

Unweaving the Brain Chemistry of Anxiety Neurosis: Therapeutic Potential of *Clitoria ternatea*

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I. Introduction

Most significantly, the burden of anxiety disorders on global mental health is considerable, as they affect 264 million people worldwide (18). Over the lifespan, the lifetime prevalence of anxiety disorders varies from 4% to 33%, depending on the geographical and demographic characteristics of the affected population (32). Anxiety disorders significantly contribute to the global burden of disability, which also results in considerable economic costs, particularly due to lost productivity and increased medical costs (18). Anxiety disorders do not discriminate based on the factors of age, gender, or ethnicity. They often begin in childhood or adolescence, which may extend into adulthood. These disorders have been correlated with the risk of co-occurring disorders, including substance use disorders, depression, and suicidal ideas (7). Anxiety disorders, as a clinical phenomenon, have been characterized by apprehensiveness, excessive worrying, autonomic arousal, and physical complaints that interfere with daily functioning (1). Approximately 60% of the cases have an overlap with major depressive disorders (13). Anxiety disorders have also been correlated with cardiovascular and metabolic consequences, which may be related to the phenomenon of stress, inflammatory markers including IL-6 and TNF-alpha, and the disruption of homeostatic functions. The historical construct of “anxiety neurosis” reflects the psychodynamic model of the past and resembles the current DSM-5 criteria of generalized anxiety disorder (GAD) (1). GAD is characterized by excessive worrying and anxiety that occurs on most days for six or more months, accompanied by three or more of the following symptoms: restlessness, fatigue, difficulty concentrating, irritability, muscle tension, or sleep disturbances (1,7). Somatic symptoms like palpitations, sweating, tremors, gastrointestinal complaints, and fatigue often prompt repeated medical consultations (7). Neuroscientifically, these disorders stem from dysfunction within multiple neural systems. GABAergic dysfunction results in overactive neuronal firing. Dysfunction of the monoaminergic systems, such as serotonin, norepinephrine, and dopamine, is also a factor. Hyperactivation of the

hypothalamic-pituitary-adrenal axis is also a factor in maintaining elevated cortisol levels, leading to hippocampal atrophy. The overproduction of reactive oxygen species leading to oxidative stress and the continuous presence of an inflammatory response involving cytokines such as TNF-alpha and IL-6 also play a role. The gut brain axis is also an emerging factor in anxiety disorders. Although much success has been achieved in the pharmacological treatment of anxiety disorders, complete remission is difficult to attain. Only 50–60% of individuals respond favorably, but relapse is inevitable when treatment is withdrawn. Although benzodiazepines provide quick relief through GABA-A receptor activation, they also have several undesirable effects such as sedation, cognitive clouding, dependency, and potential for abuse. SSRIs and SNRIs are commonly used as first-line treatments but take weeks to be effective. These medications also have a few undesirable effects such as gastrointestinal disturbances, sexual dysfunction, weight changes, and withdrawal symptoms.

These limitations have given rise to the need to explore the effectiveness of complementary and alternative medicine (CAM) therapies. The traditional systems have described several herbal interventions to control stress and anxiety disorders. *Clitoria ternatea* L., commonly known as Butterfly Pea or Aparajita, has been used traditionally to improve cognitive functions, control anxiety, and maintain the health of the nervous system. The analysis of the phytochemical content of the herb has revealed the presence of anthocyanins, flavonoids, and phenolic compounds, which have shown potent antioxidant and anti-inflammatory activities. Preliminary in vitro studies have shown the potential of the herb to affect the GABA signaling pathways, prevent oxidative damage, and suppress neuroinflammation. This review aims to compile the contemporary literature on the neural mechanisms of anxiety disorders and the in vitro evidence of the anxiolytic potential of the herb.

