A Comprehensive Review on Anxiety Disorders: Pathophysiology, Etiology, Treatment Strategies, and Experimental Models Including Molecular Docking Approaches

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Abstract

Anxiety disorders are among the most prevalent neuropsychiatric conditions worldwide, significantly affecting mental health and quality of life. This review provides a comprehensive overview of anxiety disorders, focusing on their etiology, pathophysiology, treatment strategies, and experimental evaluation models. The multifactorial nature of anxiety disorders involves genetic susceptibility, environmental stressors, neurobiological alterations, and psychological influences. Key mechanisms include dysregulation of neurotransmitters such as GABA, serotonin, dopamine, and norepinephrine, along with dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis, neuroinflammation, and oxidative stress. Current treatment approaches include pharmacological interventions such as benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), and serotonin–norepinephrine reuptake inhibitors (SNRIs), as well as non-pharmacological therapies like cognitive behavioral therapy (CBT), mindfulness, and lifestyle modifications. Despite their effectiveness, conventional drugs are associated with limitations, highlighting the need for safer alternatives.The review also emphasizes the role of herbal medicines and natural compounds, which demonstrate promising anxiolytic effects with fewer side effects. Furthermore, advanced techniques such as molecular docking, in vitro assays, and in vivo experimental models play a crucial role in drug discovery and validation. The integration of computational and experimental approaches offers new insights into the development of novel, effective, and safer anxiolytic therapies.

KeywordsGABA; Serotonin; HPA axis; Molecular docking; In vivo models; In vitro models; Herbal medicine; Anxiolytic activity; Pharmacological treatment

1. Introduction

Anxiety disorders represent one of the most widespread categories of neuropsychiatric illnesses, posing a substantial global public health burden [1]. It is estimated that over 260 million individuals are affected worldwide [2], highlighting the significant prevalence and impact of these conditions. Anxiety disorders encompass a spectrum of clinical entities, including generalized anxiety disorder (GAD), panic disorder, social anxiety disorder, and specific phobias [3], each characterized by excessive fear, persistent worry, and behavioral disturbances that interfere with daily functioning. According to the World Health Organization, these disorders are major contributors to disability, leading to reduced productivity, impaired social interactions, and diminished overall quality of life [2].

The pathogenesis of anxiety disorders is complex and multifactorial, involving intricate interactions between genetic predisposition, environmental stressors, neurobiological alterations, and psychological factors [4]. Dysregulation of key neurotransmitter systems, particularly gamma-aminobutyric acid (GABA), serotonin (5-HT), dopamine, and norepinephrine, plays a crucial role in the onset and progression of anxiety-related symptoms

[5]. In addition, growing evidence suggests the involvement of hypothalamic pituitary adrenal (HPA) axis dysfunction, neuroinflammation, oxidative stress, and altered neural circuitry especially within the amygdala, hippocampus, and prefrontal cortex in the underlying pathophysiology of anxiety disorders. [6]

Currently available pharmacological interventions, including benzodiazepines and selective serotonin reuptake inhibitors (SSRIs), remain the cornerstone of anxiety management [7]. While these agents are effective in alleviating symptoms, their clinical use is often limited by several drawbacks such as sedation, cognitive impairment, risk of dependence, withdrawal symptoms, and delayed therapeutic onset [8]. These limitations underscore the urgent need for the development of novel anxiolytic agents with improved efficacy and safety profiles.

In recent years, there has been a growing emphasis on the exploration of alternative therapeutic strategies, particularly those derived from natural products and medicinal plants [9], which are believed to offer multi-target actions with fewer adverse effects. Concurrently, advancements in experimental methodologies, including validated in vivo behavioral models and in vitro cellular assays, have enhanced the understanding of anxiolytic mechanisms.[10] Moreover, computational approaches such as molecular docking and in silico pharmacological screening have emerged as powerful tools in modern drug discovery [11], enabling the identification and optimization of bioactive compounds through the prediction of ligand–receptor interactions. The integration of these multidisciplinary approaches holds significant promise for the development of safer, more effective, and targeted therapies for the management of anxiety disorders.

