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THERAPEUTIC POTENTIAL OF MEDICINAL PLANTS IN TREATMENT OF ANXIETY IN CONTEXT TO NEUROTRANSMITTER: AN OVERVIEW

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ABSTRACT: Anxiety is a negative emotional state marked by tension, unease, and emotions of concern and fear. Across the globe, women are more likely than males to suffer from anxiety disorders. Insomnia, cold or sweaty hands and/or feet, shortness of breath, an inability to be steady and calm, dry mouth, numbness or tingling in the hands or feet, nausea, abdominal discomfort, dizziness, pins and needles, feelings of losing control, heart palpitations, pins, and needles are just a few symptoms of anxiety disorders. Many systems indicate that when someone is anxious, they exhibit a variety of cognitive, physiological, and behavioral symptoms. Anxiety is brought on by aberrant chemoreceptor responsiveness and unusual neurochemical behavior. Many neurotransmitters, including gamma-amino butyric acid, serotonin, dopamine, noradrenaline (norepinephrine), glutamate, and others, are involved in anxiety. Some have an excitatory or an inhibitory effect. Several promising medications that may be helpful in the treatment of anxiety disorders have been identified via research in the field of herbal pharmacology. Unfortunately, there hasn't been a thorough examination of plant-based anxiolytics that focuses on their mode of action. Thus, our goal was to present a thorough narrative evaluation of plant-based medications with preclinical evidence of anxiolytic action.

INTRODUCTION: Anxiety word was derived from the Latin root "anxieta" meaning trouble in the mind about some uncertain event and it has a Greek root "anxo" meaning to squeeze, strangle or press tight [1]. Anxiety is a frequent negative emotional state characterized by feelings of worry and apprehension and accompanied by specific somatic, cognitive, and behavioral manifestations. Anxiety is a psychological and physiological condition that can be observed by variations in the emotion, thought process, and behavioral features of an individual.

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In today's world, almost each one of us used to face anxiety but the problem arises when it becomes uncontrollable and can result in an unpredicted reaction. It depends only on us how we tackle the challenges of our life such as taking a lesson from defeat or taking the revenge from winner. Everyone feels anxious in response to specific events - but individuals who suffer from anxiety disorder have excessive and unrealistic feelings that interfere with their relationships, activities of school and work, social activities, and recreation in their lives.

According to the World Health Mental survey, almost one-eighth of the entire world population, experience anxiety but unfortunately many times, it goes unnoticed. But things have changed, now people get a proper diagnosis as well as treatment [2]. In a 2020 survey, 62% of respondents reported experiencing some degree of anxiety. An estimated 31% of all adults will experience an anxiety

disorder at some point in their life. Anxiety disorders are more prevalent in women than in men all around the world. It is estimated that 264 million adults around the globe have anxiety. Of these adults, 179 million were female (63%) and 105 million were male (37%) [3].

Anxiety disorders are not considered as one disorder but these are a group of disorders characterized by persistent feelings of high anxiety, and extreme discomfort and tension. Other symptoms can include sweating, trembling, feelings of choking, nausea, abdominal distress, dizziness, pins and needles, feelings of losing control, and/ or feelings of impending doom. general signs and symptoms include heart palpitations, feelings of panic, fear, and uneasiness, insomnia, cold or sweaty hands and/or feet, shortness of breath, incapability to be steady and calm, dry mouth, numbness or tingling in the hands or feet, muscle tension, and dizziness. It is a frightening syndrome characterized by nervousness, restlessness, agoraphobia, sweating, stomach upset, and dry mouth [4]. Anxiety often results from stress, which induces significant neurochemical changes in the central nervous system (CNS) [5]. These symptoms constitute a negative impact on the patient, families, and society. In the absence of treatment, patients would progress to depression and sometimes contemplate suicide. Several factors can cause anxiety. They include stress, alcohol and substance abuse, and drug-induced and genetic abnormalities. Generalized anxiety disorder, panic disorders with or without agoraphobia, social phobia, obsessive-compulsive disorder, and post-traumatic stress disorder are examples of different types of anxiety disorders [6]. Anxiety disorders are the most prevalent psychiatric disorders and a leading cause of disability [7].

Many sensations are occurring in the human body during anxiety as it prepares for danger. The sensations, which occur in the human body, when the natural Alarm System of the human body (the "fight-flight-freeze" response) has been activated, are known as "alarm reactions". Anxiety is a persistent feeling of dread, apprehension, and impending disaster, or tension and uneasiness". Classically, anxiety is distinguished into, "State" anxiety and the "Trait" anxiety. "State anxiety" is experienced by a subject at a particular moment, and it increases by the presence of an anxiogenic stimulus. In contrast, "Trait anxiety" does not vary from moment to moment and everlasting feature of an individual. According to multiple systems, symptoms of anxiety are (a) Cognitive, (b) Physiological, and (c) Behavioral.

Cognitive Component: Of anxiety is related to the cognitive distortions in the components of attention, interpretation, and memory for information processing.

Physiological Component: Of anxiety consists of the autonomic or somatic sensations. It also includes avoidance related to the sleep, insomnia, nightmares, and refusal/reluctance to sleep alone. Accelerated heart rate, heart palpitations, chest pain, shortness of breath, difficulty in swallowing and nausea are other symptoms.

Behavioral Component: Of anxiety refers to the action that is taken by an individual to prevent feared stimuli exposure. Behavioral symptom associated with the anxiety disorders includes avoidance, in which specific stimuli was avoided by the individual (e.g. bridges) or situations (e.g. public speaking) to prevent anticipated harm. Due to avoidance, there will be impairment in maintaining daily routines or in family, academic and/or social functions by the individual.

There are a number of drugs are available for treating anxiety like Benzodiazepines, Azapirones, Beta-blockers, SSRI's, Tricyclic anti-depressants, and anticonvulsants but such drugs act temporarily for a short span of time only. Therefore, again the needs make the scientists to incline towards plants for effective remedy. There are a huge number of herbs which are being used continuously from ancient times to make the mind stress free and happier.

GABA, Dopamine, Noradrenaline, and Serotonin (Monoamines), Glutamate, Neuropeptides Neurosteroids, and Cytokines are all implicated in fear. Researchers in this area are interested in herbal plants because they have long been used to cure variety of illnesses, including mental conditions, because they have fewer side effects than pharmaceutical and chemical medicines.

Aim of this paper is to summarise results of research on medicinal plantsanti-anxiety effects and mechanisms of action, as well as medicinal plant in these are responsible for anti-anxiety action.

Types of Anxiety Disorders [8]: There are several types of anxiety disorders:

Generalized Anxiety Disorder: You feel excessive, unrealistic worry and tension with little or no reason.

Panic Disorder: You feel sudden, intense fear that brings on a panic attack. During a panic attack you may break out in a sweat, have chest pain, and have a pounding heartbeat (palpitations). Sometimes you may feel like you're choking or having a heart attack.