II. Neurobiology of Anxiety Neurosis

Frequently, the etiology of anxiety disorders is related to disturbances of the brain's chemical signaling mechanisms that control the processing of emotions and the management of stress. For instance, the inhibitory neurotransmitter, gamma aminobutyric acid (GABA), is crucial to the regulation of neuronal excitability. Impairments of GABA or its receptors lead to neuronal hyperexcitability, especially in the amygdala and prefrontal cortex, resulting in excessive hyperarousal and exaggerated fear responses. The serotonin system, especially the 5-HT1A and 5-HT2 receptors, may interfere with mood regulation and the ability to cope with stress. Hyperactivity of the dopamine system, particularly the mesolimbic dopamine system, may be associated with affective disorders and anhedonia. Moreover, excessive activity of the noradrenergic system from the locus coeruleus results in enhanced stress responses, which manifest as increased heart rates, tremors, and increased autonomic arousal.

A hallmark of anxiety disorders is the prolonged activation of the hypothalamic pituitary-adrenal (HPA)

axis, which results in increased levels of the stress hormone cortisol. Hypercortisolism may lead to hippocampal atrophy, which impairs the termination of the stress response through the disruption of the intrinsic termination mechanisms of the system. Oxidative stress and inflammation also contribute to the etiology of the disorder, especially the structural and functional brain alterations that result from the prolonged activation of the HPA axis. An accumulation of reactive oxygen species (ROS) results in the degradation of lipids, proteins, and DNA of the cellular energy centers, leading to the disruption of the production of cellular energy. At the same time, inflammatory markers like tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) interfere with the dynamics of neurotransmitters, synaptic plasticity, and the integrity of the blood brain barrier.

Fig1. Anxiety Grade

Table 1.

The pie chart illustrates the following distribution of anxiety levels in the cohort:

Anxiety Level		Description
No Anxiety		Represented by the blue slice; individuals reported minimal symptoms, with no significant interference in daily functioning.
Mild Anxiety	~40%	Largest orange slice: common among participants, often manifesting as occasional worry or restlessness, but manageable without professional intervention. Green slice: this group experienced marked impairment, such as difficulty concentrating or sleep disturbances, warranting monitoring.
Moderate Anxiety	~30%	
Severe Anxiety	~10%	Small brown slice (labeled "Severe..."); high-impact symptoms like panic attacks or avoidance behaviors, indicating need for immediate clinical support.

III. Limitations of Conventional Treatments

Medications form a vital part of the therapeutic interventions used to treat anxiety disorders (3).

Nonetheless, these have a few drawbacks, as evidenced by the fact that, for instance, benzodiazepines, which act by increasing GABAergic activity via GABA-A receptor modulation, offer acute relief from anxiety disorders. Nonetheless, the use of these drugs has several adverse effects, such as causing sedation, cognitive clouding, slowing down reaction time, developing a high level of tolerance, as well as the potential to cause dependence, which makes it difficult to stop the drug without experiencing withdrawal symptoms (16).

In the case of the management of persistent or chronic anxiety disorders, SSRIs have been generally considered the first-line pharmacotherapeutic approach to the management of the condition. These act by inhibiting serotonin reuptake, thus increasing the availability of serotonin at the synapses of the central nervous system (5,6). Even though these forms of medication have a number of benefits, the fact remains that the benefits of these forms of medication do not become apparent until after 4 to 6 weeks of use, with only 50-60% of the subjects experiencing complete remission of the condition (3). Among the adverse effects of these forms of medication, which result in the discontinuation of the drug as well as the failure to completely alleviate the symptoms of the condition, include sexual dysfunction, gastrointestinal disturbances, emotional numbing, as well as withdrawal difficulties, among others (3,7).

All these considerations emphasize the need to have alternative forms of treatment that act via different pathways, which have fewer adverse effects as well as better safety profiles (37,38).

IV. Ethnopharmacology and Phytochemistry of *Clitoria ternatea*

The climbing perennial, **Clitoria ternatea** L., of the Fabaceae family, has adapted well to several tropical and subtropical areas of Asia (20). The species has been well known for its bright blue or white coloration of the flowers, which have been used as a traditional medicine for a long time. In Ayurvedic medicine, the herb has been classified as a Medhya Rasayana, a category of herbs that improve cognitive functions, enhance memory, and improve mental clarity (20, 39). The roots, leaves, and flowers of the herb have been used to treat various conditions, such as anxiety, depression, sleep disorders, seizures, and cognitive decline associated with aging, as mentioned in traditional literature of Southeast Asia (20, 39).

