy DO, Little W, Haskell CF, Scholey AB. Anxiolytic effects of a combination of *Melissa officinalis* and *Valeriana officinalis* during laboratory induced stress. *Phytother Res.* 2006 Feb;20(2):96-102.
10. Dimpfel W, Pischel I, Lehnfeld R. Effects of lozenge containing lavender oil, extracts from hops, lemon balm and oat on electrical brain activity of volunteers. *Eur J Med Res.* 2004 Sep 29;9(9):423-31.
11. Kennedy DO, Little W, Scholey AB. Attenuation of laboratory-induced stress in humans after acute administration of *Melissa officinalis* (Lemon Balm). *Psychosom Med.* 2004 Jul;66(4):607-13.
12. Available at: <http://www.nutraingredients.com/news/ng.asp?id=75166-berkem-lemon-balm-extract-stress-anxiety>. Accessed May 22, 2007.
13. Kennedy DO, Scholey AB, Tildesley NT, Perry EK, Wesnes KA. Modulation of mood and cognitive performance following acute administration of *Melissa officinalis* (lemon balm). *Pharmacol Biochem Behav.* 2002 Jul;72(4):953-64.
14. Kennedy DO, Wake G, Savelev S, et al. Modulation of mood and cognitive performance following acute administration of single doses of *Melissa officinalis* (Lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties. *Neuropsychopharmacology.* 2003 Oct;28(10):1871-81.
15. de Sousa AC, Alviano DS, Blank AF, et al. *Melissa officinalis* L. essential oil: antitumoral and antioxidant activities. *J Pharm Pharmacol.* 2004 May;56(5):677-81.
16. Available at: [http://www.pdrhealth.com/drug\\_info/nmdrugprofiles/herbaldrugs/101690.shtml](http://www.pdrhealth.com/drug_info/nmdrugprofiles/herbaldrugs/101690.shtml). Accessed May 22, 2007.
17. Ulbricht C, Brendler T, Gruenwald J, et al. Lemon balm (*Melissa officinalis* L.): an evidence-based systematic review by the Natural Standard Research Collaboration. *J Herb Pharmacother.* 2005;5(4):71-114.
18. Available at: [http://www.pdrhealth.com/drug\\_info/nmdrugprofiles/nutsupdrugs/lth\\_0296.shtml](http://www.pdrhealth.com/drug_info/nmdrugprofiles/nutsupdrugs/lth_0296.shtml). Accessed May 22, 2007.
19. Yamada T, Terashima T, Okubo T, Juneja LR, Yokogoshi H. Effects of theanine, r-glutamylethylamide, on neurotransmitter release and its relationship with glutamic acid neurotransmission. *Nutr Neurosci.* 2005 Aug;8(4):219-26.
20. Yokogoshi H, Kobayashi M, Mochizuki M, Terashima T. Effect of theanine, r-glutamylethylamide, on brain monoamines and striatal dopamine release in conscious rats. *Neurochem Res.* 1998 May;23(5):667-73.
21. Cooper R, Morre DJ, Morre DM. Medicinal benefits of green tea: Part I. Review of noncancer health benefits. *J Altern Complement Med.* 2005 Jun;11(3):521-8.

22. Egashira N, Hayakawa K, Mishima K, et al. Neuroprotective effect of gamma-glutamylethylamide (theanine) on cerebral infarction in mice. *Neurosci Lett*. 2004 Jun 3;363(1):58-61.
23. Kakuda T, Yanase H, Utsunomiya K, et al. Protective effect of gamma-glutamylethylamide (theanine) on ischemic delayed neuronal death in gerbils. *Neurosci Lett*. 2000 Aug 11;289(3):189-92.
24. Nagasawa K, Aoki H, Yasuda E, et al. Possible involvement of group I mGluRs in neuroprotective effect of theanine. *Biochem Biophys Res Commun*. 2004 Jul 16;320(1):116-22.
25. Kakuda T, Nozawa A, Sugimoto A, Niino H. Inhibition by theanine of binding of [3H]AMPA, [3H]kainate, and [3H]MDL 105,519 to glutamate receptors. *Biosci Biotechnol Biochem*. 2002 Dec;66(12):2683-6.
26. Chohan MO, Iqbal K. From tau to toxicity: emerging roles of NMDA receptor in Alzheimer's disease. *J Alzheimers Dis*. 2006 Sep;10(1):81-7.
27. Lu K, Gray MA, Oliver C, et al. The acute effects of L-theanine in comparison with alprazolam on anticipatory anxiety in humans. *Hum Psychopharmacol*. 2004 Oct;19(7):457-65.
28. Available at: [http://www.pdrhealth.com/drug\\_info/rxdrugprofiles/drugs/val1473.shtml](http://www.pdrhealth.com/drug_info/rxdrugprofiles/drugs/val1473.shtml). Accessed May 30, 2007.
29. Available at: [http://www.pdrhealth.com/drug\\_info/rxdrugprofiles/drugs/xan1491.shtml](http://www.pdrhealth.com/drug_info/rxdrugprofiles/drugs/xan1491.shtml). Accessed May 30, 2007.
30. Nathan PJ, Lu K, Gray M, Oliver C. The neuropharmacology of L-theanine(N-ethyl-L-glutamine): a possible neuroprotective and cognitive enhancing agent. *J Herb Pharmacother*. 2006;6(2):21-30.
31. Gomez-Ramirez M, Higgins BA, Rycroft JA, et al. The deployment of intersensory selective attention: a high-density electrical mapping study of the effects of theanine. *Clin Neuropharmacol*. 2007 Jan;30(1):25-38.
32. Jokisch D, Jensen O. Modulation of gamma and alpha activity during a working memory task engaging the dorsal or ventral stream. *J Neurosci*. 2007 Mar 21;27(12):3244-51.
33. Dockree PM, Kelly SP, Foxe JJ, Reilly RB, Robertson IH. Optimal sustained attention is linked to the spectral content of background EEG activity: greater ongoing tonic alpha (approximately 10 Hz) power supports successful phasic goal activation. *Eur J Neurosci*. 2007 Feb;25(3):900-7.
34. Yagyu T, Wackermann J, Kinoshita T, et al. Chewing-gum flavor affects measures of global complexity of multichannel EEG. *Neuropsychobiology*. 1997;35(1):46-50.
35. Ayoub S, Melzig MF. Induction of neutral endopeptidase (NEP) activity of SK-N-SH cells by natural compounds from green tea. *J Pharm Pharmacol*. 2006 Apr;58(4):495-501.
36. Yokogoshi H, Kato Y, Sagesaka YM, et al. Reduction effect of theanine on blood pressure and brain 5-hydroxyindoles in spontaneously hypertensive rats. *Biosci Biotechnol Biochem*. 1995 Apr;59(4):615-8.
37. Zheng G, Sayama K, Okubo T, Juneja LR, Oguni I. Anti-obesity effects of three major components of green tea, catechins, caffeine and theanine, in mice. *In Vivo*. 2004 Jan;18(1):55-62.
38. Sadzuka Y, Sugiyama T, Suzuki T, Sonobe T. Enhancement of the activity of doxorubicin by inhibition of glutamate transporter. *Toxicol Lett*. 2001 Sep 15;123(2-3):159-67.
39. Sugiyama T, Sadzuka Y. Theanine and glutamate transporter inhibitors enhance the antitumor efficacy of chemotherapeutic agents. *Biochim Biophys Acta*. 2003 Dec 5;1653(2):47-59.

your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.