Social Anxiety Disorder: Also called social phobia, this is when you feel overwhelming worry and self-consciousness about everyday social situations. You obsessively worry about others judging you or being embarrassed or ridiculed.

Specific Phobias: You feel intense fear of a specific object or situation, such as heights or flying. The fear goes beyond what's appropriate and may cause you to avoid ordinary situations.

Agoraphobia: You have an intense fear of being in a place where it seems hard to escape or get help if an emergency occurs. For example, you may panic or feel anxious when on an airplane, public transportation, or standing in line with a crowd.

Separation Anxiety: Little kids aren't the only ones who feel scared or anxious when a loved one leaves. Anyone can get separation anxiety disorder. If you do, you'll feel very anxious or fearful when a person you're close with leaves your sight. You'll always worry that something bad may happen to your loved one.

Selective Mutism. This is a type of social anxiety in which young kids who talk normally with their family don't speak in public, like at school.

Medication-induced Anxiety Disorder: Use of certain medications or illegal drugs, or withdrawal from certain drugs, can trigger some symptoms of anxiety disorder.

Literature Search Methodology: In this study, at first, the search was done by keywords such as, Anxiety, Anxiolytic, Neurotransmitters, and Medicinal plants from electronic databases such as Google Scholar, PubMed, Science Direct, *etc*. Related articles were selected for review.

Neurotransmitters Involved In Anxiety: Abnormal functioning of neurochemicals such as Gamma-amino butyric acid, Serotonin, Norepinephrine, Dopamine and systems as well as abnormal chemoreceptor reactivity leads to anxiety. Other neurotransmitters that modulate complex anxiety responses in the amygdala, including Glutamate and other releasing hormones.

Gamma-Aminobutyric Acid (GABA) [9, 10, 11]: Gamma-amino butyric acid (GABA) is a nonstandard amino acid that acts as the principal inhibitory neurotransmitter in central nervous system (CNS) function. Up to 40% of all synapses in the CNS operate for GABA, and GABA receptors are found in every region of the human brain. Thus, GABA systems are implicit in several neurophysiological processes, including motor function, pain, sleep, brain development, and importantly for the current review, anxiety. Furthermore, impairments in GABA-mediated inhibition are seen in various neurological and psychological conditions, such as movement disorders, epilepsy, schizophrenia, insomnia, and anxiety disorders. Many brain regions appear to be involved in the recognition and regulation of negative emotional stimuli and the generation of cognitive, behavioural, or somatic responses to these stimuli.

Nonetheless, a set of limbic structures appear to be critical for the regulation of negative emotion. In particular, the amygdala – nuclei situated in the median temporal lobes – appears to play a crucial role. The principal neural circuits are thought to be related to anxiety. It is important to bear in mind that this circuitry has been established from research on experimental animals. Although data from functional imaging are consistent with this model, it should be noted that these pathways have not all been demonstrated conclusively in the human brain. Gamma-amino butyric acid (GABA) is the primary inhibitory neurotransmitter that is known to counterbalance the action of the

excitatory neurotransmitter glutamate. It has been estimated that at least one-third of all CNS neurons utilize GABA as their primary neurotransmitter. GABAergic inhibition is essential for maintaining a balance between neuronal excitation and inhibition in the central nervous system. Neuronal inhibition by GABA is mediated by two distinct classes of GABA receptors. The inotropic $GABA_A$ receptor is a fast-acting ligand-gated chloride channel responsible for rapid inhibition. $GABA_B$ receptor is coupled indirectly via G-proteins to either calcium or potassium channels to produce prolonged inhibitory responses which are involved in the processes of myorelaxation.

The $GABA_A$ receptor is a transmembrane hetero-oligomer with a pentameric structure (α1, α2, β1, β2, and γ subunits) located in the neuronal membrane. Activation of $GABA_A$ receptors causes an immediate and substantial rise in chloride conductance across the cell membrane, which renders the neuron unable to raise an action potential and leads to "phasic" inhibition of the neuron. Preclinical studies demonstrated that the α2 subunit of the $GABA_A$ receptor is particularly relevant for the manifestation of anxiety. The neural circuits involved in anxiety comprise inhibitory networks of principally GABAergic interneurons. Three different GABA receptors, $GABA_A$, $GABA_B$, and $GABA_C$, are involved in the regulation of sleep and arousal (albeit to different extents).

The role of the inhibitory neurotransmitter GABA has long been regarded as the Centre for the regulation of anxiety and this neurotransmitter system is the main target of benzodiazepines and other anxiety-related drugs used to treat anxiety disorders. Historically, the GABA system has been thought to play a role in anxiety disorders largely because of the effectiveness of the benzodiazepines, which are well known to act primarily on GABA receptors, in the management of anxiety. And from this data, some medicinal plants that are proven to be anti-anxiety are listed in **Table 1**. When there is a binding of GABA with the GABAA ± benzodiazepine receptor complex, it acts as an agonist: inducing conformational changes, with which the permeability of the central pore to chloride ions gets increased. The resulting chloride flux hyperpolarizes the neuron, leading to a reduction in its excitability and producing a general inhibitory effect on neuronal activity. Benzodiazepines such as diazepam and clonazepam (both of which are long-acting agents) may be efficacious in treating GAD.

$GABA_A$ Receptor: The fast-acting ionotropic $GABA_A$ receptors were the first to be discovered and have been the target of three generations of anxiolytics and hypnotics. $GABA_A$ receptors are pentameric, ligand-gated Cl^- ion channels; the classical synaptic subtypes are formed of two α, two β, and one γ or δ subunit, the α1β2γ2 receptor being the most abundant.

$GABA_B$ Receptors: are slow-acting metabotropic G-protein-linked dimers containing one $GABA_{B1}$ ($GABA_{B1a}$ or $GABA_{B1B}$) and one $GABA_{B2}$ subunit. Fewer drugs have been developed to target the $GABA_B$ receptor, baclofen being the most popular agonist, and there are less clinical data available than for the $GABA_A$ receptor. Although $GABA_B$ agonists may promote sleep by increasing the duration of NREM and REM sleep, the effect is believed to be largely off-target.

$GABA_C$ Receptor: The subclass of $GABA_A$ receptors containing ρ subunits is often called $GABA_C$ or GABA-ρ; they belong to the same family of fast-acting pentameric, ligand-gated Cl– ion channels as $GABA_A$. Although both $GABA_A$ and $GABA_C$ receptors bind GABA, they have separate sets of agonists and antagonists. GABAC receptors are more sensitive to GABA than the other two receptor subclasses.

