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Anxiolytic Activity Of Gmelina Arborea: A Review Based On Different Experimental Models

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Abstract:

Anxiety disorders are a major global health issue and continue to create a need for safer and more effective treatment options. In recent years, medicinal plants with possible neuropharmacological effects have gained growing attention as alternative therapeutic agents. *Gmelina arborea*, an important component of *Brihat Pancha Moola*, has long been used in traditional systems of medicine and is now being explored for its wider medicinal value. The plant is rich in phytochemicals such as lignans, flavonoids, tannins, glycosides, and other bioactive compounds, which contribute to its therapeutic potential. Among its many reported pharmacological properties, its anti-inflammatory and antioxidant activities are especially significant. Recent preclinical studies, particularly those using animal models such as the Elevated Plus Maze (EPM) and Light-Dark Box (LDB), indicate that extracts of *Gmelina arborea* may help reduce anxiety-related behaviour. These effects are believed to be associated with the modulation of neurotransmitter systems, especially the GABAergic pathway, which plays a key role in anxiety regulation. In addition, the antioxidant nature of the plant may provide neuroprotective benefits. Although the preclinical findings are encouraging, clinical evidence in humans is still limited. Therefore, further studies are needed to clarify its mechanism of action, ensure proper standardisation, and establish its safety and efficacy through clinical validation. Overall, *Gmelina arborea* shows promising potential as a natural anxiolytic agent, but more research is required before it can be confidently applied in modern medicine.

Keywords: Mental Disorder, Agoraphobia, Amygdala, Gmelina Arborea.

Introduction

Anxiety disorders are among the most common mental health conditions worldwide, affecting millions of people and significantly reducing quality of life. They are characterised by excessive fear, worry, and behavioural disturbances that interfere with daily functioning. According to the World Health Organisation, anxiety disorders contribute substantially to the global burden of disease, highlighting the urgent need for effective and safe treatment strategies. Although conventional pharmacological therapies such as benzodiazepines and selective serotonin reuptake inhibitors (SSRIs) are widely prescribed, they are often associated with side effects like sedation, dependence, tolerance, and withdrawal symptoms. These limitations have encouraged researchers to explore alternative therapeutic options, particularly those derived from medicinal plants.

In recent years, the field of herbal medicine has gained considerable attention due to its holistic approach and relatively lower risk of adverse effects. Plants with neuropharmacological properties are being extensively studied for their potential role in managing central nervous system disorders, including anxiety. One such plant is *Gmelina arborea*, a well-known medicinal species in traditional Indian systems such as Ayurveda. It is a key component of *Brihat Pancha Moola*, a classical formulation used for its rejuvenating and therapeutic benefits. Historically, different parts of the plant, including roots, bark, and leaves, have been used to treat a variety of ailments such as inflammation, fever, and nervous disorders.

The pharmacological potential of *Gmelina arborea* is largely attributed to its diverse range of phytoconstituents. These include flavonoids, lignans, tannins, iridoid glycosides, and other bioactive compounds that exhibit multiple biological activities. Among these, flavonoids are particularly important due to their known effects on the central nervous system, including anxiolytic and sedative properties. Additionally, the antioxidant and anti-inflammatory activities of the plant may contribute to its neuroprotective effects, which are relevant in the management of anxiety-related conditions.

To evaluate the anxiolytic potential of plant extracts, various experimental animal models are commonly used in preclinical research. Behavioural models such as the Elevated Plus Maze (EPM), Light-Dark Box (LDB), Open Field Test (OFT), and Hole Board Test are widely used to assess anxiety-related responses in rodents. These models are based on the natural aversion of animals to open or brightly lit spaces and their tendency to explore novel environments. Studies involving *Gmelina arborea* extracts have demonstrated promising results in these models, indicating reduced anxiety-like behaviour, which supports its traditional use as a calming agent.

The mechanism underlying the anxiolytic activity of *Gmelina arborea* is believed to involve modulation of neurotransmitter systems, particularly the gamma-aminobutyric acid (GABA) pathway. GABA is the primary inhibitory neurotransmitter in the brain and plays a crucial role in regulating neuronal excitability and emotional responses. Compounds that enhance GABAergic transmission are known to produce anxiolytic effects, suggesting a possible pathway through which the plant exerts its action.

