A Review Article on Evaluation of Synergistic Anxiolytic Effects of Lemongrass (Cymbopogon citratus)and blue pea flower(Clitoria ternatea) Hydroalcoholic Extract and Topiramate in Experimental Rat Models

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ABSTRACT

Anxiety disorders are among the most prevalent neuropsychiatric conditions worldwide, often requiring long-term pharmacological management. However, conventional anxiolytic drugs are associated with adverse effects and limited patient compliance, prompting the exploration of safer and more effective alternatives. This review article evaluates the potential synergistic anxiolytic effects of hydroalcoholic extracts of *Cymbopogon citratus* (lemongrass) and *Clitoria ternatea* (blue pea flower) in combination with topiramate using experimental rat models.*Cymbopogon citratus* and *Clitoria ternatea* are medicinal plants known for their neuroprotective, antioxidant, and mild sedative properties, attributed to bioactive compounds such as flavonoids, alkaloids, and phenolic constituents. Topiramate, an anticonvulsant drug, has demonstrated anxiolytic effects through modulation of GABAergic transmission and inhibition of excitatory neurotransmission. This review highlights the therapeutic potential of integrating phytochemicals with conventional pharmacotherapy for anxiety management. Further experimental and clinical studies are warranted to elucidate the precise mechanisms, optimize dosage regimens, and confirm safety and efficacy in humans.

Keywords:
Anxiety disorders; Anxiolytic activity; *Cymbopogon citratus*; *Clitoria ternatea*; Lemongrass; Blue pea flower; Topiramate; GABAergic modulation.

Introduction

Anxiety and depressive disorders are the most common mental illnesses in the world and a prominent health care problem . The World Health Organization (WHO) estimates that the prevalence of these diseases ranges from 0.1 to 16.9% Benzodiazepines are the major class of compounds used to treat generalized anxiety disorder and acute anxiety states . However, these compounds have a number of undesirable effects such as sedation, muscle relaxation, amnesia, dependence and tolerance.

Cymbopogon citratus (DC) Stapf (Poaceae), commonly known as lemongrass, is widely used in traditional medicine as an infusion or decoction for treating nervous disturbances.In Mexico, *Cymbopogon citratus* is used as a sedative, and in Brazil, an infusion or the cold juice of the leaves has been employed as a sedative and analgesic (Hiruma-Lima et al., 2002). An antinociceptive effect of *Cymbopogon citratus* has been detected in the

rodent hot plate test, an experimental procedure related to central activity. In the previous work (Costa et al., 2006, Blanco et al., 2009), we have demonstrated that acute treatment with the essential oil (EO) from *Cymbopogon citratus* is effective against generalized anxiety disorder and epilepsy in experimental procedures in mice[1].

Anxiety is a common ailment of high co-morbidity with epilepsy, a chronic neurologic disease characterized by recurrent seizures. Current drugs used for these conditions have several limitations such as disabling side effects, relapse, and ineffectiveness in certain population necessitating the search for alternative options. The aqueous leaf extract of *Cymbopogon citratus* (CYC) is widely used for its various health-promoting effects including relief of seizures and anxiety in ethnomedicine. This present study describes its effects on convulsions, anxiety-like behaviors, and social interaction in mice [2].

The biology of anxiety is considered as an integral part of the human response to threat or danger and it affects about one-eight of the world's population. Anxiety is a generalized response to a potential threat, danger, fear, or even internal or external, and it's marked by a rise in arousal, expectancy, autonomic and neuro endocrine activation and also shows specific patterns in behavior. These changes basically are to enhance coping with an adverse or unexpected situation. Anxiety may also be referred to an elaborate form of fear, and causes an increase in the ability of an individual to adapt and plan for the future. Fear and anxiety are difficult to distinguish. The distinction between the two lies in the concept that the former is a response to an actual threat while latter is anticipatory response to a potential threat. The cause of anxiety remains unclear, but report elicits evidence that implicate societal factor, psycho-stimulant drugs (amphetamine, caffeine), genetic and environmental factors. Some anxiety states are essential mechanism for survival and are feature of all mammals[3].

1. Introduction to Anxiety and Current Treatments

Anxiety disorders are among the most common psychiatric conditions globally. They involve excessive fear, worry, restlessness, and physiological changes like increased heart rate. Common treatments include benzodiazepines, SSRIs, SNRIs, and other medications. Although effective, these drugs can cause **sedation, dependence, cognitive impairment, and withdrawal effects.** This has encouraged interest in **herbal alternatives**and **drug–herb combinations** that may improve efficacy and reduce side effects.

2. Overview of Cymbopogon citratus (Lemongrass)

Lemongrass is a medicinal plant widely used in traditional medicine across Africa, Asia, and South America. It contains essential oils and phytochemicals with therapeutic importance.

