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Review Article

A Review on Anti-anxiety Plants

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ABSTRACT

Despite is major mental health problem affecting 4% of the world population. Despite the availability of effective treatment, many people don not seek help due to barriers such as stigma and lack of knowledge. This review highlights the potential anxiolytic effects of several botanical ex-tract, including Achyranthes bidentata, coriander, lemon balm, shepherd's purse, Plec-tranthus bergamot, Melissa parviflora, purslane, kale, liquor ice root, and frangipani. This article discusses the mechanisms of anxiolytic action of these herbs, including GABA transaminase inhibition, and GABA receptor modulation, and highlights their potential as complementary and alternative treatments for anxiety disorders. The arti-cle also discusses the implication of these finding for the development of new treat-ments for stress and the need for further research to confirm the plant's efficacy and safety in humans. Anxiolytic effects, GABAergic mechanisms, complementary and mental illness.

INTRODUCTION

While anxiety is a universal feeling, individuals with nervousness conditions usually experience excessive and acute apprehension and anxiety. (1) These emotions remain usually escorted by physiological stress as well as other behavioral and cognitive markers. They can last for a long time if not treated, are difficult to manage, and cause a lot of distress. Anxiety illness can interfere with a person's family, social life, education, and profession, as well as their daily activities. (2) Currently, an estimated 4% of individuals globally experience distress from anxiety disorders. Anxiety syndromes are the most public mental health issue globally, impacting 301 million people in 2019. Despite the fact that there are very effective treatments, only about one-fourth of those in need of treatment (27.6%) receive any treatment at all. Lack of knowledge that this is a treatable illness, a lack of funding for mental health services, a shortage of qualified medical professionals, and societal stigma are all obstacles to receiving care.(3)

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What Is Anxiety?

Stress can trigger feelings of anxiety, panic, and terror. Stressed-out people may perspire, feel agitated and nervous, and beat more quickly. A condition of uncontrollable, widespread, unfulfilling, and unhappiness, anxiety is brought on by the fear of impending risks and manifests as bodily symptoms. (1)

Pathophysiology of Stress Disorder

The human body's physiological systems work to preserve homeostasis. A stressor is anything in the surroundings that throws off homeostasis. In addition to a physical challenge, the expectation of a homeostatic challenge can also set off the reaction. (4)As a result, people experience neurosis, anxiety, and paranoia when they consistently think that a homeostatic challenge is coming. The stress reaction then triggers physiological changes that restore homeostatic balance. A person's reaction to a given stressor is also influenced by their past experiences and coping mechanisms. Even though these reactions are adaptive, they can also raise the risk of sudden death and cause heart problems and hypertension if they are activated repeatedly. Three physiological pathways react to psychosocial stimuli and become active in both acute and chronic stress situations:
The initial three consist of the endocrine systems, the neuroendocrine pathway, and the neural networks. (5)

The Neural Axes

The 3 neural axes set off in response to stress remain the sympathetic nervous system, parasympathetic nervous system, and neuromuscular nervous system. These lanes react to acute stress the fastest because of their entirely neural structure, which extends from organization to target-organ innervation. Furthermore, of all the stress routes, these axes are the record straight. Short-term stress-induced alterations cause the hypothalamus, which is part of the peripheral and autonomic nervous systems, to produce norepinephrine (NEL). In addition to causing symptoms of escape danger, such as dilated pupils, dry mouth, excessive perspiration, limb tingling, elevated heart rate, and elevated blood pressure, NE also stimulates the autonomic and sympathetic nervous systems. The parasympathetic division, which is primarily involved in inhibition, slowing, and restorative function, is activated by the other neurotransmitter, acetylcholine (ACh). Fatty acids and glucose are released from storage locations into the bloodstream during this period, making them easily accessible for the muscles to use. (6)