2. Etiology of Anxiety Disorders

Anxiety disorders are multifactorial in origin, arising from a dynamic interplay between genetic susceptibility, environmental exposures, neurobiological alterations, and psychological influences. Rather than being attributed to a single causative factor, these disorders result from the cumulative effect of multiple risk determinants that interact at molecular, cellular, and behavioral levels. Contemporary research highlights that this complex interaction disrupts emotional regulation, stress response systems, and cognitive processing, ultimately contributing to the development and persistence of anxiety symptoms.[12]

2.1 Genetic Factors [13]

- Family and twin studies suggest heritability of 30–50%.
- Genes regulating neurotransmitters such as serotonin transporter (SLC6A4) are implicated.

2.2 Environmental Factors

- Chronic stress
- Trauma and abuse
- Socioeconomic instability

2.3 Neurobiological Factors [14]

- Dysregulation of neurotransmitter systems:
    - Gamma-aminobutyric acid (GABA)

- Serotonin (5-HT)
- Dopamine (DA)
- Norepinephrine (NE)

2.4 Psychological Factors

- Personality traits (neuroticism)
- Cognitive distortions
- Learned fear response

3. Pathophysiology of Anxiety Disorders [15]

The pathophysiology of anxiety disorders is highly complex and involves a combination of neurochemical imbalances, structural and functional alterations in specific brain regions, dysregulation of neuroendocrine systems, and the contribution of inflammatory and oxidative mechanisms. These interconnected processes collectively disrupt emotional regulation, stress responsiveness, and cognitive function, ultimately leading to the manifestation of anxiety-related symptoms.

3.1 Neurotransmitter Imbalance

One of the central mechanisms underlying anxiety disorders is the dysregulation of key neurotransmitter systems that are responsible for maintaining emotional stability and neuronal excitability. Gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the central nervous system, plays a crucial role in reducing neuronal overactivity. A decrease in GABAergic transmission leads to heightened neuronal excitability, thereby contributing to increased anxiety and hyperarousal.

In addition, serotonergic dysfunction is widely implicated in the pathogenesis of anxiety disorders. Reduced levels of serotonin (5-hydroxytryptamine, 5-HT) are associated with impaired mood regulation, increased fear perception, and emotional instability. Furthermore, enhanced activity of the noradrenergic system, particularly increased norepinephrine release, is linked to heightened alertness, autonomic arousal, and exaggerated stress responses. Together, these neurotransmitter imbalances create a neurochemical environment that predisposes individuals to persistent anxiety.

3.2 Brain Regions Involved

Anxiety disorders are also associated with functional and structural alterations in specific brain regions that regulate emotional processing and stress responses. The amygdala, a key component of the limbic system, is primarily responsible for fear perception and threat detection. Hyperactivity of the amygdala has been consistently observed in individuals with anxiety disorders, leading to exaggerated fear responses even in non-threatening situations.

The hippocampus, which plays a vital role in memory formation and contextual processing of stress, is often affected by chronic anxiety. Prolonged exposure to stress hormones can result in hippocampal atrophy and impaired neurogenesis, thereby affecting memory and emotional regulation. The prefrontal cortex, particularly the medial and dorsolateral regions, is involved in executive function and top-down regulation of emotional responses. Reduced activity or

impaired connectivity of the prefrontal cortex diminishes its ability to modulate amygdala activity, resulting in poor emotional control and increased anxiety.

3.3 Hypothalamic–Pituitary–Adrenal (HPA) Axis Dysfunction

The hypothalamic–pituitary–adrenal (HPA) axis plays a critical role in the physiological response to stress. In anxiety disorders, this system is often dysregulated, leading to excessive and prolonged activation. Chronic stress stimulates the hypothalamus to release corticotropin-releasing hormone (CRH), which subsequently triggers the secretion of adrenocorticotropic hormone (ACTH) from the pituitary gland, ultimately resulting in increased cortisol production from the adrenal cortex.

Elevated cortisol levels over extended periods can have detrimental effects on brain function, including impaired synaptic plasticity, reduced neurogenesis, and neuronal damage, particularly in the hippocampus and prefrontal cortex. This persistent hyperactivation of the HPA axis contributes significantly to the development and maintenance of anxiety symptoms.

