A SYSTEMATIC REVIEW ON ANXIETY AND THEIR TREATMENT WITH HERBAL AND NON-HERBAL DRUG

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Abstract

Anxiety is a common emotional response characterized by feelings of worry, dread, and unease. It can manifest physically as sweating, agitation, and a rapid heartbeat. Anxiety is often triggered by stress, past trauma, or certain medical conditions. A mental illness like anxiety can drastically change a person's way of life and make it very difficult for them to afford therapy. Your body may begin to perspire, you may feel agitated and anxious, and your heart rate may increase. The various types of anxiety in this article with their systems are "Obsessive- compulsive disorder (OCD), Post-traumatic stress disorder (PTSD), Social phobia or social anxiety disorder (SAD), Specific phobia (SP) and Generalized anxiety disorders (GAD)". The 14% populations are experiencing and 2.5% children also in 1 year. The amygdala is a part of the brain that is essential for processing and controlling fear and anxiety. It takes in sensory information from the environment and communicates with other brain regions to start the "fight or flight" response. The treatment for antianxiety drug including Azapirones, Benzo-diazepines, Monoamine Oxidase inhibitor. In this article used the 32 herbal plant with part of plant treatment, types of extract, dose and various animal model used with significance of result

Keyword: Anxiety, Obsessive compulsive disorder, Drug Treatment, Herbal treatment, Social phobia.

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INTRODUCTION

Anxiety is a natural human response to stress or danger, and it has likely existed throughout human history. However, the concept of anxiety as a distinct disorder is a relatively recent development. In ancient times, anxiety was often attributed to supernatural or spiritual causes. For example, in ancient Greece, anxiety was thought to be caused by an imbalance of bodily fluids or by the displeasure of the gods. In ancient China, anxiety was associated with a disruption in the flow of qi, or life force energy. History is a detailed narrative of humankind's past. It offers a way to assess and evaluate the development of human affairs and historical events, putting them into context. Through historical awareness and the present is more fully disclosed, judged, and understood, and it can be more successfully interpreted and described given how it has influenced and molded the past (Crocq 2015). Man is not only able to live in the present more successfully as a result of this improved understanding of the past via assessment and interpretation of the present, but he is also more equipped to forecast the better future and to predict. As a result, history is a product of the past and the present, and the future will be a product of both as impacted by both past and present circumstances and situations (Kiel and Kalomiris 2019). The emotion of anxiety predates the development of man(Janszky et al. 2010). While anxiety manifests itself in different ways for children, adolescents, and adults, it can also be deduced from other people's physiological and

Types of symptoms of anxiety disorder

psychological reactions in some cases. You could feel more energized or more focused as a result of the worry. The symptoms can obstruct daily tasks including job performances, homework, and interpersonal connections. Even in reaction to the same stimuli, anxiety might vary in frequency and intensity amongst individuals. It is a widespread feeling of unease or foreboding. There are numerous reasons to worry. Our health, social interactions, tests, occupations, and environmental conditions are just a few examples of potential worry-causing factors. Being a little concerned about these areas of life is natural and even appropriate. When anxiety encourages us to study for exams or prompts us to seek out routine medical examinations, it serves a useful purpose (Kiel and Kalomiris 2019). Changes in your lifestyle might successfully reduce some of the stress and worry you might experience daily. Among psychiatric conditions, anxiety disorders are among the most prevalent. A generalized, uncomfortable, hazy sense of unease is what defines anxiety. Autonomic symptoms including sweating, chest stiffness and palpitations, slight stomach discomfort are frequently present along with it. The main family of substances used to treat anxiety is called benzodiazepines, and these medications continue to be the most often prescribed ones Anxiety is connected yet distinct. When you are anxious about a specific event, such as an approaching test, presentation, wedding, or other significant shift in your life, stress is a common and appropriate response (Baxter et al. 2014).

Types of Disorder	Symptoms	Reference
Obsessive-compulsive disorder (OCD)	Most consistent obsessions are examinations about spoiling, kept washing, addressing, forcefulness, relief pursuing, extreme sexual contemplations, checking/counting, and asking for are the most generally perceived motivations	(Stein et al. 2020)