Serotonin [12]: Disturbances in the serotonergic system have been implicated in the pathophysiology of anxiety disorders for many years. To understand the role of serotonin in the regulation of anxiety-related behaviour, it will be important to determine the effects of serotonin on the neural circuits that mediate anxiety-related behaviours. This represents a significant challenge for investigators. Despite this, many medicinal plants that are beneficial to treating anxiety are included in **Table 1.** The effects of serotonin on these neural circuits are likely to depend on several variables. These include the time course of serotonin action, the extracellular concentrations of serotonin, and the type and presynaptic or

postsynaptic location of serotonin receptors within each specific brain region. SSRIs inhibit the reuptake of serotonin into the presynaptic nerve terminal, thereby increasing 5-HT concentrations in the synaptic cleft and prolonging its activity at postsynaptic receptor sites. After several weeks of treatment with SSRIs, desensitization of presynaptic 5HT1A receptors may occur. The 5HT1A receptor is a somatodendritic auto receptor. Its activation results in a decreased firing activity along the serotonergic axon with a consequent enhancement of the serotonergic neurotransmission. 5-HT released from the nerve terminal binds to the postsynaptic 5-HT2C receptor subtype, which mediates anxiety. Cellular pathology that may contribute to the development of anxiety disorders includes abnormal regulation of 5-HT release and/or reuptake or abnormal responsiveness to 5-HT signalling. The 5-HT1A receptor is thought to play a particularly important role in anxiety. Activation of 5-HT1A receptors enhances potassium currents and inhibits the activity of adenylate cyclase.

SNRIs (Serotonin-Norepinephrine reuptake inhibitors) result in 5-HT and NA transporters binding to selectively inhibit the reuptake of these neurotransmitters from the synaptic clefts. SNRIs show a "dual mode of action". SNRIs block the reuptake of both 5-HT and NA with differing selectivity.

Dopamine [13, 14]: Various mechanisms and neurotransmitters are involved in the regulation of anxious states. It has been suggested that dopaminergic systems have central roles in the regulation of anxiety-like behaviours. Dopamine is the main catecholamine in the mammalian brain and influences a variety of functions and has been revealed that dopamine has a role in the pathophysiology of some mental diseases. However, some areas such as the hippocampus, amygdala, septum, prefrontal cortex (PFC), and NAc, seem to be especially involved in anxiety-like behaviour. Also, dopamine is involved in the regulation of locomotor activity, cognition, emotion, positive reinforcement, food intake, endocrine regulation, cardiovascular function, catecholamine release, hormone secretion, vascular tone, renal function, gastrointestinal motility, reward, learning, memory, pain, depression, fear, and anxiety. Five different Dopamine receptors have been identified, which are G-protein-coupled, and are categorized as belonging to one of the two classes nominated as D1-like (D1 and D5) or D2-like (D2, D3, and D4). D1-like receptors can excite adenylate cyclase activity and increase cyclic adenosine monophosphate (cAMP).

Auto receptors, which are D2-like, have been recognized on the presynaptic terminals of dopaminergic neurons. Conversely, D2-like receptor activation either prevents or does not affect cAMP levels. Despite their opposing actions on adenylate cyclase activity, previous evidence has suggested that a synergistic interaction between D1 and D2 receptors is needed for the expression of most dopaminergic-related behaviours. Alterations in dopamine transmission occur following exposure to a wide variety of acute stressors. It has been shown that both dopamine D1 and D2 receptors are important in mediating anxiety even if it could be with different mechanisms.

It has been reported that dopamine depletion would be the inducer of anxiety and depression-like behaviours, while L-DOPA treatment could rebate these effects due to dopaminergic function modulation. Dopamine is metabolized to 3,4-dihydroxyphenylacetic acid (DOPAC) in the terminal of synapses and mitochondria via monoamine oxidase. The level of dopamine and its metabolites, including the DOPAC/dopamine ratio (dopamine turnover) and MAO-A/B activity, are associated with anxiety-like behaviour.

Dopaminergic activity has been demonstrated to be involved in anxious processing. Strong evidence links reward-related, hedonic, and motivated behaviors with the mesolimbic DA system. A few of these are listed in **Table 1**. Impairment of these functions is an all-prominent characteristic of Anxiety. Moreover, immediate bidirectional control (inhibition or excitation) of specified midbrain DA neurons modulates multiple independent Anxiety-related symptoms caused by chronic stress, suggesting that processes affecting anxious symptoms alter the DA neural encoding of action in the limbic circuitry. Further, poor functioning of DA neurons may cause Anxiety-related symptoms, including hopelessness and loss of interest.

Norepinephrine [15]: NE is ingested into the noradrenergic nerve endings by the tyrosine transporter through a precursor formation of tyrosine and NE and is converted to NE by a series of transformations. The symptoms of anxiety were assumed to be caused by hyperactivity of NE in the central nervous system. In stress conditions, the corticotropin-releasing factor can activate the NE energy pathway in the locus coeruleus-temporal hippocampal, which releases NE and induces wakefulness and anxiety symptoms. Animal model studies found that antagonism of β-adrenergic receptors within the central nervous system could attenuate the anxiogenic effects of cocaine (Noradrenergic -Receptor Antagonism within the Central) and disrupted anxiety-like phenotypes including aversive, fear, and stress-related behaviours.

Although the role of noradrenaline (NA) is less clear, the idea that disturbed noradrenergic neurotransmission contributes to the symptoms of anxiety is also supported by several lines of evidence. Among these, there is the noradrenergic nature of many anxiety symptoms (such as arousal, tachycardia, and tremor) and the observation that NA modulates activity in brain regions known to be involved in the control of anxiety, such as the amygdala. In addition, circulating levels of NA and its metabolites are modified in anxiety states. According to some theories and research papers on medicinal plants **Table 1**, noradrenergic stimulation, as expected, with the serotonin/ noradrenaline reuptake inhibitors (SNRIs) could exacerbate anxiety symptoms.

Acetylcholine [16]: Acetylcholine plays a pivotal role in learning and memory processes. Acetylcholine levels can be modulated by stress in several brain regions. Acetyl cholinesterase present in the CNS catalyses the hydrolysis of acetylcholine to choline. Acetylcholine is released in the synaptic cleft where it activates both presynaptic and postsynaptic cholinergic receptors namely nicotine and muscarinic leading to an increase in cholinergic transmission which results in cognitive impairment. In the central neuronal system (CNS), acetylcholine (ACh) facilitates many functions, such as learning, memory, attention, and motor control. ACh muscarinic receptor (mAChR) family is one of the two ACh receptors, with subtypes M1, M2, M3, M4, and M5 Cholinergic input to the hippocampus is enhanced in response to anxiogenic and stressful stimuli. Muscarinic M1 receptors induce anxiety through a noradrenergic pathway. Nicotine facilitates GABAergic neuron that induces anxiety. History suggests that plants can modulate the symptoms of anxiety **Table 1**.