3.4 Neuroinflammation and Oxidative Stress

Recent advances in neuropsychiatric research have highlighted the important role of neuroinflammation and oxidative stress in the pathophysiology of anxiety disorders. Increased levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), have been observed in individuals with anxiety, suggesting an activated immune response within the central nervous system.

In parallel, oxidative stress resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms leads to cellular and molecular damage. This oxidative damage affects neuronal integrity, disrupts neurotransmitter function, and impairs synaptic signaling. The combined effects of neuroinflammation and oxidative stress further exacerbate neuronal dysfunction and contribute to the progression of anxiety disorders.

4. Treatment Strategies

The management of anxiety disorders requires a comprehensive and multidimensional approach that integrates both pharmacological and non-pharmacological interventions. The choice of treatment is typically guided by the severity of symptoms, patient-specific factors, comorbid conditions, and the risk–benefit profile of therapeutic agents. While conventional pharmacotherapy remains the cornerstone of treatment, increasing attention is being directed toward alternative therapies and holistic approaches to improve safety and long-term outcomes. [16]

4.1 Pharmacological Treatment

Pharmacological agents are widely used for the symptomatic relief and long-term management of anxiety disorders. These drugs primarily act by modulating neurotransmitter systems involved in emotional regulation, particularly GABAergic and serotonergic pathways.

4.1.1 Benzodiazepines

Benzodiazepines, such as Diazepam, are among the most rapidly acting anxiolytic agents. They exert their therapeutic effect by enhancing the activity of gamma-aminobutyric acid (GABA), the principal inhibitory neurotransmitter in the central nervous system. This results in reduced neuronal excitability and a calming effect.

Despite their efficacy in acute anxiety management, long-term use is limited due to adverse effects such as sedation, cognitive impairment, tolerance, and the risk of physical and psychological dependence. Therefore, benzodiazepines are generally recommended for short-term or adjunctive use. [17]

4.1.2 Selective Serotonin Reuptake Inhibitors (SSRIs) [18]

Selective serotonin reuptake inhibitors, including Fluoxetine, are considered first-line pharmacological agents for the treatment of anxiety disorders. These drugs function by inhibiting the reuptake of serotonin (5-HT) into presynaptic neurons, thereby increasing its availability in the synaptic cleft and enhancing serotonergic neurotransmission.

SSRIs are preferred over benzodiazepines due to their improved safety profile and lower risk of dependence. However, they are associated with a delayed onset of action and may cause side effects such as gastrointestinal disturbances, sleep disturbances, and sexual dysfunction.

4.1.3 Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs) [19]

Serotonin–norepinephrine reuptake inhibitors, such as Venlafaxine, act by inhibiting the reuptake of both serotonin and norepinephrine. This dual mechanism enhances mood regulation and reduces anxiety symptoms.

SNRIs are particularly beneficial in patients who do not respond adequately to SSRIs. However, they may be associated with side effects such as hypertension, nausea, and insomnia.

4.1.4 Herbal and Natural Therapies [20]

In recent years, there has been growing interest in plant-based therapies as potential alternatives to conventional anxiolytics. Medicinal plants such as *Hamelia patens*, *Withania somnifera*, and *Passiflora incarnata* have demonstrated significant anxiolytic activity in preclinical and clinical studies.

These natural agents are believed to exert their effects through multiple mechanisms, including modulation of GABAergic and serotonergic systems, antioxidant activity, and reduction of neuroinflammation. Importantly, they are generally associated with fewer adverse effects and better tolerability, making them promising candidates for long-term use.

Drug Class	Example	Mechanism of Action	Advantages	Limitations
Benzodiazepines	Diazepam	Enhances GABA activity	Rapid onset of action	Sedation, dependence, tolerance
SSRIs	Fluoxetine	Inhibits serotonin reuptake	First-line therapy, safer profile	Delayed onset, mild side effects
SNRIs	Venlafaxine	Inhibits serotonin & norepinephrine reuptake	Effective in resistant cases	Hypertension, insomnia
Herbal Drugs	*Hamelia patens*, *Withania somnifera*	Multi-target action (GABA, antioxidants)	Fewer side effects, natural origin	Limited clinical standardization

4.2 Non-Pharmacological Treatment [21]

Non-pharmacological interventions play a crucial role in the comprehensive management of anxiety disorders, particularly in mild to moderate cases or as adjuncts to pharmacotherapy. These approaches primarily target cognitive, behavioural, and lifestyle factors that contribute to anxiety.