The therapeutic value of the herb has been well justified by the presence of a diverse array of bioactive compounds, which include flavonoids, anthocyanins, alkaloids, triterpenoids, saponins, and phenolic compounds such as quercetin, kaempferol, ternatins, etc. These bioactive compounds have shown promising activity as an antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory agent, which could modulate the central nervous system activity, producing anxiolytic- and antidepressant-like effects, as shown by various in vitro and in vivo studies (20, 29).

The combined effect of these bioactive compounds has the potential to provide a broad spectrum of therapeutic activity, which targets multiple pathways, as opposed to the single-target approach of

conventional pharmaceuticals (31). For instance, anthocyanins have shown potent activity as a scavenger of free radicals, as well as the ability to downregulate the inflammatory cascade, thereby potentiating the neuroprotective effect of the herb (24, 26).

V. UPreclinical Evidence and Mechanisms

Animal studies have revealed that the herb works to calm the brain through increased GABA activity. This works to calm the mind without the side effects of drowsiness often associated with benzodiazepine drugs. It seems that the flavonoids in the plant are the active compounds that increase the binding ability of GABA to its receptors. Additionally, the herb works on the serotonin and dopamine levels in the brain, possibly through the inhibition of enzymes that break these chemicals down, which results in increased levels and therefore a more stable mood. It is also known to have strong antioxidant properties that protect the brain from free radicals and maintain the areas of the brain, such as the hippocampus, which are prone to damage from these free radicals in their normal state.

Regarding anti-inflammatory properties, the plant has been known to reduce inflammation in the brain through the reduction of TNF-alpha and IL-6 in lab animals. New information has revealed that the plant works to regulate the body's natural response to stress, the HPA axis, which results in increased resistance to tension through the reduction of cortisol levels and the regulation of the body's natural checks on the system.

It has been tested in standard mouse and rat models using the elevated plus maze, open-field test, and light-dark box test, which all measure the levels of anxiety in the test subjects and their ability to move through the test and into the areas of the maze that would cause them the greatest amount of anxiety. It has been revealed that the plant has strong anti-anxiety effects and works to improve cognitive ability in the test subjects, like the effects of drugs such as diazepam and alprazolam. A study in 2025 has revealed that the plant works to reduce anxiety in maze tests using 300 mg/kg of methanol leaf extracts, like the effects of 2.5 mg/kg of the drug alprazolam, without the side effects of drowsiness. A review in 2025 has revealed that the plant's alkaloids have been known to ease the tension and worry felt in the body through the modulation of the body's natural response to stress, which results in increased emotional well-being.

Safety studies indicate it's quite safe, with no signs of addiction liability, withdrawal symptoms, or problems in animal studies at effective doses and with long-term use [9]. However, it's worth noting that the chemical content of the plant may vary depending on how it's grown, and therefore quality control must be exercised before use by humans. Recent studies from 2023-2024 are investigating brain-protective properties and other benefits such as prevention of asthma and diabetes through inhibition of certain enzymes, which may help with anxiety-related health issues.

Case Study: Prevalence and Distribution of Anxiety Levels Among Young Adults in Urban India (Fig.1)

Mental health issues, such as anxiety, are an important problem that is being faced globally, affecting many

people every day. This is causing people to slow down, making work or school more challenging, as well as increasing medical expenses. In this analysis, we will investigate the ways severe anxiety manifests itself in 500 people between the ages of 18 and 35, living in urban areas of Uttar Pradesh, India, focusing on Lucknow. The data was obtained by using the results of the pie chart analysis of the data. The data was obtained by reporting the anxiety experienced by people during the early part of 2026, when the job market was uncertain, as was the outcome of the COVID-19 pandemic. The objective is to look for patterns that exist regarding the anxiety experienced by many, as well as the ways we can assist the anxious. The data was obtained by using a tool that is like the GAD-7, consisting of seven simple questions that determine the level of anxiety experienced by an individual, categorized as none, mild, moderate, or severe, as illustrated by the visual data provided.

Table 2.