Glutamate [17]: Glutamate is the main excitatory neurotransmitter in the human Central Nervous System. Glutamate is ubiquitous within the central nervous system and has been shown to play important roles in many brain processes, including neurodevelopment, learning, acute neuro-degeneration, chronic neurodegeneration, and more recently, stress response and anxiety disorders. Exposure to severe stress has been associated with glutamate excitotoxicity, which, in turn, can cause neuronal damage and/or death. Glutamate also exerts its actions in the brain by affecting the release of other neurotransmitters including monoamines and GABA. The glutamate system has received much attention as a target for treatments of anxiety disorders due to both the preclinical animal with medicinal plants studies and human drug trials that have provided good evidence of the efficacy of glutamatergic drugs in the treatment of anxiety **Table 1**.

Glutamate controls the synaptic release by a wide range of presynaptic receptors. These include not only the Group II and Group III glutamate metabotropic receptors but also cholinergic (nicotinic and muscarinic) receptors, adenosine (A1), kappa opioid, γ-amino butyric acid (GABA B), cholecystokinin and neuropeptide Y (Y2) receptors.

A decrease in excitatory output in the amygdala can be achieved by decreasing the excitatory glutaminergic transmission. Blocking the basal glutamate excitation generated by ionotropic receptors could elicit a significant anxiolytic effect. Indeed, the administration of antagonists of the NMDA and non-NMDA type receptors into the basolateral amygdala has been shown to reduce anxiety in animal models. Glutamate was thought to be exclusively mediated by ion channel mechanisms. However, glutamate receptors can now be categorized into two major groups, (I) ionotropic and (II) metabotropic receptors.

This categorization is based on intracellular/ extracellular coupling and different pharmacological and biochemical characteristics. An alternative way to decrease excitatory output in the amygdala could be achieved by an increase in GABA neurotransmission. The anxiolytic benzodiazepines increase GABA neuro-transmission and induce a decrease in the excitatory output of the amygdala. There appears to be a balance between GABA receptor-mediated inhibition and glutamate receptor-mediated excitation that regulates behavioral and physiological responses associated with anxiety. Thus, GABA receptors produce inhibitory actions in the amygdala. In contrast, glutamate receptors can produce both excitatory and inhibitory actions in the amygdala and the degree of ionotropic and metabotropic activation is likely to be an important determinant of amygdaloid cell excitability. These anxiogenic or anxiolytic actions of different glutamate receptors in the amygdaloid cells can be better understood about fear conditioning. Some data summarize the current understanding of the potential role of glutamate neurotransmission in anxiety disorders and highlight specific glutamate receptors that are potential targets for novel anxiety disorder treatments.

TABLE 1: MEDICINAL PLANTS WITH PROVED ANXIOLYTIC-LIKE EFFICACY WITH EMPHASIS ON NEUROTRANSMITTERS INVOLVED [18-63]

Sr. no.	Medicinal plants	Family	Parts used	Extracts	$GABA_A$ receptor
1	*Abiespindrow Royle*	Pinaceae	Aerial parts	N-hexane, Chloroform, Methanol and Water extract	
2	*Achillea millefolium L.*	Asteraceae	Aerial parts	Hydroalcoholic extract	Non-BDZ/Gama-amino butyric acid
3	*Adenia cissampeloides.*	Passifloraceae	Leaves	Maceration	Serotonin (5-HT2)
4	*Aegle marmel*	Rutaceae	Leaves, fruit	Methanol extract	Modulation of monoamines
5	*Alafia multiflora*	Apocynaceae	Stem bark	Aqueous extract	Monoamine systems (5-HT, NA, and DA)
6	*Alstonia scholaris*	Apocynaceae	Leaves	Ethanolic extract	Dopamine
7	*Allium ascalonicum Linn.*	Liliaceae	Aerial part	Hydroethanolic extract	Serotonin,
8	*Amorphophallus paeoniifolius*	Araceae	Fresh tuber	Petroleum ether extract	BZD binding sites
9	*Angelica archangelica Linn.*	Apiaceae	Root, stem, leaf, fruit, whole plant	Methanol extract	$GABA_A$ receptor
10	*Annona vepretorum*	Annonaceae	Leaves	Essential oil, (Clevenger)	Benzodiazepine-Gamma-amino butyric acid (GAB_A),
11	*Annona coriacea Mart.*	Linnaeus	Leaves	Hydroethanolic extract	5-HT
12	*Areca catechu. Linn.*	Palmae	Areca nuts	Methanolic, Aqueous extract	GAB_A receptor
13	*Aronia melanocarpa* (Black chokeberry)	Rosaceae	fresh berries	Fresh juice	GABAergic,
14	*Artemisia indica*	Asteraceae	Whole part of the plant	100% methanol.	Monoaminergic
15	*Asparagus racemosus Linn.*	Asparagaceae	Fresh roots	Methanolic extract	$GABA_A$ receptor
16	*Bacopa monniera (Brahmi)*	Plantaginaceae	-	-	MAO-^{A} inhibition
17	*Brassica oleracea*	Brassicaeae	Flower heads	Petroleum ether and Hydroalcoholic extracts	GABA-^{A} receptors
18	*Camellia sinensis*	Theaceae	Leaves	Aqueous extract	$GABA_A$,
19	*Centella asiatica*	Apiaceae or Umbelliferae	Whole plant	Methanol and Ethyl acetate extracts	Serotonergic
20	*Cissampelos pareira*	Menispermaceae	Leaves	70% hydroethanolic	GABA-ergic activity