4.2.1 Cognitive Behavioural Therapy (CBT)

Cognitive Behavioural Therapy (CBT) is one of the most effective psychological interventions for anxiety disorders. It focuses on identifying and modifying maladaptive thought patterns and behaviours that contribute to anxiety. CBT helps patients develop coping strategies, improve emotional regulation, and reduce avoidance behaviours. [22]

4.2.2 Mindfulness and Meditation

Mindfulness-based interventions and meditation techniques have gained significant attention for their role in reducing stress and anxiety. These practices promote present-moment awareness and help individuals manage intrusive thoughts and emotional distress. Neuroimaging studies have shown that mindfulness can modulate brain regions involved in emotional regulation, such as the prefrontal cortex and amygdala. [23]

4.2.3 Lifestyle Modifications

Lifestyle interventions, including regular physical activity, balanced nutrition, adequate sleep, and stress management techniques, are essential components of anxiety management. Exercise has been shown to enhance endorphin release and improve mood, while proper sleep hygiene helps regulate circadian rhythms and reduce stress levels. [23]

Approach	Mechanism/Principle	Clinical Benefits
Cognitive Behavioral Therapy (CBT)	Modifies negative thoughts and behaviors	Long-term symptom control
Mindfulness & Meditation	Enhances emotional regulation and awareness	Reduces stress and relapse
Lifestyle Modifications	Improves physical and mental health	Supports overall well-being

5. Molecular Docking Studies

Molecular docking has emerged as a fundamental computational tool in modern drug discovery, particularly in the field of neuropsychiatric disorders such as anxiety. It enables the prediction of the preferred orientation, binding affinity, and interaction patterns between a ligand (drug candidate) and a target protein at the molecular level. This approach plays a critical role in identifying potential anxiolytic compounds by simulating their interactions with key biological targets involved in anxiety pathophysiology.

Recent Scopus-indexed studies have demonstrated that molecular docking is widely employed alongside in vitro and in vivo models to validate the pharmacological potential of novel compounds. It provides mechanistic insights into receptor binding and helps in optimizing lead compounds prior to experimental validation.[24]

5.1 Target Proteins in Anxiety Research [25]

In anxiety disorder research, several key protein targets are frequently selected for docking studies due to their involvement in neurotransmission and stress regulation.

- **GABA-A Receptor:**
  The gamma-aminobutyric acid (GABA-A) receptor is the primary inhibitory receptor in the central nervous system. Docking studies have shown that many anxiolytic agents, including benzodiazepines, exert their effects by binding to this receptor and enhancing inhibitory neurotransmission. Recent studies have confirmed strong ligand–receptor interactions between novel compounds and GABA receptors, supporting their anxiolytic potential .
- **Serotonin Transporter (SERT):**
  The serotonin transporter regulates synaptic serotonin levels and is a major target for antidepressants and anxiolytics. Docking studies targeting SERT help in identifying compounds that can modulate serotonergic signaling, which is crucial in anxiety regulation.
- **Monoamine Oxidase-A (MAO-A):**
  MAO-A is responsible for the degradation of monoamine neurotransmitters such as serotonin and norepinephrine. Inhibition of this enzyme increases neurotransmitter availability, thereby reducing anxiety symptoms. Docking approaches are extensively used to identify potent MAO-A inhibitors.

5.2 Software Tools Used in Molecular Docking [26]

Several computational tools are employed for molecular docking studies, each offering distinct advantages in terms of accuracy and efficiency.

- Auto Dock:
  Widely used open-source software that utilizes Lamarckian genetic algorithms for predicting ligand–protein interactions and binding energies.
- Schrödinger:
  A comprehensive computational platform that includes Glide for docking, offering high precision and advanced visualization of molecular interactions.