Summary of Key Preclinical Studies on *Clitoria ternatea*

Study	Model	Key Findings	Citation
Jain et al. (2003)	Rodent CNS models (e.g., maze tests)	Anxiolytic effects via GABA modulation; reduced hyperexcitability	[20]
Rai et al. (2002)	Stress-induced models (e.g., forced swim)	Improved HPA regulation, nootropic effects; enhanced stress resilience	[22]
Samarth et al. (2008)	Oxidative stress assays (in vitro/in vivo)	Antioxidant protection against ROS; mitigated neuronal damage	[27]
Recent study	Elevated	extract (300 mg/kg)	[24]
(2021)	in rats	Alprazolam review (2025) Various models Relaxing effects from alkaloids; Literature reduced anxiety and stress	

VI. Conclusion

Generalized Anxiety Disorder, formerly known as Anxiety Neurosis, is a complex psychological state

that is the result of a variety of biological factors. Some of the main factors that contribute to the development of Generalized Anxiety Disorder include imbalances in neurotransmitters such as GABA and serotonin, a hyperactive stress system that causes cortisol to be in a heightened state in the brain, oxidative stress that damages brain cells, and inflammation that is the result of chemicals such as TNF-alpha and IL-6. Overall, the combined effect of all these factors causes the brain to lose its ability to cope and results in the manifestation of Generalized Anxiety Disorder. However, the use of drugs such as SSRIs and benzodiazepines to treat Generalized Anxiety Disorder has its own limitations, such as the presence of side effects, the development of tolerance, the development of dependency, the difficulty in withdrawal, and the lack of relief in a considerable number of patients. Thus, in the quest to find a solution to Generalized Anxiety Disorder, a variety of alternative options have come into the limelight. One such natural remedy that has come into the limelight as a possible solution to Generalized Anxiety Disorder is the medicinal herb known as *Clitoria ternatea*. It has been found to have the potential to treat Generalized Anxiety Disorder in a variety of ways, such as the modulation of neurotransmitters such as GABA and serotonin, the manifestation of anti-inflammatory and antioxidant properties, the regulation of stress hormones via the HPA axis, and a good safety profile along with the manifestation of neuroprotective effects such as the support of BDNF activity.

References

- [1] Diagnostic and Statistical Manual of Mental Disorders (DSM-5). 5th ed. Washington, DC: APA; 2013.
- [2] Stahl SM. Stahl's Essential Psychopharmacology: (2). 4th ed. Cambridge University Press; 2013.
- [3] Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders. *Int J Neuropsychopharmacol.* 2014;17(3):403–439.
- [4] Charney DS, Nestler EJ. *Neurobiology of mental illness.* 4th ed. Oxford University Press; 2017.
- [5] Ressler KJ, Nemeroff CB. Role of serotonergic and noradrenergic systems in the pathophysiology of anxiety disorders. *Depress Anxiety.* 2000;12(S1):2–19. 6. Millan MJ. The neurobiology and control of anxious states. *Prog Neurobiol.* 2003;70(2):83–244.
- [6] Stein MB, Sareen J. Clinical practice: generalized anxiety disorder. *N Engl J Med.* 2015;373:2059–2068.
- [7] Nutt DJ. The neuropharmacology of anxiety disorders. *Pharmacol Ther.* 1990;47(2):233–252.
- [8] Bremner JD. Stress and brain atrophy. *CNS Neurol Disord Drug Targets.* 2006;5(5):503–512.
- [9] McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med.* 1998;338:171–179.
- [10] Chrousos GP. Stress and disorders of the stress system. *Nat Rev Endocrinol.* 2009;5(7):374–381.
- [11] Leonard BE. Inflammation, depression and anxiety. *J Psychopharmacol.* 2011;25(3):373–384.
- [12] Salim S. Oxidative stress and psychological disorders. *Curr Neuropharmacol.* 2014;12(2):140–147.
- [13] Ng F, Berk M, Dean O, Bush AI. Oxidative stress in psychiatric disorders. *Int J Neuropsychopharmacol.* 2008;11(6):851–876.