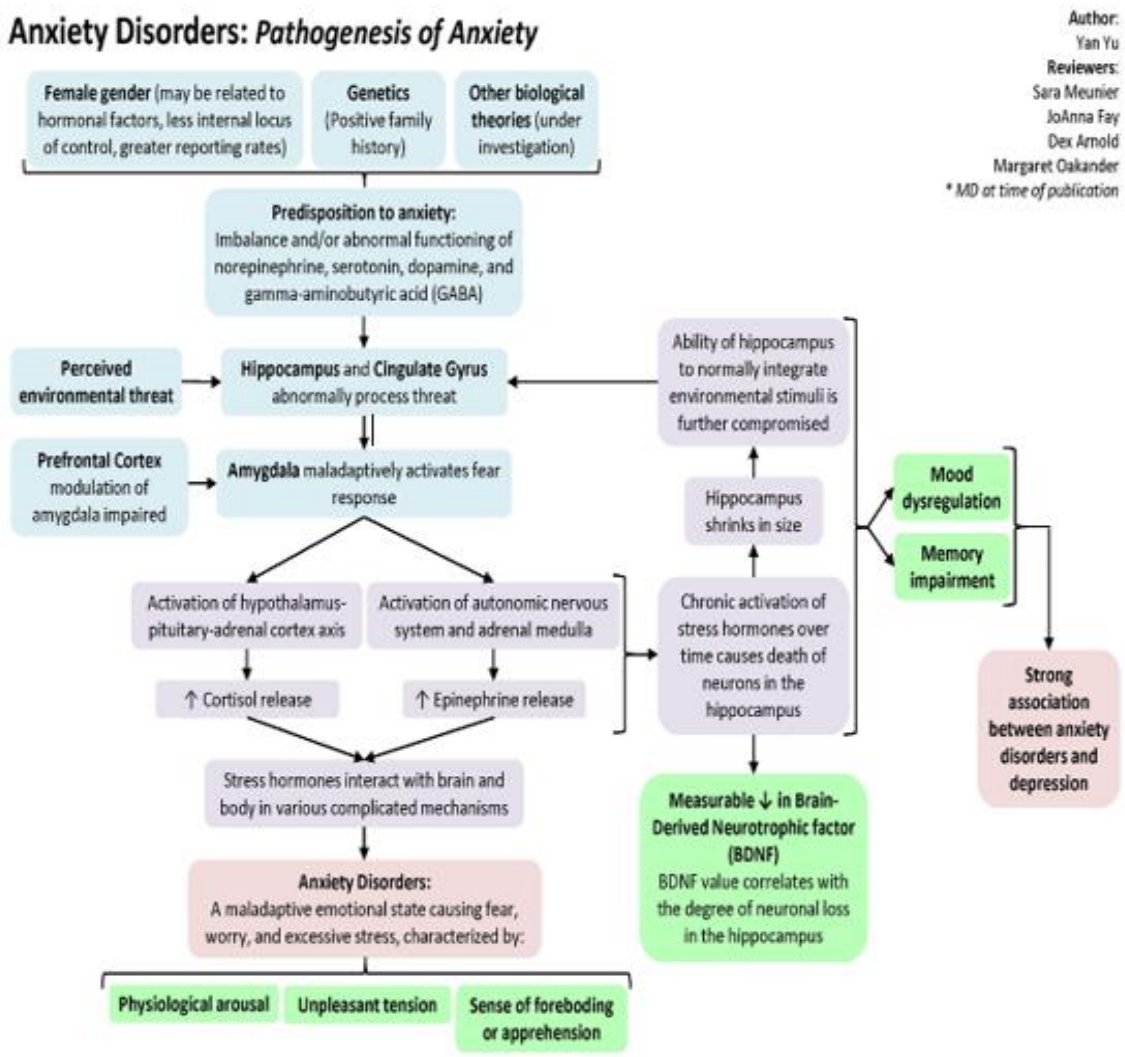
Neuroendocrine Axes

This axis has a delayed stress response and necessitates longer-lasting stress conditions. The neuroendocrine stress axis begins in the dorsomedial amygdala, passes through the lateral and posterior hypothalamic areas, relies on the spinal cord, and eventually innervates the adrenal gland, namely the adrenal medulla. Catecholamines (epinephrine and NE) are produced and secreted by the chromaffin cells in the adrenal medulla. The adrenal medulla and sympathomimetic neurons in both central and peripheral nervous systems produce NE, but its impact remains consistent regardless of its origin. Frequently Knowns sympathetic hub catecholamines prime the body for energetic strong activity by redirecting blood stream from the kidney, gastrointestinal framework, and skin to the musclesand hindering absorption to preserve vitality. For those who are vulnerable, this reaction raises the risk of angina pectoris, thrombus development, and hypertension. Additionally, it

raises the risk of arrhythmias, which raises the potential for unexpected death. (7)