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Post-traumatic stress disorder (PTSD)	Striking re-experiencing of the damage: intrusive memories, awful dreams, flashbacks	(Bisson et al. 2015)
	Avoiding of damage related enhancements: effortful undertakings to keep up a vital separation from spots, people, or memory of the damage	
	Eager desensitizing: inconvenience in experiencing close enthusiastic relationship with different people	
	Hyper energy: hypervigilance, irritability, a dozing issue [9] [10].	
Social phobia or social anxiety disorder (SAD)	dread of numerous social circumstances like eating, composing, talking out in the open non-summed up social nervousness issue: open talking fears	(Id and Ungar 2020)
Specific phobia(SP)	Persevering fear due to: Animals: bugs, snakes, canines, et cetera.	(Miloyan, Sciences, and Hopkins 2020)
	Consistent living space: obscurity, storms, statures, water, et cetera. Situation: flying, encased spaces, lifts, et cetera.	
	Blood/implantation/harm: seeing blood, getting shots or mixtures, et cetera.	
	Irregular: smothering, uproarious sounds, costumed characters, et cetera	
Generalized anxiety disorders(GAD)	Instability, exhaustion, obsession inconvenience, crabbiness, muscle strain and rest disturbance	(Newman et al. 2016)

EPIDEMIOLOGY

In fact, one of the most prevalent categories of mental illness in Europe is anxiety disorders. According to a study by the European College of Neuropsychopharmacology, anxiety disorders—which affect 14% of the population in Europe—are the most common mental illnesses. The study also emphasises that the most prevalent mental health diseases are anxiety disorders in the European Union, Switzerland, Iceland, and Norway, which have a combined population of over 500 million people. The field of psychology continued to evolve in the 20th century, and anxiety disorders became better understood and more widely recognized. Sigmund Freud's psychoanalytic theory posited that anxiety was the result of repressed, unconscious conflicts. Other psychological approaches, such as behaviorism and cognitive-behavioral therapy, also provided new insights into the nature of anxiety and how it could be treated. Anxiety disorders can have a significant impact on a person's daily life and can lead to a range of physical and psychological symptoms, making it important to seek appropriate treatment and support. With a 14 percent prevalence over a 12-month period and 61.5 million people afflicted, they are more prevalent than any other type of mental disorder among older people in Europe14 to 65. Two to three times as many women are impacted as typically as males. Disorders of anxiety may start in childhood or adolescence. For specific phobias and social phobias, this is

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especially true. A youngster can develop selective mutism as early as their third year. Most kids experience a temporary a normal aversion to strangers, this frequently begins at about eight or nine months of age (Bandelow and Michaelis 2015). 2-3% of kids experience severe separation anxiety throughout preschool or school. Treatment is necessary if separation anxiety hinders a child's ability to develop normally, such as by preventing them from participating in crucial social interactions. The World Health Organisation (WHO) reports that among the chronic illnesses that significantly impacted patients' lives in 2015 were anxiety disorders. According to the WHO Global Burden of Disease Study, anxiety disorders rank as the sixth most common global cause of "years lived with disability" (YLD) and the fourth in highly developed nations. The study highlighted that anxiety disorders are associated with a substantial burden on individuals, The most prevalent type of anxiety illness is specific phobias(Miloyan, Sciences, and Hopkins 2020). Millions of people worldwide suffer from anxiety disorders, which are among the most prevalent mental health diseases today. Treatments range from therapy to medication, and ongoing research continues to deepen our understanding of this complex and often debilitating condition.

Anxiety can be treated with both herbal and non-herbal therapies. Here are some examples:

Non-Herbal Treatments:

1. Psychotherapy - talking with a trained mental health professional can help to identify and address the root causes of anxiety, as well as develop coping strategies.

2. Medication - A doctor may recommend a variety of drugs to treat anxiety symptoms, including beta-blockers, benzodiazepines, and selective serotonin reuptake inhibitors (SSRIs).

3. Cognitive-behavioral therapy (CBT) - This type of therapy aids in identifying and changing the unfavourable attitudes and conduct that fuel worry.

4. Relaxation practises can assist to lessen the symptoms of anxiety. Examples include yoga, meditation, deep breathing, and progressive muscle relaxation.

Herbal Treatments:

1. Kava - Kava, which is made from the root of the kava plant, has long been used to ease anxiety and encourage relaxation.

2. Passionflower - this herb has been used for centuries as a natural treatment for anxiety and insomnia.

3. Valerian root - valerian root has been shown to have sedative effects and is often used to promote relaxation and improve sleep.

4. Chamomile - chamomile is known for its calming properties and has been used to reduce anxiety and promote sleep.

While herbal medicines can be helpful in treating anxiety, it's vital to keep in mind that they should always be used with a doctor's supervision because they may have unwanted side effects or interfere with other prescriptions.

PATHOPHYSIOLOGY OF ANXIETY

Anxiety has a complicated pathophysiology that is influenced by a number of physiological and psychological components. In general, it is believed that a mix of genetic, environmental, and developmental variables contribute to anxiety disorders.