These tools allow researchers to perform virtual screening of large compound libraries and predict binding conformations with high reliability.

5.3 Molecular Docking Procedure [28]

The molecular docking workflow involves several systematic steps to ensure accurate prediction of ligand–receptor interactions:

1. **Protein Preparation:**
   The three-dimensional structure of the target protein is retrieved from databases such as the Protein Data Bank (PDB). The structure is then refined by removing water molecules, adding hydrogen atoms, and optimizing geometry.
2. **Ligand Preparation:**
   The chemical structures of potential compounds are drawn or retrieved from databases and subjected to energy minimization to obtain stable conformations.
3. **Docking Simulation:**
   The ligand is positioned within the active site of the target protein using docking algorithms to predict the most favorable binding orientation.
4. **Binding Energy Calculation:**
   The strength of interaction is evaluated using scoring functions, where lower binding energy indicates stronger and more stable interactions.
5. **Interaction Analysis:**
   The docked complex is analyzed to identify key interactions such as hydrogen bonding, hydrophobic interactions, and electrostatic forces.

Recent studies have integrated molecular docking with molecular dynamics simulations and ADMET analysis to enhance prediction accuracy and validate biological relevance .

5.4 Significance of Molecular Docking in Anxiety Research [28]

Molecular docking plays a crucial role in the early stages of drug discovery and development. Its significance includes:

- **Identification of Lead Compounds:**
  Docking enables rapid screening of large libraries of natural and synthetic compounds to identify potential anxiolytic candidates.
- **Mechanistic Insight:**
  It provides detailed information about ligand–receptor interactions at the molecular level, helping to elucidate the mechanism of action.

- **Cost and Time Efficiency:**
  By reducing the need for extensive experimental trials, docking significantly lowers research costs and accelerates drug development.
- **Integration with Experimental Models:**
  Recent Scopus-indexed studies highlight the integration of molecular docking with in vivo and in vitro models, enhancing the reliability of findings. For example, a 2024 study combining network pharmacology and docking validated anxiolytic effects through both computational and animal models .
- **Support for Herbal Drug Discovery:**
  Docking studies have demonstrated that phytochemicals can interact with multiple targets such as GABA receptors and serotonin transporters, supporting their potential as multi-target anxiolytic agents .

6. In Vivo Experimental Models for Anxiety

Preclinical in vivo models play a crucial role in the evaluation of anxiolytic activity and the screening of novel therapeutic agents. These models are designed to mimic human anxiety-like behaviors in animals, primarily rodents, by exploiting their natural aversion to open, brightly lit, or unfamiliar environments. Behavioral responses observed in these models provide valuable insights into the neurobiological mechanisms underlying anxiety and are widely used to assess the efficacy of pharmacological and natural compounds. [29]

6.1 Elevated Plus Maze (EPM) [30]

The Elevated Plus Maze is one of the most extensively validated and widely used behavioral models for assessing anxiety-like behavior in rodents. The apparatus consists of two open arms and two closed arms arranged in a plus (+) configuration and elevated above the ground.This model is based on the natural conflict between the exploratory drive of rodents and their aversion to open, elevated spaces. Anxiolytic agents increase the willingness of animals to explore the open arms.

Key Parameters:

- Number of entries into open and closed arms
- Time spent in open arms

Interpretation:
An increase in the duration and frequency of open arm exploration is indicative of reduced anxiety and suggests anxiolytic activity of the test compound.

Elevated Plus Maze (EPM) [38]

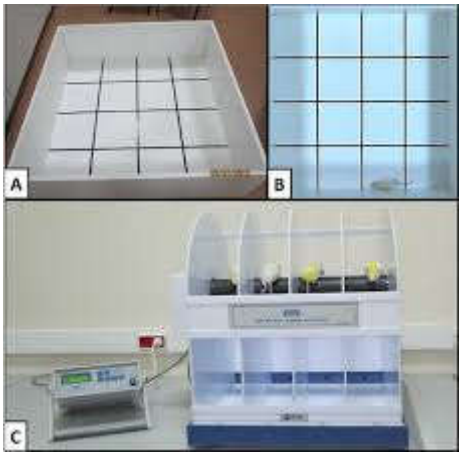
6.2 Open Field Test (OFT) [31]

The Open Field Test is a widely used behavioral paradigm for evaluating both locomotor activity and anxiety-related responses. The apparatus typically consists of a large, enclosed arena divided into central and peripheral zones. Rodents naturally prefer to stay close to the walls (thigmotaxis) due to fear of open spaces. Anxiolytic treatments reduce this fear, leading to increased exploration of the central area.