Despite encouraging findings from preclinical studies, there is still a lack of well-designed clinical trials to confirm the safety and efficacy of *Gmelina arborea* in humans. Therefore, a comprehensive review of its anxiolytic activity across different experimental models is essential to better understand its therapeutic potential. This review aims to compile and critically analyse existing research on *Gmelina arborea*, focusing on its pharmacological effects, mechanisms of action, and prospects as a natural anxiolytic agent.

Classification of Anxiety Disorder:

Anxiety disorders are classified based on their clinical presentation, triggers, and duration. According to standard diagnostic systems such as the *DSM-5 (Diagnostic and Statistical Manual of Mental Disorders)*, anxiety disorders can be grouped into the following major types:

1. Generalised Anxiety Disorder (GAD)

Generalised Anxiety Disorder is characterised by persistent and excessive worry about everyday events such as work, health, or personal relationships.

- The anxiety is often difficult to control
- Symptoms last for at least 6 months
- Common symptoms include restlessness, fatigue, poor concentration, irritability, and sleep disturbances

2. Panic Disorder

Panic Disorder involves recurrent and unexpected panic attacks, which are sudden episodes of intense fear.

- Symptoms include palpitations, sweating, trembling, shortness of breath, and dizziness
- Patients may develop fear of future attacks (anticipatory anxiety)
- Often associated with avoidance behaviour

3. Social Anxiety Disorder (Social Phobia)

This disorder is marked by intense fear of social situations where the individual may be judged or embarrassed.

- Common in situations like public speaking, meeting new people, or eating in public
- Leads to avoidance of social interactions
- Can significantly affect academic and professional performance

4. Specific Phobias

Specific phobias involve an irrational and excessive fear of a particular object or situation.

- Examples include fear of heights (acrophobia), animals, flying, or injections
- Exposure to the trigger leads to immediate anxiety response
- Individuals often recognize that the fear is excessive

5. Agoraphobia

Agoraphobia is the fear of situations where escape might be difficult or help may not be available.

- Includes fear of crowded places, public transport, or being outside alone
- Often develops after repeated panic attacks
- May lead to complete avoidance of leaving home in severe cases

6. Separation Anxiety Disorder

This disorder involves excessive fear or anxiety about separation from attachment figures.

- Commonly seen in children but can occur in adults
- Symptoms include distress on separation, fear of losing loved ones, and reluctance to be alone

7. Selective Mutism

Selective Mutism is a rare anxiety disorder where an individual is unable to speak in certain social situations despite having the ability to speak normally.

- Commonly observed in children
- Often linked with social anxiety
- Interferes with academic and social functioning

Neurobiology of Anxiety

The neurobiology of anxiety explains how different parts of the brain and chemical messengers work together to produce feelings of fear and worry. In simple terms, anxiety is not just a psychological state—it is strongly linked to biological processes in the central nervous system.

Several key areas of the brain play an important role in anxiety:

- **Amygdala**: This is the main centre for processing fear and emotional responses. It becomes overactive during anxiety and sends signals that trigger fear reactions.
- **Hippocampus**: It is involved in memory formation and helps the brain recognise whether a situation is threatening based on past experiences.
- **Prefrontal Cortex**: This part of the brain helps in decision-making and controlling emotional responses. In anxiety disorders, the ability to regulate fear signals may be reduced.

Together, these regions form a network that controls how we perceive and respond to stress and fear.

Neurotransmitters and Their Role

Neurotransmitters are chemical messengers that transmit signals between nerve cells. They play a major role in regulating anxiety:

- **GABA (Gamma-Aminobutyric Acid)**: It is the main inhibitory neurotransmitter in the brain. It reduces nerve activity and produces a calming effect. Low levels of GABA are commonly associated with anxiety.
- **Serotonin**: It helps regulate mood, sleep, and emotions. An imbalance in serotonin levels can lead to anxiety and depression.
- **Dopamine**: It is involved in motivation and reward, and its imbalance may also influence anxiety-related behaviour.
- **Norepinephrine**: It is responsible for the “fight or flight” response and increases alertness during stress.

Role of the HPA Axis (Stress Response System)

The Hypothalamic–Pituitary–Adrenal (HPA) axis is the body’s main stress response system.

