

## A Systematic Review on Herbs Exhibiting Anxiolytic Activity

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### ABSTRACT

Mental disorders are very common of which anxiety disorder is the most prevalent one affecting approximately 10- 30% of the general population. Anxiety is a maladaptive emotional state causing fear, worry and excessive stress characterized by physiological arousal, unpleasant tension and feeling of apprehension. DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders) criteria classifies anxiety as panic disorder, agoraphobia, social phobias, obsessive compulsive disorder, post traumatic stress disorder, generalized anxiety disorder. This review of literature aims to discuss the anxiolytic potential of some 40 medicinal plants with their botanical name, family, chemical constituents and the anxiolytic properties of those plants had been tested in the animal models. Most of these plants have been found to act through modulation of serotonin, GABA (gamma amino butyric acid), noradrenaline (NA) neurotransmitters. Nowadays herbal medicines are preferred over the allopathic medications because of its adverse effects. It is hoped that an more efficient and effective screening of herbal medicines will help to unveil newer anxiolytic drugs of plant origin with fewer side effects. The review has focused on some of the medicinal plants exhibiting anxiolytic activity. However use of specific medicinal plants for management of specific subtypes of anxiety disorder is yet to be substantiated.

**Keywords:** Anxiety, anxiolytics, medicinal plants, less side effects

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### INTRODUCTION

Anxiety is an emotional state caused by the perception of real or perceived danger that threatens the security of an individual [1]. Anxiety is characterized by psychologic symptoms such as tension, fear, apprehension, lack of concentration as well as somatic symptoms such as tachycardia, tremor, sweating, GIT distress [2].

#### EPIDEMIOLOGY:

Anxiety disorders affect 16.6% of population worldwide [3]. It is found that the prevalence of all anxiety disorders using Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria is 14.4% (boys = 4.8%, girls = 9.6%) [4]. It is found that girls are more affected than the boys.

The lifetime prevalence rate of generalized anxiety disorder (GAD) is 4.1 - 6.6%, post-traumatic stress disorder is 7- 8% and obsessive compulsive disorder (OCD) ranges from 1.2 - 3.3%. The life time prevalence of panic attacks is around 7-9%.

#### THE DMS-IV-TR CLASSIFIES ANXIETY AS FOLLOWS:

- Panic disorder  
Panic attacks have intense autonomic arousal such as lightheadedness, a racing heart, difficulty breathing, chest discomfort, sweating, weakness, trembling, abdominal discomfort and hot flushes.
- Agoraphobia

Agoraphobic individuals will always stay at home and will avoid standing in line or in a crowd. Severe agoraphobia leads to individuals being house bound.

- Generalized anxiety disorder  
Major symptoms of GAD include restlessness, muscle tension, irritability, fatigue, difficulty concentration and difficulty in sleeping.
- Obsessive compulsive disorder  
People suffering from OCD tend to have intrusive thoughts that cause anxiety (obsession) and perform repetitive actions (compulsion).
- Posttraumatic stress disorder (PTSD)  
Exposure to a terrifying or life threatening trauma may produce post-traumatic Stress disorder.

#### **PATHOPHYSIOLOGY:**

Stress is an important factor causing anxiety disorder. The stress related anxiety disorder is produced by persistent changes in the stress responsive CNS -CRF system. Cell bodies containing CRF are highly found in medial parvocellular region of hypothalamic paraventricular nucleus (PVN). The parvocellular region of hypothalamic PVN is considered as the neuroendocrine stress response system. The stress response in humans involves a series of hormonal events by the activation of hypothalamus pituitary adrenal axis which leads to the increased release of cortisol and adrenaline (stress hormones). These stress hormones reacts with body and brain in various complicated mechanism producing anxiety disorders (a maladaptive emotional state causing fear, worry and excessive stress characterized by physiological arousal, unpleasant tension and feeling of apprehension).

Pathophysiology of anxiety is associated with multiple regions of the brain such as

- (a) Amygdala, a temporal lobe structure which assess the fearful stimuli and produces responses to fear.

- (b) Locus ceruleus a noradrenaline (NA) containing site located in the brain stem with widespread projections to areas responsible for producing fear responses (vagus, lateral and paraventricular hypothalamus).

- (c) Hippocampus region.

- (d) The hypothalamus is the principle area for generating neuroendocrine and autonomic responses to fear.