The Endocrine Axes

Endocrine axis activation necessitates higher intensity stimulation and is characterized by slower firing and longer somatic effects. When a person lacks coping mechanisms in a stressful circumstance, these axes are activated. The adrenal cortical pivot, somatotrophic hub, thyroid hub, and back pituitary pivot are the four endocrine tomahawks that make up the endocrine push reaction. Neural impulses are released to the hypothalamus via the septal-hippocampal complex in the adrenal corneal axis during situations of prolonged stress. The anterior pituitary releases adrenocorticotropic hormone (ACTH) into the bloodstream in response to corticotropin-releasing factor (CRF), which is then formed by the hypothalamus. At that point, in response to the ACTH, the adrenal cortex discharges glucocorticoids (cortisol and corticosterone). Glucocorticoids ordinarily have a negative criticism impact. At that point, in reac-tion to the ACTH, the adrenal cortex discharges glucocorticoids (cortisol and corti-costerone). The hypothalamus usually receives negative feedback from glucocorticoids, which reduces CRF release. Among the trademark impacts are expanded ketone body generation and glycogenesis, wors-ened gastric damage, expanded urea generation, expa ded discharge of free greasy acids into the circulatory system, diminished craving, resistant framework concealment, and expanded vulnerability to atherosclerotic forms and myocardial rot. Excessive glucocorticoids in the central nervous system (CNS) change sleep patterns, resulting in mood swings and insomnia, and lower the threshold for convulsive seizures. The anterior pituitary secretes somatotropic hormone, also known as growth hormone, which is the hallmark of the somatotropic axis. Beneath persistent stretch condition, the development hormone is accepted to deliver a diabetic-like insulin-resistant impact, as well as mobilize fats put away within the body, which increase-es the concentration of free fatty acids and glucose within the blood. Additionally, human psychosocial stimuli raise thyroidal activity, which causes the thyroid glands to release thyroxine (T4) and triiodothyronine (T3). It is well recognized that thyroid hormones raise blood weight, heart rate, common digestion system, and the affectability of a few tissues to catecholamines. Moreover, people with depressive episodes exhibit hypothyroidism. The enactment of the back pituitary hub leads to the discharge of vasopressin and oxytocin into the systemic circulation. Vasopressin, also known as antidiuretic hormone, results in water retention. Oxytocin is believed to be involved in stress response, particularly in women.(7)



❖ Neurotransmitters Involved in Anxiety

Serotonin

• Function: Mainly affects appetite, memory, sleep, and mood regulation.

• Anxiety disorders, particularly panic and obsessive-compulsive disorder (OCD), have been linked to low serotonin levels. Selective serotonin reuptake inhibitors (SSRIs), commonly used to treat anxiety and depression, work by expanding serotonin levels.

Gaba

• Role: GABA is the main inhibitory neurotransmitter that lowers anxiety and calms the brain.

• In Anxiety: Freeze clutter and generalized anxiety disorder (GAD) have remained linked to low GABA levels. The effects of GABA are amplified by benzodiazepines, a type of drugs used to treat anxiety.

Norepinephrine

Norepinephrine plays a part in the "fight-or-flight" response by directing blood pressure, heart rate, and attention.
• In Anxiety: Anxiety disorders, particularly panic

attacks, can be exacerbated by excessive norepinephrine activity. In addition to lowering norepinephrine levels and easing anxiety symptoms, beta-blockers are frequently used to manage excessive blood pressure.

Dopamine

• Function: Linked to motivation, reward, and pleasure.

• In Anxiety: Research indicates that dopamine imbalances may play a role in anxiety disorders, especially those characterized by obsessive behaviours, although the exact role of dopamine in anxiety is complicated.