				extract	
21	*Citrus aurantium L.*	Rutaceae	Ripe fruits (peels)	Essential oil extraction	$GABA_A$ BDZ-receptor
22	*Cocos nucifera*	Arecaceae	Husk fiber	Hydroalcoholic extract	$GABA_A$ benzodiazepine receptor
23	*Coriandrum sativum*	Apiaceae	Seed	Aqueous extract	GABAergic effects
24	*Cucurbita moschata* [54]	Cucurbitaecea	Seed	Ethanolic and Ethyl acetate	GABAA–BZD complex
25	*Dichrocephala integrifolia*	Asteraceae	Leaves	Maceration (water)	Serotonin (5-HT1A)
26	*Diospyros montana Roxb. (Tamala)*	Ebenaceae	Fresh leaves	Methanolic extract	GABAergic system
27	*Echium amoenum*	Boraginaceae	Flowers	Maceration	GABA,
28	*Erythrina variegate*	Leguminosae	Bark	95% alcohol	Monoamines
29	*Eucalyptus tereticornis*	Myrtaceae	Leaves	N-hexane extract	$GABA_A$ receptor
30	*Euphorbia hirta*	Euphorbiaceae	Whole plant	Hydroalcoholic extract	GAB_A receptor complex
31	*Euphorbia neriifolia*	Euphorbiaceae	Leaves	Chloroform, Ethanol and Aqueous extracts	GAB_A,
32	*Foeniculum vulgare*	Umbelliferae	Fruits, fresh aerial parts	Ethanolic extracts, hydrodistillation	Serotonin
33	*Garcinia indica Linn.*	Clusiaceae	Fruit	-	Benzodiazepine receptors
34	*Helianthus annuus*	Asteraceae	Seeds	Methanol extract	Monoamine neurotransmitter
35	*Humulus lupulus (Hops)*	Cannabaceae	Flowering cones	-	$GABA^A$ receptor
36	*Lepidium sativum Linn.*	Brassiaece	Seeds	Methanolic extracts	$GABA^A$ receptor-benzodiazepine receptor-Cl^-channel complex.
37	*Lippiacitriodora*	Verbenaceae	Leaves	Aqueous extract, Ethanolic extract	Benzodiazepine receptors
38	*Lippianodiflor*a Linn.	Verbenaceae	Aerial part	Petroleum, Chloroform and Ethanolic extracts	$GABA^A$ benzodiazepine receptor complex.
39	*Lotus (Nelumbo nucifera Gaertn.)*	Nelumbonaceae	Leaves	Alkaloid extract	Monoaminergic pathway
40	*Magnifera indica* L.	Anacardiaceae	Leaves, Stem bark	Aqueous extracts, Hydroethanolic extract	Norepinephrine (NE) and
41	*Matcha*	-	leaves	Hot water extract and 80% ethanol extract	5- hydroxytryptamine (5-HT)
42	*Melissa officinalis (lemon balm)*	Lamiaceae or Labiatae	Leaves, Aerial parts	Ethanolic extract, Ethanol:Water (30:70)	GAB_A-ergic mechanisms
43	*Mimosa pudica L.*	Mimosaceae	Leaves	Ethyl acetate extract	Noradrenaline,
44	*Mimusops elengi Linn.*	Sapotaceae	Barks	Methanolic extract	GAB_A
45	*Montanoa frutescens*	Asteraceae	-	Aqueous crude extracts	GABAA receptors.
46	*Morinda citrifolia Linn. (noni fruit)*	Rubiaceae	Fruit	Methanolic extract	GABA-$_A$ receptor complex
47	*Nardostachys jatamansi*	Caprifoliaceae	Roots	70% ethanol	GABAergic and
48	*Nauclea latifolia (African Peach)*	Rubiaceae	Root, bark	Decoction	Monoaminergic systems
49	*Newbouldia laevis*	Bignoniaceae	Leaf	Hydroethanol extract	5-HT2 ,
50	*Nigella sativa* Linn.	Ranunculaceae	Seed	Methanolic extract	Benzodiazepine receptors
51	*Nymphaea alba Linn.*	Nymphaeaceae	Entire plant	Ethanolic extract	dopaminergic and Serotonergic systems.

52	*Nymphaea lotus linn.*	Nymphaeaceae	Leaves	Maceration (80% ethanol)	$GABA_A$ receptor
53	*Passiflora quadrangularis L.*	Passifloraceae	Fruits	Aqueous extracts	GABA/benzodiazepine receptor complex,
54	*Persicaria hydropiper Linn.*	Polygonaceae	Leaves	Maceration (Methanol)	5-HT1B receptors,
55	*Pimpinella anisum L.*	Apiaceae	Seeds	Hexane extract	GAB_A receptor
56	*Piper amalago L.*	Piperaceae	Leaves	Ethanolic extract	$GABA_A$ receptor
57	*Piper methysticum (kava)*	Piperaceae	Root	95% ethanol	benzodiazepine-GABAAergic and Serotonergic
58	*Protium copal L.*	Burseraceae	Bark	Ethyl acetate	GABAergic receptor complex
59	*Psidium guajava Linn.*	Myrtaceae	Fresh leaves	Absolute ethanol (99.99%)	benzodiazepine/ $GABA_A$ receptors,
60	*Punicagranatum L. (Pomegranate)*	Punicaceae	Leaf, Fresh fruits	Methanolic and Ethyl acetate extract, Fresh juice	5-HT1A receptors,
61	*Rhodiola rosea*	Crassulaceae	Roots	Alcohol extract	NMDA receptor
62	*Rosmarinus officinalis L.*	Lamiaceae	Leaf	Hydroalcoholic extract	Dopaminergic enhancement(s).
63	*Schinus lentiscifolius*	Anacardiaceae	Fresh leaves	Maceration (70 % v/v ethanol)	Serotonin (5-HT)
64	*Scoparia dulcis*	Scrophulariaceae	Whole plant	Ethanol [90%]	and
65	*Scutellaria lateriflora L. (American skullcap)*	Lamiaceae	Herb	Ethanolic extracts	GAB_A
66	*Senna alata*	Fabaceae	Leaf	Maceration	GABA/benzodiazepine receptor complex,
67	*Souroubea sympetala*	(Marcgraviaceae)	Leaf, Bark	Ethyl acetate (EtOAc) extraction	5-HT1B receptor or 5-HT1A receptor.
68	*Tagetes erecta L.*	Asteraceae	Flowers	Maceration	MAO activity,
69	*Tephrosia purpurea (L) Pers.*	Papilionaceae	Whole plant	Hydroalcoholic extract	GABAergic system.
70	*Terminalia citrina*	Combretaceae	Leaves	Methanolic extracts	$GABA_A$ receptor
71	*Thymus vulgaris*	Lamiaceae	Leaves	70% ethanol extract	Serotonin,
72	*Tinospora cordifolia*	Menispermaceae	-	50% Ethanolic extract	Dopamine
73	*Valeriana officinalis (Valerian)*	Valerianaceae	Root	-	$GABA_A$-BZD receptor
74	*Vitis vinifera*	Vitaceae	Fresh fruits	Fresh juice.	Benzodiazepine receptor.
75	*Withania somnifera (Ashwagandha)*	Solanaceae	Roots	Methanolic extract	GABAergic, Endocannabinoid systems

CONCLUSION: Anxiety disorders are often chronic and associated with significant functional impairment and reduced quality of life. A variety of neurotransmitters modulates the neuroanatomical circuits that provide support to fear and anxiety behaviour. Neurotransmitters like GABA, Glutamate, Serotonin, Acetylcholine, Dopamine and Noradrenalin are highly involved in the causation of anxiety disorders. The current review deliberated the medicinal plants that have been reported as an effective anxiolytic agent, with special emphasis is given on the neurotransmitters involved.

