"Anxiolytic Effects of L-Theanine: A Component of Green Tea, when Combined with Midazolam, in the Male Sprague-Dawley Rat"

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www.vetmed.ucdavis.edu/Animal_Alternatives/LabHAI.html

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Problem Statement

- It is not known if L-theanine, a component of green tea, has an anxiolytic effect via activation of benzodiazepine site on the GABA$_A$ receptor.
Significance

- Anxiety Disorders are prevalent in American culture, affecting approximately 40 million adults (16%) age 18-54. (surggeneral.gov, 2006)
- A recent review of the literature indicates as many as 77% of patients do not disclose use of alternative medicines; this has prompted a JCAHO mandate that all health care providers screen for use of alternative medications. (Complementary Therapies in Medicine, 2006)
- The incidence of herbal use in preoperative patients approaches 22%, compared to 18% of the general population. (Anesthesiology, 2000)
- Herbal products can interact with frequently used medications—including anesthesia—and may cause serious unforeseen consequences or complications. (JAMA, 2001)
- Few studies address the therapeutic effects of L-theanine.
Research Questions

- Does L-theanine (a component of green tea) have anxiolytic effects in the laboratory rat?
- Is the anxiolytic effect of L-theanine a result of modulation of the benzodiazepine site on the GABA<sub>A</sub> receptor?
Theoretical Framework

Anxiety

Stress

↑ Serum Corticosterone

↑ Catecholamine

Behavioral Changes (EPM)
Theoretical Framework

Anxiety

Decrease

Stress

L-theanine

GABA<sub>A</sub> Receptor

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<tr>
<th>Decrease</th>
<th>Stress</th>
<th>Anxiety</th>
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- Serum Corticosterone?
- Catecholamine?
- Behavioral Changes? (EPM)
Literature Review


Research Design

- Prospective Experimental Between Groups Design
  1. Control (vehicle)
  2. L-theanine 10 mg/kg
  3. Midazolam 1.5 mg/kg
  4. Flumazenil 3 mg/kg + L-theanine 10 mg/kg
  5. Midazolam 1.5 mg/kg + L-theanine 10 mg/kg
Methodology

- Medication injected intraperitoneally 30 minutes prior to testing
- Test 5 minutes on the elevated plus maze (EPM)
- Data was collected via the MotorMonitor software
  Hamilton-Kinder
Instrumentation

- Elevated Plus Maze (EPM)
  - Valid and reliable instrument for anxiolytic studies using the rat model

Montgomery (1955), Pellow (1985)
Statistical Analysis

- Multivariate Analysis of Variance (MANOVA two-tailed)
- Sheffe Post Hoc Test
Methodology
Ratio Open Arm Time/Total Time

Mean Open Arm/Total Time +/- SEM

- Control
- Theanine
- Midazolam
- Flumazenil
- Midazolam + Theanine

* Indicates significant difference.
Discussion

- L-theanine and anxiolysis
- L-theanine and GABA$_A$ receptor
- L-theanine and midazolam
Future Study

- Explore L-theanine’s motor effects
- Establish the molecular mechanism of action and its potential effects in other neurotransmitter systems
- Determine significant clinical interactions of L-theanine
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Questions?