Key Parameters:

- Number of entries into the central zone
- Time spent in the center
- Total locomotor activity

Interpretation:
Enhanced exploration of the central area and increased locomotion are indicative of reduced anxiety levels.



Open Field Test (OFT) [37]

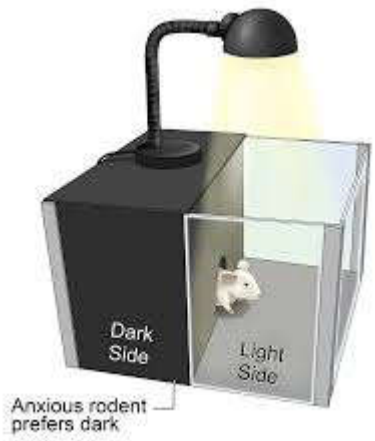
6.3 Light–Dark Box Test [32]

The Light–Dark Box Test is based on the innate aversion of rodents to brightly illuminated environments and their spontaneous exploratory behaviour. The apparatus consists of two compartments: a brightly lit chamber and a dark, enclosed chamber connected by a small opening. Anxiolytic agents reduce the aversion to light, encouraging animals to spend more time in the illuminated compartment.

Key Parameters:

- Time spent in light compartment
- Number of transitions between compartments

Interpretation:
An increase in time spent in the light compartment and higher transition frequency indicate anxiolytic effects.



Light–Dark Box Test [40]

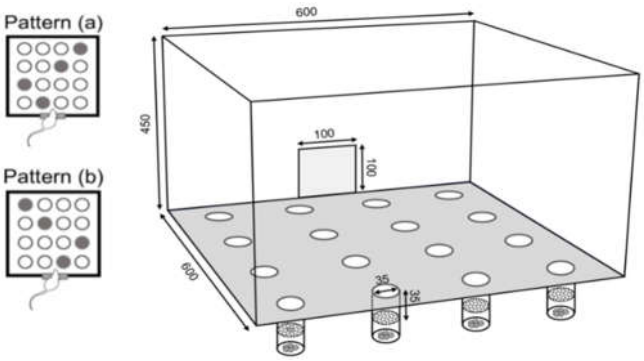
6.4 Hole Board Test [33]

The Hole Board Test is used to evaluate exploratory behaviour and anxiety by measuring head-dipping activity in rodents. The apparatus consists of a flat board with evenly spaced holes. This model assesses the natural curiosity of animals, where increased exploratory behavior is associated with reduced anxiety.

Key Parameters:

- Number of head dips
- Duration of head-dipping behaviour

Interpretation:
An increase in head-dipping activity reflects enhanced exploratory behaviour and reduced anxiety levels.



Hole Board Test [39]

Model	Principle	Key Parameters	Interpretation
Elevated Plus Maze (EPM)	Conflict between fear and exploration	Open arm entries, time spent	↑ Open arm activity = anxiolytic
Open Field Test (OFT)	Fear of open spaces	Center exploration, locomotion	↑ Center activity = reduced anxiety
Light–Dark Box	Aversion to light	Time in light area, transitions	↑ Light time = anxiolysis
Hole Board Test	Exploratory behaviour	Head dipping frequency	↑ Head dips = reduced anxiety

6. In Vitro Models

In vitro experimental models play a crucial role in the preliminary screening of anxiolytic agents by elucidating their interaction with neurotransmitter systems, neuronal survival pathways, and enzyme activity. These models provide mechanistic insights into drug action before in vivo validation.