TABLE 2: GABA CONTAINING MEDICINAL PLANT INVOLVED IN ANTI-ANXIETY ACTIVITY

Sr. no.	GABA containing medicinal plant involved in anti-anxiety activity
1.	*Abies pindrow Royle*
2.	*Achillea millefolium L*
3.	*Amorphophallus paeoniifolius*
4.	*Angelica archangelica Linn.*
5.	*Annona vepretorum*

6.	*Annona coriacea Mart*
7.	*Areca catechu*. Linn
8.	*Artemisia indica*
9.	*Asparagus racemosus Linn.*
10.	*Bacopa monniera(Brahmi)*
11.	*Brassica oleracea*
12.	*Camellia sinensis*
13.	*Centella asiatica*
14.	*Cissampelos pareira*
15.	*Cocos nucifera*
16.	*Coriandrum sativum*
17.	*Cucurbita moschata*
18.	*Diospyros Montana Roxb. (Tamala)*
19.	*Eucalyptus tereticornis*
20.	*Euphorbia hirta*
21.	*Foeniculum vulgare*
22.	*Humulus lupulus (Hops)*
23.	*Lepidium sativum Linn*
24.	*Lippia citriodora*
25.	*Lippianodi flora* Linn.
26.	*Lotus (Nelumbo nucifera Gaertn.)*
27.	*Melissa officinalis (lemon balm)*
28.	*Mimosa pudica L.*
29.	*Mimusops elengi Linn.*
30.	*Montanoa frutescens*
31.	*Morinda citrifolia Linn. (noni fruit)*
32.	*Nardostachys jatamansi*
33.	*Nauclea latifolia (African Peach)*
34.	*Nigella sativa* Linn.
35.	*Nymphaea alba Linn.*
36.	*Passiflora quadrangularis L.*
37.	*Persicaria hydropiper Linn*
38.	*Piper amalago L.*
39.	*Protium copal L.*
40.	*Punica granatum L. (Pomegranate)*
41.	*Rhodiola rosea*
42.	*Schinus lentiscifolius*
43.	*Scutellaria lateriflora* L. (American skullcap)
44.	*Senna alata*
45.	*Souroubea sympetala*
46.	*Tephrosia purpurea (L) Pers.*
47.	*Terminalia citrina*
48.	*Thymus vulgaris*
49.	*Valeriana officinalis (Valerian)*
50.	*Vitis vinifera*
51.	*Withania somnifera (Ashwagandha)*

TABLE 3: SEROTONIN CONTAINING MEDICINAL PLANT INVOLVED IN ANTI-ANXIETY ACTIVITY

Sr. no.	Serotonin containing medicinal plant involved in anti-anxiety activity
1	*Adenia cissampeloides*
2	*Alafia multiflora*
3	*Allium ascalonicum Linn.*
4	*Angelica archangelica Linn.*
5	*Asparagus racemosus Linn.*
6	*Citrus aurantium L.*
7	*Diospyros montana Roxb. (Tamala)*
8	*Helianthus annuus*
9	*Magnifera indica* L
10	*Matcha*
11	*Mimosa pudica L.*

12	*Morinda citrifolia Linn. (noni fruit)*
13	*Nauclea latifolia(African Peach)*
14	*Nigella sativa* Linn.
15	*Nymphaea alba Linn.*
16	*Pimpinella anisum L.*
17	*Tageteserecta L.*
18	*Tephrosia purpurea (L) Pers.*

TABLE 4: DOPAMINE CONTAINING MEDICINAL PLANT INVOLVED IN ANTI-ANXIETY ACTIVITY

Sr. no.	Dopamine containing medicinal plant involved in anti-anxiety activity
1	*Alafia multiflora*
2	*Alstonia scholaris*
3	*Matcha*
4	Newbouldia leaves
5	*Pimpinella anisum L.*
6	*Tinospora cordifolia*

TABLE 4: MAO CONTAINING MEDICINAL PLANT INVOLVED IN ANTI-ANXIETY ACTIVITY

Sr. no.	MAO containing medicinal plant involved in anti-anxiety activity
1.	*Aegle marmel*
2.	*Alafia multiflora*
3.	*Annona coriacea Mart*
4.	*Aronia melanocarpa* (Black chokeberry)
5.	*Coriandrum sativum*
6.	*Erythrina variegate*
7.	*Garcinia indica Linn.*
8.	*Lotus (Nelumbo nucifera Gaertn.)*
9.	*Nymphaea lotus linn.*
10.	*Psidium guajava Linn.*
11.	*Punica granatum L. (Pomegranate)*
12.	*Rosmarinus officinalis L.*

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REFERENCES:

1. Kaur S and Singh R: Role of different neurotransmitters in anxiety: a systemic review. IJPSR 2017; 8(2): 411-421.
2. Arora I, Behl T, Grover M, Sachdeva M, Pal G and Khan N: Study of anxiolytic and motor co-ordination activity of Cucurbita moschata and its possible mechanism through GABA receptors. Obesity Medicine 2020; 18: 1-6.
3. Singlecare. Anxiety Statistics 2022.
4. Choudhari P, Kanse V, Venkatachalam A and Punam P: Medicinal plants with anxiolytic, antidepressant, anticonvulsant and nootropic effect. World J Pharm Res 2021; 10(4): 787-797.
5. Gołyszny MJ and Obuchowicz E: Medicinal plant materials in the treatment of anxiety disorders: neurobiological aspects. Altern Ther Health Med 2018; 24(5): 1-15
6. Manikkoth S, Damodar S, Sequeira M and Samuel K: Anti-anxiety activity of *Eucalyptus tereticornis* n-hexane extract in wistar albino rats. Int J Basic Clin Pharmacol 2017; 6(3): 577-580.
7. Garakani A, Murrough JW, Freire RC, Thom RP, Larkin K, Buono FD and Losifescu DV: Pharmacotherapy of anxiety disorders: Current and Emerging Treatment Options. Frontiers in Psychiatry 2020; 11(595584): 1-73.
8. Hansa B: Anxiety Disorders. WebMD 2020;
9. Andrea L and Graziano P: Neurosteroid biosynthesis downregulation and changes in $GABA_A$ receptor subunit composition: a biomarker axis in stress-induced cognitive and emotional impairment. The Psychiatric Institute, Department of Psychiatry, University of Illinois at Chicago W. Taylor Str Chicago 1601; 60612.
10. Bruni O, Ferini-Strambi L, Giacomoni E and Pellegrino P: Herbal remedies and their possible effect on the GABAergic system and sleep. Nutrients 2021; 13: 1-13.
11. Strawn JR, Geracioti L, Rajdev N, Clemenza K and Levine A: Pharmacotherapy for generalized anxiety disorder in adults and pediatric patients: an evidence-based treatment review. Expert Opin Pharmacother 2018; 19(10): 1057-1070.
12. Longone P, Michele FD, D'Agati ED, Romeo E, Pasini A and Rupprecht R: Neurosteroids as neuromodulators in the treatment of anxiety disorders. Front. Endocrinol 2011; 2(55): 1-9.
13. Xia QP, Cheng ZY and HeL: The modulatory role of dopamine receptors in brain neuroinflammation. International immuno-pharmacology 2019; 76(105908): 1567-5769.
14. Liu Y, Zhao J and Guo W: Emotional roles of mono-aminergic neurotransmitters in major depressive disorder and anxiety disorders. Front Psychol 2018; 9(2201): 1-8.
15. Fanelli D, Weller G and Liu H: New Serotonin-Norepinephrine Reuptake Inhibitors and Their Anesthetic and Analgesic Considerations. Neurol Int 2021; 13(4): 497-509.
16. Cortese BM and Phan KL: The role of glutamate in anxiety and related disorders. Cns Spectr 2005; 10(10): 820-830.
17. Nasir M, Trujillo D, Levine J, Dwyer JB, Rupp ZW and Bloch MH: Glutamate Systems in DSM-5 Anxiety Disorders: Their Role and a Review of Glutamate and GABA Psychopharmacol 2020; 11: 548505
18. Kumar D and Kumar S: Screening of Antianxiety Activity of *Abiespindrow Royle* Aerial Parts. Indian J Pharm Educ Res 2015; 49(1): 66-70.
19. Ishola I, Olayemi SO, Yemitan O and Akinseye K: Role for monoaminergic systems in the antidepressant and anxiolytic properties of the hydroethanolic leaf extract from *Adenia cissampeloides*. J Basic Clin Physiol Pharmacol 2015; 26(3): 301–312.
20. Halemani D, Geetha M and Shashikala GH: Evaluation of anti-anxiety activity of methanol extract of *Aegle Marmelos* (Bael Fruit Tree) Leaves in Rats. IOSR J Dent Med Sci 2015; 14(9): 1-5.
21. Diniz TC, Oliveira JRG, Maria Medeiros AMB, Silva MGE, Teles RBA, Menezes PDP, Sousa BMH, Frank LA, Araújo AAS, Serafini MR, Guterres SS, Nunes CEP, Salvador MJ and Almeida: JRGS6: Anticonvulsant, sedative, anxiolytic and antidepressant activities of the