Dysregulation of the amygdala, a tiny brain region that is crucial in the processing of emotional information, is a significant factor in anxiety. The amygdala may become excessively sensitive or active in people with anxiety disorders,

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which causes heightened emotional reactions and higher levels of anxiety.

The hypothalamic-pituitary-adrenal (HPA) axis' dysfunction is a key component in the pathophysiology of anxiety. The hypothalamus, pituitary, and adrenal glands are all part of the intricate HPA axis system, which controls how the body reacts to stress. The HPA axis may become overactive in people with anxiety disorders, which would result in higher amounts of stress hormones like cortisol.

Imbalances in neurotransmitters may also contribute to anxiety disorders. "Serotonin, norepinephrine, and gamma-aminobutyric acid (GABA) imbalances in particular have been linked to the emergence of anxiety. In addition to these biological aspects, environmental and psychological factors can also influence how anxiety develops. An individual's chance of having anxiety disorders may be boosted by traumatic events, ongoing stress, and adverse life circumstances. Overall, the pathophysiology of anxiety is intricate and influenced by a variety of genetic, environmental, and developmental variables as well as physiological system abnormalities. A deeper comprehension of these underlying processes might guide the creation of anxiety disorder therapies that are more potent." (Bandelow, Michaelis, and Wedekind, 2017).

Treatment of anxiety Disorder

S. No	Types	Name of Drugs	Mechanism of action	Uses	Reference
1.	Azapirones	Buspirone	Serotonin agonist	GAD	(Bandelow, Michaelis, and Wedekind 2017)
2.	Benzo-diazepines	Lorazepam Flurazepam Clonazepam Diazepam Alprazolam	GABA Agonist	GAD SAD PD	(Melaragno 2021)
3.	Monoamine Oxidase inhibitors (MAOIs)	Selegilene Isocarboxid Phenelzine Tranylcypromine	Prevent breakdown of serotonin	PD SAD, PTSD	(Mangolini et al. 2019)
4.	Selective Serotonin reuptake inhibitors (SSRIs)	Citalopram Fluvoxamine Paroxetine Fluoxetine Sertraline	Serotonin concentration affected	PD OCD, SAD GAD	(Stein 2021)

"GAD = Generalized anxiety disorder OCD= obsessive compulsive disorder PD= Panic disorder PTSD= Post traumatic stress disorder SAD= Social anxiety disorder"

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Herbal treatment of anxiety

Plant Name	Plant Part	Plant Extracts	Dose	Model	Result	Reference
Coriandrum sativum (Linn.) Family: Apiaceae	Fruits	Hydroalcoholic Extract	50mg/kg 100/kg 200mg/kg	Open field test, light/dark model, elevated plus maze, and social interaction	At dosages of 100 mg/kg and 200 mg/kg, *C. sativum* had anti-anxiety effects that were very similar to those of anti-anxiety prescription medications.	(Mahendra and Bisht 2011)
Murraya koenigii Family: Rutaceae	Leaf	Aqueous extract	200mg/kg 300mg/kg 400mg/kg	EPM Measurement of spontaneous locomotor activity	M. koenigii produced anti-anxiety effects at doses of 300 and 400mg/kg that were nearly identical to those of a conventional medication.	(S. Sharma et al. 2017)
Achillea millefoliun Family: Asteraceae	leaf	Petroleum ether	100mg/kg	Open maze test	A. millefolium at 100mg/kg give positive result reference due to standard drug	(Life Science Journal 2013)
Actaea spicata Linn. Family: Ranunculaceae	Root	Methanolic, Petroleum ether, Chlorofor	100mg/kg 200mg/kg,	EPM	In mice, only methanol extract, at a dose of 100	(Madaan and Sharma 2016)

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		m and Aqueous extract	400mg/kg		mg/kg, significantly reduced anxiety compared to both control and conventional treatments.	
Allium ascalonicum Linn. Family: Liliaceae	Aerial parts	Hydroethanolic extract	50mg/kg 100mg/kg 200mg/kg 400mg/kg	"Hole-board test, elevated plus maze, Open-field, Light/dark test, social interaction test."	At 100 mg/kg, anti-anxiety benefits were primarily seen.	(Akindele, Sanni, and Edeh 2012)
Amorphophallus paeoniifolius Family: Araceae	Tuber	Petroleum Ether	100mg/kg 150mg/kg 200mg/kg	Elevated Plus maze, open field test, light/dark test	Most anti-anxiety effects were seen at a 200 mg/kg dosage.	(Saha, Bose, and Banerjee 2013)
Angelica archangelica Linn Family: Apiaceae	Whole Plant	Methanolic	200mg/kg 400mg/kg	EPM	At a dose of 400 mg/kg, the whole plant and leaves had the greatest anxiolytic action, followed by the root and fruit and stem.	(D. Kumar and Bhat 2011)
Argyreia Speciosa Family: Convolvulaceae	Root	Hydroalcoholic	100mg/kg 200mg/kg	EPM Open field test Forced	The plant shows the anti-anxiety activity as	(Galani and Patel 2011)