2.1 Phytochemical Composition

Major active compounds include:

- **Citral (geranial + neral)**
- **Myrcene**
- **Flavonoids (quercetin, luteolin)**
- **Phenolic compounds**
- **Tannins and saponins**

2.2 Traditional Uses

Lemongrass has been used as a folk remedy for:

- Anxiety, stress, and insomnia
- Headache
- Stomach ailments
- Fever and inflammation
- Antimicrobial purposes

***Cymbopogon citratus* (Lemongrass)**

3. Anxiolytic Potential of Lemongrass

Several studies support the calming and anti-anxiety potential of *C. citratus*.

3.1 Essential Oil Studies

- Inhalation of lemongrass essential oil has shown **reduced anxiety-like behavior** in animal models.
- Aroma therapy using lemongrass has improved autonomic nervous system activity and reduced subjective anxiety in human volunteers (measured by questionnaires and physiological parameters).

3.2 Extract-Based Studies

Hydroalcoholic extracts, methanolic extracts, and aqueous extracts of lemongrass have shown:

- Increased open-arm time in Elevated Plus Maze (EPM)
- Increased central zone activity in Open Field Test (OFT)
- Reduction in stress-induced behaviors

These effects are believed to be due to:

- **GABAergic modulation**
- **Antioxidant action reducing oxidative stress in the brain**
- **Reduction of corticosterone levels**

3.3 Mechanisms Proposed

1. **GABA receptor enhancement** – similar to mild benzodiazepine-like action.
2. **Decrease in oxidative stress** – protects neural circuits involved in anxiety.
3. **Serotonergic modulation** – flavonoids may influence serotonin levels.

Thus, lemongrass extract demonstrates **mild to moderate anxiolytic effects**.

4. Overview of Topiramate

Topiramate is primarily an **antiepileptic drug,** but research suggests it may have anxiolytic properties.

4.1 Pharmacological Actions

Topiramate works through multiple mechanisms:

- Enhances **GABA-A receptor** activity
- Inhibits **glutamate** neurotransmission (AMPA/kainate receptors)
- Blocks voltage-gated sodium channels
- Reduces oxidative stress and neuro inflammation

These mechanisms are important in anxiety regulation.

4.2 Topiramate in Anxiety Studies

- Several preclinical studies have shown that Topiramate reduces anxiety-like behavior in rodent models.
- Clinically, it has been tested for **PTSD, alcohol dependence**, and **bipolar disorder**, where anxiety is a major component.
- Some studies report reductions in **anticipatory anxiety** and stress-induced behavior.

5. Herbal–Drug Synergism in Anxiety Treatment

There is increasing scientific interest in combining herbal extracts with standard medications.

Why combination therapy?

- Many herbal extracts act on multiple pathways.
- Low doses of drugs + herbs may produce **better therapeutic effects**.

- Reduced risk of side effects from high-dose synthetic drugs.
- Synergistic antioxidant and neurotransmitter-regulating effects.

6.Overview of Blue Pea Flower (Clitoria ternatea)

6.1. Introduction

The **blue pea flower**, also called **butterfly pea**, **Asian pigeonwings**, or **Shankhpushpi** (in some traditions), comes from the plant *Clitoria ternatea*, a perennial climber native to Southeast Asia. It is widely used for its vibrant blue flowers and traditional medicinal properties.

6.2.Botanical Description

- **Family:** Fabaceae (legume family)
- **Growth habit:** Fast-growing perennial vine
- **Leaves:** Pinnate with 5–7 leaflets
- **Flowers:** Bright blue (sometimes white), with a unique shape resembling a conch-shell or butterfly
- **Fruit:** Flat pods with several seeds

The flowers contain **anthocyanins**—specifically **ternatins**—responsible for the intense blue pigment.

6.3. Traditional Uses

A. Culinary Uses

- Natural food dye for rice, desserts, and drinks
- Popular in Southeast Asian cuisines
- Color-changing properties: turns **purple with lemon/lime (acid)**

B. Herbal & Traditional Medicine-Used in Ayurveda, Traditional Chinese Medicine, and Thai folk medicine for:

- Memory enhancement
- Reducing stress/anxiety
- Improving eye health
- Anti-inflammatory effects

6.4. Nutritional & Phytochemical Profile

Contains:

- **Anthocyanins (ternatins)** – antioxidant pigment
- **Flavonoids (quercetin, kaempferol)**
- **Alkaloids**
- **Triterpenoids**
- **Cyclotides** – small proteins with antimicrobial/cell-protective properties

Blue Pea Flower (Clitoria ternatea)

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