- When a person faces stress, the hypothalamus releases signals to the pituitary gland
- The pituitary then stimulates the adrenal glands to release cortisol (stress hormone)
- Excess or prolonged cortisol release can lead to increased anxiety levels

Neurochemical Imbalance and Anxiety

Anxiety disorders often occur due to an imbalance between excitatory and inhibitory signals in the brain.

- Reduced inhibitory control (low GABA activity) leads to overexcitation
- Increased stress hormones and altered neurotransmitter levels further worsen the condition
- This imbalance results in symptoms like restlessness, fear, and hyperactivity

Relation to Herbal Medicines (Research Perspective)

From a pharmacological point of view, many medicinal plants—including *Gmelina arborea*—are believed to act on these neurobiological pathways.

- Certain phytochemicals (like flavonoids) may enhance GABA activity
- Antioxidant compounds help protect neurons from stress-induced damage
- Anti-inflammatory effects may also support brain function

Gmelina Arborea: Plant profile

Gmelina arborea, commonly known as Gambhari, is a fast-growing medicinal plant widely found in India and other parts of Southeast Asia. It belongs to the family Lamiaceae and holds an important place in traditional systems of medicine, especially Ayurveda. The plant is valued for its wide range of therapeutic properties and is included as a key component in the classical Ayurvedic formulation known as *Brihat Pancha Moola*. Due to its rich phytochemical composition, it has gained attention in modern pharmacological research as well.

Taxonomical Classification

- **Kingdom**: Plantae
- **Division**: Angiosperms
- **Class**: Dicotyledons
- **Order**: Lamiales
- **Family**: Lamiaceae
- **Genus**: *Gmelina*
- **Species**: *Gmelina arborea*

Pharmacological Importance

Modern research has shown that *Gmelina arborea* possesses several pharmacological activities such as anti-inflammatory, antioxidant, antimicrobial, hepatoprotective, and neuroprotective effects. Recent studies have also suggested its potential role in managing anxiety, which may be linked to its effect on the central nervous system and neurotransmitter modulation.

Different Experimental Models For Anxiolytic Screening :

Evaluation of anxiolytic activity is an essential step in the development of new therapeutic agents, including plant-based drugs such as *Gmelina arborea*. Since anxiety cannot be measured directly in animals, researchers rely on well-established behavioural models that reflect anxiety-like responses. These experimental models are primarily conducted in rodents and are designed to reflect their natural behaviour, such as fear of open spaces, bright light, or unfamiliar environments. The results obtained from these models help in predicting the potential anxiolytic effects of test substances.

1. Elevated Plus Maze (EPM)

The Elevated Plus Maze is one of the most commonly used models for screening anxiolytic activity. It consists of four arms arranged in a plus shape—two open arms and two closed arms—elevated above the ground.

Rodents naturally avoid open and elevated spaces due to fear of predators. When an anxiolytic agent is administered, the animal tends to spend more time in the open arms.

- **Parameters observed**: Number of entries into open arms and time spent in open arms
- **Interpretation**: Increased open-arm activity indicates reduced anxiety

2. Light-Dark Box (LDB) Test

This model is based on the natural preference of rodents for dark and enclosed spaces. The apparatus consists of two compartments—one brightly lit and the other dark.

An anxious animal spends more time in the dark compartment. After administration of an anxiolytic drug, the animal shows increased exploration of the light area.

- **Parameters observed**: Time spent in light compartment, number of transitions
- **Interpretation**: Increased time in the light area suggests anxiolytic effect

3. Open Field Test (OFT)

The Open Field Test is used to assess general locomotion and anxiety-related behaviour. It consists of a large square arena divided into central and peripheral zones.

Rodents usually prefer to stay near the walls (thigmotaxis) due to anxiety. A reduction in anxiety leads to increased movement towards the centre.

- **Parameters observed**: Number of squares crossed, time spent in centre, rearing behaviour
- **Interpretation**: Increased central activity indicates reduced anxiety

4. Hole Board Test

This model is used to measure exploratory behavior in rodents. The apparatus contains evenly spaced holes on a flat surface.

When anxiety is reduced, animals show increased curiosity and explore the holes by dipping their heads.