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			500mg/kg	swimming test Tail suspension test	the dose of 200mg/kg and 500mg/kg	
Calluna vulgaris (L.) Hull Family: Ericaceae	Arial Part	Hydroethanolic	100mg/kg	EPM	The plant shows anxiety activity with the respected dose on 100mg/kg	(Szewczyk, Rka, and Polakowska 2018)
Citrus paradisi Family: Rutaceae	Leaf	Petroleum ether Chloroform Methanol water	50mg/kg 100mg/kg 200mg/kg 400mg/kg	EPM	"Employing an elevated plus maze model and methanolic extracts at a concentration of 100 mg/kg body weight. The outcomes clearly support the use of Citrus paradisi leaf extracts as an anxiety therapy."	(Modules 2017)
Cynodon dactylon Family: Poaceae	Leaf, Flower, Stem	aqueous extract	200mg/kg 400mg/kg	EPM Light/dark model	When compared to a conventional medication, C. dactylon demonstrated anti-anxiety activity at doses of 200 and 400mg/kg.	
Datura stramonium Family: Solanaceae	Leaf	Ethanolic extract	100mg/kg 200mg/kg	EPM	The outcome demonstrated that Datura stramonium leaf	(Tiwari et al. 2018)

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					ethanolic extract (100 and 200 mg/kg) at the response in accordance with standard drug	
Equisetum arvense Linn. Family: Equisetaceae	Stem	Petroleum ether Chloroform Ethanol Aqueous	25mg/kg 50mg/kg 100mg/kg	EPM	The ethanolic extract of E. arvense showed the anti-anxiety on 50mg/kg and 100mg/kg dose.	(Singh et al. 2011)
Echium italicum L. Family: Boraginaceae	Aerial Parts	Aqueous extract Ethanolic Extract	300mg/kg 600mg/kg 1200mg/kg 2100mg/kg	Open-field test EPM	"The ethanolic and aqueous extracts of E. italicum, at doses of 1.2 and 2.1 g/kg, increased the percentage of time-spent and the percentage of arm entries in the open arms of the EPM and decreased the percentage of time-spent in the closed arms of the EPM."	(Hosseinzadeh, Shahandeh, and Shahsavand 2012)
Eucalyptus tereticornis	Leaf	n-hexane	100mg/kg	EPM Light/dar	The anti-anxiety activity of *E.*	(Manikkoth et al. 2017)

				k model	*terteticornis* can be due to its effect on brain neurotransmitters	
Ficus hispida Family: Moraceae	Leaf	Methanol	200mg/kg 400mg/kg	EPM Zero maze	Show the anti-anxiety effect on the dose of 400mg/kg.	(Dhanasekaran and Rahman 2012)
Gelsemium sempervirens Family: Gelsemiaceae	Root	Petroleum ether Chloroform Methanol	50mg/kg 100mg/kg 150mg/kg 200mg/kg	EPM	The methanolic extract show the anti-anxiety effect on 150mg/kg and 200mg/kg dose.	(Dutt, Dhar, and Sharma 2010)
Gloriosa superba Linn. Family: Colchicaceae	Seeds	Petroleum ether Chloroform Ethanol	300mg/kg	EPM	In the current investigation, Gloriosa superba Linn. ethanolic extract showed good anti-anxiety effect at a dose of 300 mg/kg.	(Sundaraganapathy et al. 2013)
Hibiscus rosa sinensis Family: Malvaceae	Root	Ethanol	100mg/kg 500mg/kg	EPM Hole-board test Light/dark test	The findings suggest that inhibition of ionotropic GABA receptors underlies the potential calming effects of the ethanol extract of Hibiscus	(Begum and Younus 2018)