The adrenal glands release the stress hormone cortisol.

• In Anxiety: Post-traumatic stress disorder (PTSD) and generalized anxiety disorder (GAD) can be exacerbated by prolonged stress and high cortisol levels. Techniques for dcmanaging stress and drugs that lower cortisol levels can be beneficial.

Additional Neurotransmitters

• **Glutamate**: The main excitatory neurotransmitter that acting a character in recall and learning. Glutamate overactivity may be a factor in anxiety disorders.

• **Substance P**: An inflammatory and pain perception-related neuropeptide. Anxiety disorders have been associated with elevated levels of substance P.

• **Neuropeptide Y**: A neurotransmitter that controls hunger and the body's reaction to stress. Anxiety problems have been linked to decreased neuropeptide Y levels.(8)

Literature Review of Some Plants Which Show Antianxiety Action

1. *Achyranthes Aspera* Leaves



Fig. No.: - 2{*Achyranthes aspera leaves}*

Mr. Rajkumar Mathur claims that hydroalcoholic extracts of Achyranthes aspera leaves have anti-anxiety qualities. The study's goal was to determine whether hydroalcoholic extracts of Achyranthes aspera plant leaves could alleviate anxiety in animals like mice. Swiss albino mice were utilized to assess the anti-anxiety effect. After being allowed to air dry, the Achyranthes aspera plant's leaves were ground into coarse powders. For this anti-anxiety effect, the Soxhlet extraction method was employed. Achyranthes aspera hydroalcoholic extracts were screened for phytochemicals qualitatively. The anti-anxiety characteristics of Achyranthes aspera plant leaves were evaluated using a variety of models, including the hole board technique, an elevated plus-maze model, the light-dark method, and the interaction with others model. Diazepam, a common anxiolytic, was combined with a dose of tincture administered orally at 300 and 600 mg/kg, respectively. The results revealed that tincture of Achyranthes aspera leaves had anxiety-reducing properties and reduced aversion fear. (9)

***Coriandrum sativum* leaves**



Fig. No.: - 3{*Coriandrum sativum* leaves}

According to the study conducted by author K. Latha, the water-soluble extract of CS Linn. leaves displays dependent on dose anxiolytic action. The purpose of this study is to investigate the calming effects of a water-soluble extract of Coriandrum sativum (CS) on mice. To compare CS's capacity to alleviate anxiety to the commonly used drug diazepam (3 mg/kg). Swiss albino mice weighing between 18 and 25 grams were assigned at random to five groups of six each, with clearance from the Institutional Animal Ethics Committee. After boiling with distilled water, the dried up powder of CS leaves was cooled, filtered, placed on a hotplate to completely evaporate, weighed, and stored. The saline CS extract (50, 100, and 200 mg/kg), and diazepam (3 mg/kg) were given orally to the control, test, and traditional medication groups, respectively. The Elevated Plus Maze (EPM) was utilized to assess the antianxiety impact on rats. EPM found that CS 50 mg/kg (Group III), 100 mg/kg (Group IV), and 200 mg/kg (Group V) significantly enhanced the number of open arms ($P < 0.001$) compared to the control. In all CS extract dosages, the amount of time spent in open arms also increased noticeably. The current investigation shows that CS leaves have dose-dependent antianxiety action that is statistically significant.(10)

3.*Cymbopogon Citratus* leaves



Fig. No.: - 4{*Cymbopogon Citratus* leaves}

The author Paul Alan Arkin Alvarado-García claims that essential oils are intricate compounds that are frequently used in aromatherapy procedures. It is known that several essential oils can help reduce the symptoms of anxiety. The goal of this study was to determine the way vital oil from Cymbopogon citratus affects anxiety. Gas chromatography with flame-ionization detection (GC-FID) and gas chromatography-mass spectrometry (GC-MS) were employed to determine the chemical composition of the extracted essential oil. Furthermore, a pretest-posttest experimental study was conducted with 128 participants divided into two groups: a treatment group that received scent therapy using Cymbopogon citratus vital oil and a waiting-list (WL) control group. The stress level was assessed using the Zung Self-Rating Anxiety Scale (SAS). According to the chemical study, the main ingredients were neral (35.2%) and geranial (52.1%). During the posttest phase, the experimental group's anxiety levels dropped.(11)