- [14] Kulkarni SK, Dhir A. An overview of anxiolytic drugs. *Indian J Exp Biol.* 2007;45(6):463–470.
- [15] Lader M. Benzodiazepines revisited. *Br J Psychiatry.* 2011;199(6):445–446.
- [16] Bandelow B, Michaelis S. Epidemiology of anxiety disorders. *Dialogues Clin Neurosci.* 2015;17(3):327–335.
- [17] Mukherjee PK. *Quality Control and Evaluation of Herbal Drugs.* Elsevier; 2019.
- [18] Jain NN, Ohal CC, Shroff SK, Bhutada RH, Somani RS, Kasture VS, Kasture SB. *Clitoria ternatea* and the CNS. *J Ethnopharmacol.* 2003;84(2–3):197–202.
- [19] Kulkarni C, Pattanshetty JR, Amruthraj G. Effect of *Clitoria ternatea* root extract on cognition. *Indian J Exp Biol.* 1988;26:957–960.
- [20] Rai KS, Murthy KD, Karanth KS, Nalini K, Rao MS. *Clitoria ternatea* as a nootropic agent. *Pharmacol Biochem Behav.* 2002;73(3):529–536.
- [21] Mukherjee PK, Kumar V, Mal M, Houghton PJ. Acetylcholinesterase inhibitors from plants. *Phytomedicine.* 2007;14(4):289–300.
- [22] Jeyaraj EJ, Lim YY, Choo WS. Antioxidant, cytotoxic, and anti-inflammatory activities of *Clitoria ternatea*. *Food Chem.* 2021;354:129505.
- [23] Kazuma K, Noda N, Suzuki M. Malonylated flavonol glycosides in butterfly pea. *Phytochemistry.* 2003;62(2):229–237.
- [24] Terahara N, Takeda Y, Nesumi A, Honda T. Anthocyanins from *Clitoria ternatea* flowers. *Phytochemistry.* 1998;48(6):1141–1143.
- [25] Samarth RM, Panwar M, Kumar M, Soni A, Kumar M, Kumar A. Protective effects of *Clitoria ternatea* on oxidative stress. *Indian J Pharmacol.* 2008;40(6):250–254.
- [26] Ponnusamy S, Mohan M, Nagaraja HS. Neuroprotective role of *Clitoria ternatea*. *Int J Pharm Sci Rev Res.* 2011;7(1):32–36.
- [27] Dhingra D, Valecha R. Screening of antidepressant-like activity of *Clitoria ternatea*. *Pharm Biol.* 2007;45(7):593–598.
- [28] Heinrich M, Barnes J, Gibbons S, Williamson EM. *Fundamentals of Pharmacognosy and Phytotherapy.* 2nd ed. Elsevier; 2012.
- [29] Williamson EM. Synergy and other interactions in phytomedicines. *Phytomedicine.* 2001;8(5):401–409.
- [30] Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence of anxiety disorders. *Arch Gen Psychiatry.* 2005;62(6):593–602. (3)
- [31] Nemeroff CB. The role of corticotropin-releasing factor in anxiety disorders. *Psychiatr Clin North Am.* 2001;24(3):551–573.
- [32] Haroon E, Raison CL, Miller AH. Psychoneuroimmunology of mood disorders. *Trends Cogn Sci.* 2012;16(1):18–27.
- [33] Chandra V, Maurya PK, Kulshreshtha R, Mohanty S, Pant AB. Oxidative stress in neuropsychiatric disorders. *Neurosci Lett.* 2017;640:24–36.
- [34] Butterweck V, Schmidt M. St. John's wort and neurobiology of depression. *CNS Drugs.* 2007;21(8):667–681.
- [35] Ernst E. Herbal medicines for anxiety. *CNS Drugs.* 2006;20(8):633–644.
- [36] Sarris J, Moylan S, Camfield DA, et al. Complementary medicine for anxiety and depression. *Evid Based Complement Alternat Med.* 2012;2012:1–21.

- [37] World Health Organization. WHO Monographs on Selected Medicinal Plants. Vol. 4. WHO Press; 2009.
- [38] Russo E, Guy GW. A tale of two cannabinoids. *Br J Pharmacol.* 2006;147(S1):S138–S148.