6.1 Neurotransmitter Binding Assays [34]

Neurotransmitter receptor binding studies are widely used to evaluate the affinity of compounds toward key receptors involved in anxiety regulation, particularly γ-aminobutyric acid (GABA) and serotonin (5-HT) receptors.

GABA-A receptor binding assays typically involve radio ligand displacement techniques to determine the interaction of test compounds with receptor subunits. Compounds demonstrating significant binding affinity may enhance inhibitory neurotransmission, which is a well-established mechanism underlying anxiolytic effects. Experimental studies have reported that several plant extracts and synthetic compounds exhibit moderate binding to GABA-A receptors, indicating their potential to modulate neuronal excitability.

Similarly, serotonergic receptor interaction assays assess the modulation of receptors such as 5-HT_1A and 5-HT_2A, which are critically involved in mood and anxiety regulation. In vitro findings using neuronal cell systems have shown that certain bioactive compounds can regulate gene expression and functional activity of both GABAergic and serotonergic pathways, thereby contributing to anxiolytic effects.

Overall, these assays provide a direct measure of receptor-level interactions and are essential for identifying compounds that act via central neurotransmitter systems.

6.2 Cell Line Studies [35]

Neuronal cell lines such as PC12 (rat pheochromocytoma cells) and SH-SY5Y (human neuroblastoma cells) are extensively employed to evaluate neuroprotective and cytotoxic effects of potential anxiolytic agents. These models mimic neuronal behavior under controlled laboratory conditions.

SH-SY5Y cells, in particular, are widely used to study oxidative stress-induced neuronal damage and neuroprotection. Exposure to toxic agents such as hydrogen peroxide (H_2O_2) significantly reduces cell viability, while treatment with test compounds can restore viability in a concentration-dependent manner. This indicates neuroprotective potential, which is closely associated with anxiolytic and antidepressant activity.

Cell viability assays such as MTT and LDH release are commonly employed to assess cytotoxicity and membrane integrity. Studies have demonstrated that compounds with anxiolytic potential not only improve neuronal survival but also enhance neurotrophic factors such as brain-derived neurotrophic factor (BDNF), supporting neuronal growth and function.

Additionally, these models are useful for investigating intracellular signalling pathways, oxidative stress responses, and apoptosis mechanisms, which are often dysregulated in anxiety disorders.

6.3 Enzyme Inhibition Assays [36]

Enzyme-based assays are important tools for evaluating the effect of compounds on neurotransmitter metabolism. Monoamine oxidase (MAO), particularly MAO-A, plays a key role in the degradation of monoamines such as serotonin, norepinephrine, and dopamine.

In vitro MAO inhibition assays typically use fluorometric or spectrophotometric methods to measure enzyme activity in the presence of test compounds. A reduction in MAO activity indicates the potential of the compound to increase monoamine levels in the brain, thereby producing anxiolytic and antidepressant effects.

Recent studies have shown that several natural extracts and synthetic molecules exhibit dose-dependent inhibition of MAO-A, supporting their role in modulating mood and emotional behaviour.

Furthermore, inhibition of MAO enzymes also reduces the formation of reactive oxygen species generated during monoamine metabolism, contributing to neuroprotection and improved neuronal function.

7. Conclusion

Anxiety disorders are complex and multifactorial conditions that arise from the interaction of genetic, environmental, neurobiological, and psychological factors. Advances in understanding their pathophysiology have highlighted the critical roles of neurotransmitter imbalance, brain circuitry alterations, HPA axis dysfunction, neuroinflammation, and oxidative stress. Although conventional pharmacological treatments such as benzodiazepines, SSRIs, and SNRIs are effective, their limitations necessitate the exploration of alternative therapeutic approaches. Herbal and natural products have emerged as promising candidates due to their multi-target mechanisms and improved safety profiles. The integration of modern research methodologies, including molecular docking, in vitro assays, and in vivo behavioural models, has significantly enhanced the process of drug discovery and validation. These approaches provide valuable insights into the mechanisms of action and therapeutic potential of new compounds. Overall, future research should focus on developing safer, more effective, and targeted therapies by combining traditional knowledge with advanced scientific techniques, ultimately improving the management and treatment outcomes of anxiety disorders.

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