4. Piper betle leaf



Fig. No.: - 5{*Piper betle* leaf}

The author Uttara Krishna claims that numerous native medicinal herbs with inherent antioxidant and neuroprotective qualities have been helpful in treating a range of behavioural problems, including anxiety disorders. The aim is to investigate the antianxiety activities of Piper betle L. leaf ethanol and aqueous decoction in Swiss White mice. Aqueous and tincture of the leaves of Piper betle L. [PBEE and PBAE] at 100 and 200 mg/kg were contrasted with the control (distilled water) and standard (Diazepam 1 mg/kg). For each group, six Swiss albino mice weighing 25–30g were utilized, three of each sex. The Elevated Plus Maze [EPM] and Light Dark Arena [LDA] behavioral models were used to study anxiety levels. The extracts underwent phytochemical investigation and comparison. Tukey Kramer's multiple comparison test was performed at P = 0.05 after a one-way ANOVA was used to evaluate the data. Mean ± SEM was used to represent the results. Results: When compared to the control in the EPM model, PBEE 100 mg/kg significantly increased the amount of time spent in the open arm and the number of entries to the open arm. In the LDA method, the identical dosage was discovered to be relevant. for both the number of bright area entrances and the amount of time spent in a bright area. However, there was no discernible difference between the PBAE doses and the control. Both extracts included flavonoids, a beneficial component, according to preliminary phytochemical screening; nevertheless, the water-soluble extract lacked saponins. At a dosage of 100 mg/kg, the ethanolic extract of Piper betle L. exhibited notable antianxiety properties.(12)

5**. *Plectranthus amboinicus* leaves**



Fig. No.: -6 {*Plectranthus amboinicus* leaves}

The author Dilip Kumar Tiwari investigate the calming impact of Plectranthus odorifera leaves and alcohol (AQPA and ALPA) utilizing the elevated plus maze (EPM) and light-dark maze (LDT). Control mice received the equivalent of a 2% acacia slurry, whereas positive control animals received diazepam (2mg/kg). A single treatment with L. elegans perfume/alcoh ol extract (250 and 350 mg/kg, i.p.) I creased the time spent entering the right arm of th e EPM and decreased the time spent entering and entering the closed arm compared to saline treatm ent. (P< 0.05 His.).In the light and dark test, AQP A and ALPA (250 and 350 mg/kg, i.p.) and diaze pam (2 mg/kg, i.p.) delayed entry and exit to the bright area.Neither diazepam nor AQPA and ALP A extracts caused behavioral or physiological cha nges in EPM and LDT. These results indicate that AQPA and ALPA extracts are potent anxiolytis. (13)

6. *Melissa Parviflora*



Fig. No.: -7{*Melissa parviflora*}

Melissa parviflora Benth. (Family: Lamiaceae) has been used traditionally as a nervine, relaxing, tranquilizer, and sleeping aid all over the world, according to authors Kundan Singh Bora and Aruna Dubey. The herb is prized for its relaxing qualities and is said to reduce stress and anxiety reactions. Despite a lengthy history of use, this promising herb has never been the subject of any scientific pharmacological research. Therefore, the present study was design to evaluate anti-anxiety activity of M. parviflora in rats. Various extracts viz. petroleum ether, chloroform, methanol and aqueous were prepared by successive Soxhlet extraction method. The elevated plus-maze apparatus and the light and dark stress test paradigm in Wistar rats of both sexes were used to evaluate the anxiolytic impact of various plant extracts. The biologically active extract has been standardized by estimating its complete phenolic and flavonoid content using the colorimetric technique. Only the methanol extract of M. parviflora shown significant anxiolytic action (100 and 200 mg/kg, p.o.) in contrast to the vehicle-treated control and the positive control of diazepam (2 mg/kg, p.o.) in the elevated plus maze test and the light and dark test models of anxiety. Estimates indicate that the bioactive methanol extract contains 15.21 ± 0.72 mg gallic acid equivalents and 8.06 ± 0.58 mg rutin equivalents per gram. The current investigation concludes that the plant's methanol extract exhibited primarily anxiolytic action. As a result, M. parviflora may offer a novel therapy option for central nervous system conditions including anxiety.(14)