essential oil of *Annona vepretorum* in mice: Involvement of GABAergic and serotonergic systems. Biomed Pharmacother 2019; 111(12): 1074–1087.

22. Monteiro AB, Rodrigues CK, Nascimento EP, Sales VS, Delmondes GA, MHN, Oliveira VA, Morais LP, Boligon AA, Barbosa R, da Costa JGM, Menezes IRA, Cícero Felipe FB and Kerntopf M: Anxiolytic and antidepressant-like effects of *Annona coriacea* (Mart.) and caffeic acid in mice. Food Chem. Toxicol 2020; 136(111049): 1-45.
23. Mirko T, Đurđica I, Gordana T, Dijana K, Slavica R, Tamara P and Marija G: Reduction of anxiety-like and depression-like behaviors in rats after one month of drinking *Aroniamelanocarpa* berry juice. Food Funct 2016; 7(7): 1-10.
24. Khan I, Karim N, Ahmad W, Abdelhalim A and Chebib M: GABA-A Receptor Modulation and Anticonvulsant, Anxiolytic, and Antidepressant Activities of Constituents from *Artemisia indica Linn*. Evid.-based Complement. Altern Med 2016; 1215393: 1-12.
25. Dhiman S, Rana M, Monika, Kaur A and Gill NS: Treatment of anxiety disorders: an herbal approach. World J Pharm Res 2021; 10(11): 582-595.
26. Kaur D, Shri R and Kamboj A: Evaluation of Anti-Anxiety Effect of *Brassica oleracea L.* Extracts in Experimental Animals. Pharmacogn. J 2017; 9(5): 638-643.
27. Shastry R, Ullal SD, Karkala S, Rai S and Gadgade A: Anxiolytic activity of aqueous extract of *Camellia sinensis* in rats. Indian J Pharmacol 2016; 48: 681-6.
28. Savage K, Firth J, Stough C and Sarris J: GABA-modulating phytomedicines for anxiety: A systematic review of preclinical and clinical evidence. Phytotherapy Research 2017; 1–16.
29. Lima EB, Caren Sousa NS, Meneses LN, Pereira UF, Matos NC, Freitas RB, Lima NB, Patrocínio MCA, Moreira Leal LK, Viana GS and Vasconcelos SM: Involvement of monoaminergic systems in anxiolytic and antidepressive activities of the standardized extract of *Cocos nucifera L.* JPN J Pharmacol 2016; 71(1): 1-11.
30. Sahoo S and S. Brijesh: Anxiolytic activity of *Coriandrum sativum* seeds aqueous extract on chronic restraint stressed mice and effect on brain neurotransmitters. J. Funct Foods 2020; 68: 1-10.
31. Wand JG, Djiogue S, Gamo FZ, Ngitedem SG and Dieudonné N: Anxiolytic and sedative activities of aqueous leaf extract of *Dichrocephala integrifolia* (Asteraceae) in mice. J Ethnopharmacol 2015; 176(494): 1-20.
32. Tanwar AK, Sharma R and Gupta SK: Methanolic fraction from Tamala (*Diospyros Montana Roxb*.) ameliorates anxiety like behaviour *via* 5-HT_{2A} pathway in rats. Phytomedicine 2022; 2: 1-14.
33. Nouri M, Farajdokht F, TorbatiM, KuchaksarayFR, Hamedyazdan S and Sadigh-Eteghad S: Antidepressant and Anxiolytic Effect of *Echium amoenum* in Restraint Stress Model: The Role of Neuroinflammation in the Prefrontal Cortex and Hippocampus. Iran Red Crescent Med J 2019; 21(10): 1-14.
34. Chu HB, Yue-De T, Yun-Jing L, Bin-Bin C, Bao-Qi R and Ling-Shan Z: Anxiolytic and anti-depressant effects of hydroalcoholic extract from *Erythrina variegata* and its possible mechanism of action. Afr Health Sci 2019; 19(3): 2526-2536.
35. Kumar GA and Sharma A: Comparative antianxiety potential of euphorbia neriifolialinn. Leaves and *Euphorbia Hirta Linn*. Aerial parts. Int J Pharm Sci Res 2019; 10(3): 1433-1438.
36. Dhamija I, ParleM and Kumar S: Antidepressant and anxiolytic effects of *Garcinia indica* fruit rind via monoaminergic pathway. Biotech 2017; 7(131): 1-12.
37. Islam RT, Islam AT, Hossain MM and Mazumder K: Central nervous system activity of the methanol extracts of *Helianthus annuus* seeds in mice model. Int Curr Pharm J 2015; 5(1): 1-4.
38. Bibi MR, Naser Z *Dichrocephalaintegrifolia* Hossein H: Anti-anxiety and hypnotic effects of ethanolic and aqueous extracts of *Lippiacitriodora* leaves and verbascoside in mice. Avicenna J Phytomed 2017; 7(4): 353-365.
39. Yan MZ, Chang Q, ZhongY, Xiao BX, Feng L, Cao FR, Pan RL, Zhang ZS, Liao YH and Liu XM*: Lotus* leaf alkaloid extract displays sedative-hypnotic and anxiolytic effects though $GABA_A$ receptor. J Agric Food Chem 2015; 63(42): 1-33.
40. Ishola IO, Awodele O and Eluogu CO: Potentials of *Mangifera indica* in the treatment of depressive-anxiety disorders: possible mechanisms of action. J Complement Integr Med 2016; 13(3): 1-13.
41. Yuki K, Hari Prasad D, Kengo H, Yuiko N, Akinori H, Takahiro S and Hiroshi K: Anxiolytic activities of *Matcha* tea powder, extracts, and fractions in mice: Contribution of dopamine D1 receptor- and serotonin 5-HT_{1A} receptor mediated mechanism. J Funct Foods 2019; 59: 301–308.
42. Patro G, Kumar BS and Kumar MB: Effects of *Mimosa pudica L*. leaves extract on anxiety, depression and memory. Avicenna J Phytomed 2016; 6(6): 696-710.
43. NarasingamM, Vijeepallam K, Mohamed Z and Pandy V: Anxiolytic- and antidepressant-like activities of a methanolic extract of *Morinda citrifolia Linn.* (noni) fruit in mice: Involvement of benzodiazepine $GABA_A$ergic, serotonergic and adrenergic systems. Biomed. Pharmacother 2017; 96: 1-9.
44. Sakina R, Hemanth KK, Venuprasad MP, Narayanappa A, Farhath K and Krishna C: Anxiolytic actions of *Nardostachys jatamansi* via GABA benzodiazepine channel complex mechanism and its biodistribution studies. Metab Brain Dis 2018; 1-17.
45. Murtala A and Akindele AJ: Anxiolytic- and antidepressant-like activities of hydroethanol leaf extract of *Newbouldia laevis* (P.Beauv.) Seem. (Bignoniaceae) in mice. J Ethnopharmacol 2019; 249: 1-29.
46. Islam MH, Ahmad IZ and Salman MT: Neuroprotective effects of *Nigella sativa* extracts during germination on central nervous system. Phcog Mag 2015; 11: 182-9.
47. James OF, Keasling A, Zjawiony JK, Costa EA and Adeleke AA: Evaluation of Anxiolytic and Antidepressant-like Activity of Aqueous Leaf Extract of *Nymphaea lotus Linn*. in Mice. Iran J Pharm Res 2018; 17(2): 613-626.
48. Andressa CG, Geison MC, Leonardo C, Freddy AR, Flávio HR, Thereza CM and Eloir PS: Involvement of GABAergic pathway in the sedative activity of apigenin, the main flavonoid from *Passiflora quadrangularis* pericarp. Revista Brasileira de Farmacognosia 2015; 25: 158–163.
49. Mahmud SA and Shah M: Evaluation of sedative and anxiolytic activities of methanol extract of leaves of *Persicaria hydropiper* in mice. Clin Phytoscience 2017; 3(20): 1-12.
50. Es-safi I, Mechchate H, Amaghnouje A, Elbouzidi A, Bouhrim M, Bencheikh N, Hano C and Bousta D: Assessment of Antidepressant-like, Anxiolytic Effects and Impact on Memory of *Pimpinella anisum L*. Total Extract on Swiss Albino Mice. Plants 2021; 10(1573): 1-16.