- **Parameters observed**: Number and duration of head dips
- **Interpretation**: Increased head-dipping behavior reflects anxiolytic activity

5. Social Interaction Test

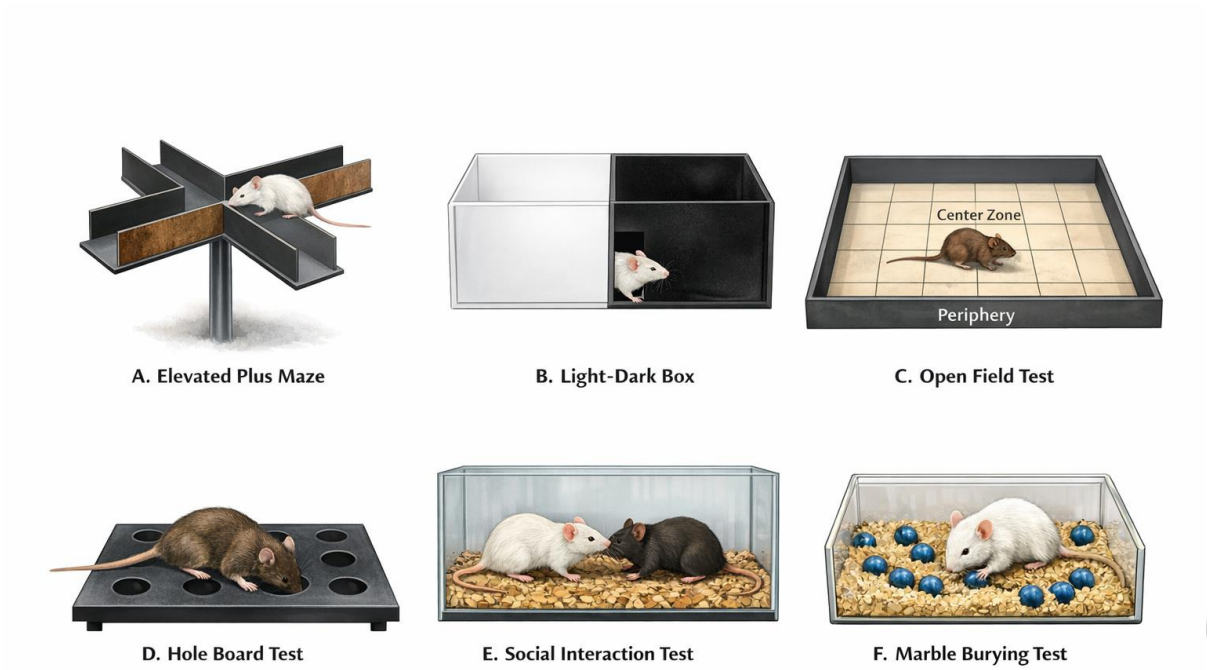
This model evaluates anxiety based on social behavior between two animals. Anxiety tends to reduce social interaction, while anxiolytic agents enhance it.

- **Parameters observed**: Time spent in active interaction (sniffing, grooming, following)
- **Interpretation**: Increased social interaction indicates reduced anxiety

6. Marble Burying Test

In this test, rodents are placed in a cage containing bedding and small marbles. Anxious animals tend to bury more marbles as a defensive behavior.

- **Parameters observed**: Number of marbles buried
- **Interpretation**: Decrease in marble burying suggests anxiolytic effect



Importance in Herbal Research

These experimental models are widely used in evaluating the anxiolytic potential of medicinal plants. In the case of *Gmelina arborea*, studies using models like Elevated Plus Maze and Light-Dark Box have shown promising results, supporting its traditional use in managing anxiety. These models also help in understanding the possible mechanism of action, such as interaction with the GABAergic system.

Conclusion

In summary, anxiety disorders continue to be a major health concern, and existing treatments often come with unwanted side effects. This has increased interest in plant-based alternatives that may offer safer therapeutic options. *Gmelina arborea*, a traditionally valued medicinal plant, has shown promising anxiolytic effects in various experimental models. Its activity is mainly linked to its rich phytochemical content and its influence on brain neurotransmitters, especially the GABA system.

Although the preclinical findings are encouraging, there is still a need for well-designed clinical studies to confirm its safety and effectiveness in humans. Overall, *Gmelina arborea* has good potential as a natural anti-anxiety agent, but further research is necessary before it can be widely used in modern therapy.

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