7. Actaea spicata roots



***Fig. No.: -8{Actaea spicata* roots}**

According to author Reecha Madaan, Actaea spicata Linn. (Ranunculaceae) has historically been used to cure a variety of ailments, including rheumatism, inflammation, nerve problems, lumbago, scrofula, and chorea. This potential plant has been utilized for a long time, but no systematic phytochemical and pharmacological studies have been conducted on it. To test the validity of its traditional usage as an anxiolytic, A. spicata underwent preliminary anti-anxiety screening trials. The solvents utilized in the current investigation to extract the roots of the plant were petroleum ether (60-80°C), chloroform, methanol, and distilled water, in sequence with higher polarity. Using an elevated plus maze equipment, the anti-anxiety properties of all the crude extracts were assessed in mice. Only the methanol extract, at a level of 100 mg/kg, had considerable anti-anxiety action in mice compared to both the control and standard (diazepam, 2 mg/kg). Alkaloids and polyphenols were detected by phytochemical screening in the methanol extract of A. spicata. Therefore, specific techniques were used to extract the plant material's total alkaloidal fraction and the polyphenol fraction from the plant's methanol extract, respectively. At a dosage

of 50 mg/kg, the polyphenol fraction showed notable anxiolytic efficacy, whereas the alkaloidal fraction showed no activity at all. (15)

7. Brassica olera



Fig. No.: -9{Brassica oleracea}

The author, Divneet Kaur, claims the nervous system is hampered by oxidative stress in the brain. Antioxidants may therefore be a useful strategy for preventing conditions like anxiety. It has been reported that plants with phenolic components are strong antioxidants. Broccoli, or *Brassica oleracea L*., is a plant that is high in phenolics, primarily flavonoids, and has good antioxidant qualities. Its potential as an anxiolytic has not been studied, though. Therefore, the current study assessed the antianxiety properties of broccoli extracts in experimental mice. Standard protocols were followed in the study of the plant material's various pharmacogenetic characteristics. The mice were divided into groups of six for each treatment. The test groups were given petroleum ether and hydroalcoholic extracts (50, 100, and 200 mg/kg body weight, p.o.), the control group was given a vehicle (1% carboxymethyl cellulose), and the positive control was given Diazepam (2 mg/kg) as a normal medication. Mirror chamber, hole board, and Elevated Plus Maze (EPM) tests were used to assess the effects. ANOVA and Turkey's post-hoc test were used for the statistical analysis. With regard to the control, the extract with hydroalcoholic content showed a dose-specific rise in the mean amount of time spent and the number of entries in the EPM's open arms; a decrease in latency; an increase in the time spent and frequency of entries in the mirror chamber; and a higher number of head dips in the hole board test. These effects were similar to what diazepam produced. Phytochemical screening was used to identify whether the bioactive extract included alkaloids, phenols, flavonoids, or tannins. Our research indicates that *Brassica oleracea* hydroalcoholic extract, at a dosage of 200 mg/kg, exhibits important anxiolytic action. (16)

8. Glycyrrhiza glabra roots and rhizomes



***Fig. No.: -10{Glycyrrhiza glabra* roots and rhizomes}**

S. Ambawade, the author, claims to investigate the anxiolytic properties of a tincture of *Glycyrrhiza glabra* roots and rhizomes. This glabra hydroalcoholic extract was given to mice at several dosages (10-300 mg/kg i.p.), and its anxiolytic efficacy has been evaluated using a range of paradigms, including amphetamine-induced judgment, foot shock-induced aggression, and elevated plus maze. Ondansetron and diazepam were the most commonly used anxiolytics. Lower dosages of hydroalcoholic extract were more successful in reducing anxiety in all animal models of the condition. The extract and conventional anxiolytic drugs enhanced mice's open arm occupancy time, increased latency to foot shock generated aggressiveness, decreased the frequency of fighting bouts, and delayed the

initiation of amphetamine-induced grooming, biting, sniffing, and repeated head movements. *Glycyrrhiza glabra's* hydroalcoholic extract of roots and rhizomes is anxiolytic.(17)