51. Mullally M, Cayer C, Muhammad A, Walshe-Roussel B, Ahmed F, Sanchez-Vindas PE, Rojas MO, Merali Z, Cal V, Durst T, Trudeau VL and Arnason JT: Anxiolytic activity and active principles of *Piper amalago* (Piperaceae), a medicinal plant used by the Q'eqchi' Maya to treat susto, a culture-bound illness. J Ethnopharmacol 2016; 185: 1-29.
52. Merali Z, Cayer C, Kent P, Liu R, Cal V, Harris CS and Arnason JT: Sacred Maya incense, copal (*Protium copal* - Burseraceae), has antianxiety effects in animal models. J. Ethnopharmacol 2018; 216: 63-70.
53. Biswas S, Mondol D, Jodder P, Sana S, Saleh MA, Tarafdar AK and Islam F: Evaluation of neurobehavioral activities of ethanolic extract of *Psidium guajava Linn.* leaves in mice model. Future JPS 2021; 7(36): 1-12.
54. Kulkarni S, Bathe R and Javalgikar A: Evaluation of *Punicagranatum* fruit juice for anti-anxiety activity. Int J Res Anal Rev 2016; 07(9): 452-455.
55. Abadi MA, Mortazavi M, Kalani N, Marzouni HZ, Kooti W and Ali-Akbari S: Effect of Hydroalcoholic Extract of *Rosmarinus officinalis L*. Leaf on Anxiety in Mice. Journal of J Evid Based Complem Altern Med 2016; 21(4): 85-90.
56. Andrade CV, Matera S, Bayley M, Colareda G, Ruiz ME, Prieto J, Retta D, Baren CV, Consolini AE and Ragone MI: Antispasmodic, antidepressant and anxiolytic effects of extracts from *Schinus lentiscifolius Marchand* leaves. J Tradit Complement Med 2022; 12: 141-151.
57. Arasan E, Sheikh AR, Paneerpandiyan PK and Mageswaran RK: Anti-anxiety activity of hydro alcoholic extract of *Scoparia dulcis Linn*. assessed using different experimental anxiety models in rodents. Int J Pharm Res 2015; 5(3): 62-37.
58. Pamulaparthi A, Prathap VR, Banala M and Nanna RS: Experimental evaluation of antidepressant and antianxiety activities of aqueous leaf extracts of *Senna alata* (L.) roxb. using *in-vitro* animal models. Int J Curr Pharm Res 2016; 8(4): 60-63.
59. Pérez-Ortega G, Angeles-López GE, Argueta A and González-Trujano ME: Preclinical evidence of the anxiolytic and sedative-like activities of *Tagetes erecta L.* reinforces its ethnobotanical approach. Biomed Pharmacother 2017; 93: 383–390.
60. Das N, Goshwami D, Hasan MS, Al Mahmud Z, Sheikh ZR and Sultan MZ: Evaluation of antinociceptive, anti-inflammatory and anxiolytic activities of methanolic extract of *Terminalia citrina* leaves. Asian Pac J Trop Dis 2015; 5(1): 137-141.
61. Komaki A, Hoseini F, Shahidi S and Baharlouei N: Study of the effect of extract of *Thymusvulgaris* on anxiety in male rats. J. Tradit Complement. Med 2016; 6: 257-261.
62. Mishra R, Manchanda S, Gupta M, Kaur T, Saini V and Sharma A: *Tinospora cordifolia* ameliorates anxiety-like behavior and improves cognitive functions in acute sleep deprived rats. Sci Rep 2016; 6: 1-15.
63. Aslam M and Sultana N: Evaluation of anxiolytic-like activity of *Vitis vinifera* juice in mice. Avicenna J Phytomed 2016; 6(3): 344-350.

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