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					rosa sinensis in mice.	
Actaea acuminata Wall Family: Ranunculaceae	Root	Petroleum ether Methanol	50mg/kg 100mg/kg 200mg/kg	EPM Light/dark Model	Methanolic extract showed the anti- anxiety activity respected dose on 100mg/kg and 200mg/kg	(Akindele, Sanni, and Edeh 2012)
Murraya paniculata Family: Rutaceae	Leaf	Petroleum ether Chloroform Ethanol Aqueous	100mg/kg 200mg/kg 400mg/kg	EPM	Only Chloroform extract show the anxiolytic activity on 400mg/kg dose	(P. Sharma et al. 2017)
Nerium oleander linn Family: Apocynaceae	flower	Petroleum ether, chloroform, ethyl acetate, and methanol extracts	100mg/kg 200mg/kg 400mg/kg	EPM	Only Ethyl acetate show the anxiolytic activity on 100mg/kg dose	(Kg and Gd 2011)
Ocimum sanctum Family: Lamiaceae	leaf	Ethanol	25mg/kg 50mg/kg 100mg/kg	EPM Light/dark model	Only 100mg/kg dose show anxiolytic activity	(Chatterjee et al. 2011)
Onosma bracteatum Family: Boraginaceae	Whole Plant	Aqueous ethanolic extract	50mg/kg 100mg/kg 200mg/kg	EPM	Only 200mg/kg dose show anxiolytic activity	(Asif et al. 2019)
Passiflora incarnata Linneaus Family:	Aerial Part	Petroleum Ether Chloroform	400mg/kg	EPM	Give the anxiolytic activity of chloroform and	(Dhawan, Kumar, and Sharma 2001)

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Passifloraceae		Methanol Aqueous			methanol extract	
Scoparia dulcis Linn. Family: Plantaginaceae	Whole plant	Ethanolic	100mg/kg 200mg/kg	Open - field test EPM EZM	Give the anxiolytic activity on 100mg/kg and 200mg/kg dose	(Elayaraja, Rahaman, and Kumar 2015)
Stachys tibetica Vatke Family: Lamiaceae	Whole Plant	Methanolic	200mg/kg 400mg/kg	EPM	Give the anxiolytic activity on 200mg/kg and 400mg/kg as per standard drug	(D. Kumar et al. 2013)
Terminalia chebula Family: Combretaceae	fruits	Alcohol	25mg/kg 50mg/kg 100mg/kg	EPM	100mg/kg dose give anxiolytic activity	(Chandrasekhar and Kumar 2018)
Turnera aphrodisiaca Ward Family: Passifloraceae	Whole plants	Ethanolic	50mg/kg 75mg/kg 100mg/kg 125mg/kg 150mg/kg	EPM	Give the anxiolytic activity on the 125mg/kg dose	(S. Kumar and Sharma 2005)
Urtica urens Family: Urticaceae	Arial Part	Methanolic Extract	100mg/kg 200mg/kg 400mg/kg	Light/dark model Hole board test	Give the anxiolytic effect of only 200mg/kg dose as per reference to standard drug	(Doukkali et al. 2015)

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FUTURE PRESPECTIVE

The information offered in this review study offers insightful information about the biology of anxiety and the state of both pharmacological and non-pharmacological treatments at the time of writing. Young researchers may use the material provided to direct their study into the creation of novel therapy strategies for anxiety disorders.

The review study also emphasizes the possibility for using medicinal plants as a source for anti-anxiety drugs, which may have consequences for the creation of new drugs in the future. The creation of more potent and secure phytomedicines for the treatment of anxiety and other mental diseases could result from additional study in this field, including the standardization of extracts and plant isolates.

The need for proper legislation and regulatory authorities is also highlighted, emphasizing the importance of ensuring that any new treatments for anxiety disorders are safe and effective. This underscores the need for ongoing research in this field, as well as collaboration between researchers, healthcare providers, and regulatory agencies to ensure that patients receive the best possible care.

Overall, this review paper provides a valuable perspective on the current state of research and treatment for anxiety disorders, and could serve as a starting point for future research and development in this field.

Conclusion

A review paper that may be used by young researchers to assess anxiolytic medicines in this field sheds insight on the various components of the animal model of anxiety illness. In therapeutic practice, anxiety has not yet shown results that are favorable. There are still certain first-line and new pharmaceuticals that reportedly belong to the existing therapeutic classifications that are linked to negative effects. There were many chances for the creation of anti-anxiety medications thanks to medicinal plants. The increased quality of herbal medications has increased the acceptance of using them to treat certain mental illnesses. The development of anti-anxiety and depression phytomedicine still requires standardization of extracts and plant isolates, adequate scientific evidence on safety and efficacy, protection of the diversity of medicinal plants, and proper legislation and regulatory authorities.

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