***Plumeria rubra* flowers**



Fig. No.: -11 {Plumeria rubra flowers}

The intent of the current study, according to author Manavi Chatterjee, was to examine the effects of *Plumeria rubra* (PR) flower ethanolic extract and its fractions in the elevated plus-maze (EPM) model of anxiety. One hour before the behavioral evaluation, male Swiss mice were given graded oral dosages of *P. rubra* extract or its fractions. The amount of time spent in the EPM's open arms was considerably extended by the PR extract at a dose of 100 mg/kg p.o. Additionally, the EPM task revealed the anxiolytic qualities of the soluble and insoluble fractions of butanolic, hexane, and chloroform at a fifth of the initial dosage. Of these, the butanol insoluble fraction exhibited notable anxiolytic efficacy on par with diazepam, a common anxiolytic medication. Furthermore, the mouse rotarod test found no evidence of motor incoordination, and prior to treatment with unrefined ethanolic extract and butane unsolvable fraction had no obvious effects on horizontal activity, the overall distance traveled, or stereotypy count in the rodent's movement monitors. These findings show that *P. rubra* flower extract as well as its insoluble butanolic component may have substantial anxiolytic characteristics that deserve further exploration in the course of medicine development. (18)

DISCUSSION:

Achyranthes aspera, Coriandrum sativum, Cymbopogon citratus, Piper betel, Plectranthus amboinicus, Melissa parviflora, Actaea spicata, Brassica oleracea, Glycyrrhiza glabra, and *Plumeria rubra* are among the plant extracts that have been shown in the studies reviewed in this article to have potential anxiolytic effects. According to these results, using traditional medicinal plants to treat anxiety problems may be a promising strategy.
These plant extracts' capacity to alter neurotransmitter function, lower stress hormone levels, and encourage relaxation may be the cause of their anxiolytic effects. For example, the aqueous extract of *Coriandrum sativum* leaves demonstrated dose-dependent anxiolytic effect, whereas the hydroalcoholic extract of *Achyranthes aspera* leaves demonstrated reduced aversion fear-induced anti-anxiety activity. Significant anxiolytic effects were also shown in the research on *Plumeria rubra, Melissa parviflora, Actaea spicata, Brassica oleracea, Glycyrrhiza glabra, Plectranthus amboinicus, and Melissa parviflora,* underscoring the promise of these plant extracts as alternative therapeutic methods for anxiety disorders.
Interestingly, the following chemical components give these plant extracts their anti-anxiety properties:

- Flavonoids in *Piper betel* leaf extract
- Phenolic components in *Brassica oleracea* extract
- Alkaloids and polyphenols in *Actaea spicata* root extract
- Geranial and neral in *Cymbopogon citratus* essential oil

- The butanol insoluble fraction of *Plumeria rubra* flower extract, which demonstrated notable anxiolytic effect;
- Glycyrrhizin in *Glycyrrhiza glabra* root and rhizome extract

CONCLUSION

Although anxiety disorders are prevalent psychological disorders which have a significant impact on people's daily lives, many people do not get the therapy they need due to a number of difficulties. There are effective treatments available, such as psychiatric counseling and prescription drugs, underscoring the significance of awareness and care availability for individuals impacted. The intricate interactions between the neuronal, neuroendocrine, and endocrine axes in the body's reaction to stress are highlighted in the text, which also describes how these systems trigger different hormones and neurotransmitters that affect physiological and psychological states. It also talks about the possible anxiolytic properties of a number of plant extracts, indicating that they may be used therapeutically to treat anxiety disorders. The importance of traditional medicinal plants in treating anxiety disorders is highlighted by the studies on a variety of plant extracts, such as *Actaea spicata*, *Brassica oleracea*, *Glycyrrhiza glabra*, and *Plumeria rubra*, which show potential anxiolytic qualities. These results call for more research into their development and pharmaceutical uses.

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