The neurochemical theory of anxiety includes the abnormal functioning of several neurotransmitters such as NA, gamma aminobutyric acid (GABA) and serotonin (5-HT). The autonomic nervous system of anxious patient is hypersensitive and over reacts to various stimuli such as threat or fear, in such condition the locus ceruleus acts as an alarm center causing NA release and stimulate the sympathetic and parasympathetic nervous system producing anxiety symptoms. 5-HT is primarily an inhibitory neurotransmitter and the abnormalities in its function through release and uptake at the presynaptic autoreceptors (5-HT<sub>1A</sub> / 1D), the serotonin reuptake transporter site or effect of 5-HT at the postsynaptic receptors plays a major role in the development of anxiety. The greater 5-HT activity reduces the release of NA from locus ceruleus, inhibits the defense response and reduces hypothalamic release of corticotropin-releasing factor (CRF). The lesser 5-HT activity may lead to dysregulation of other neurotransmitters. GABA the major inhibitory neurotransmitter in the central nervous system (CNS) has a strong regulatory or inhibitory role on the 5-HT, NA or dopamine [6].

#### **HERBAL REMEDIES TO TREAT ANXIETY DISORDERS:**

Ayurveda, the Indian traditional system of medicine uses herbs and polyherbal preparation to treat various neuropsychiatric disorders [2]. Traditional medicines are emerging as an evidence based medicine and they are more popular because of minimal side effects. A number of drugs from

natural source either in the form of extracts or as active principles is isolated or evaluated for anxiolytic properties [5]. The polyherbal

formulations currently used for anxiety disorders are OCTA, Mentat (BR-16A), Geriforte, Euphytose.

**Table 1: Medicinal Plants Exhibiting Anxiolytic Activity**

SL. NO	COMMON NAME	BIOLOGICAL NAME & FAMILY	CHEMICAL CONSTITUENT	SCREENING METHODS	REFERENCE
1.	Fools parsley	<i>Aethusa cynapium</i> (Apiaceae)	Unsaturated fatty acid	Elevated plus maze (EPM)	[7]
2.	Sage leaved alangium	<i>Alangium ssalvifolium</i> (Alangiaceae)	Flavonoids and tannins	EPM	[8]
3.	Shallot	<i>Allium ascalonium</i> (Liliaceae)	Alkaloids, flavonoids and tannins	EPM, Holeboard apparatus, Open field test	[9]
4.	Purple joyweed	<i>Alternanthera brasiliiana</i> (Amaranthaceae)	Alkaloids, steroids and triterpenes	EPM, Hole board apparatus, Light dark model	[10]
5.	Brahmi	<i>Bacopa monniera</i> (Scrophulariaceae)	Bacosides A and B, triterpinoid, saponins	EPM, Hole board apparatus, Light dark model	[11]
6.	Daisy	<i>Bellis perennis</i> (Asteraceae)	Alkaloids, phenolic compounds and flavonoids	Open field test	[12]
7.	Wax gourd	<i>Benincasa hispida</i> (Cucurbitaceae)	Triterpinoids, flavonoids, carotenes, uronic acid	Hole board apparatus	[13]
8.	Hog weed	<i>Boerhaavia diffusa</i> (Nyctaginaceae)	Alkaloids(punarnavine), Boeravinones A-F, Flavonoids	Barbituric narcosis in swiss albino mice	[14]
9.	Short pod	<i>Byrsocarpus coccineus</i> (Connaraceae)	Flavonoids, alkaloids and terpenoids	EPM, Hole board apparatus	[15]
10.	Deodar cedar	<i>Cedrus deodara</i> (Pinaceae)	Alkaloids and tannins	EPM, Light dark model	[16]
11.	Gotu kola	<i>Centella asiatica</i> (Apiaceae)	Asiaticoside (triterpinoid)	EPM, Open field test	[17]
12.	Wood calamint	<i>Clinopodium mexicanum</i> (Lamiaceae)	Neoponricin	Open field test, Hole board apparatus	[18]
13.	May blossom	<i>Crataegus oxycantha</i> (Rosaceae)	Flavonoids, triterpenes	EPM, Light dark model	[19]
14.	Lemon grass	<i>Cymbopogon citratus</i> (Poaceae)	Alkaloids, tannins	EPM, Open field test, stress induced hyperthermia	[20]
15.	Medhshingi	<i>Dolichandrone falcata</i> (Bignoniaceae)	Flavonoids, phenolic compounds	EPM, Marble burying test	[21]
16.	Red feathers	<i>Echium amoenum</i> (Boraginaceae)	Flavonoids	EPM	[22]
17.	Pangra	<i>Erythrina suberosa</i> ( fabaceae)	Erysodine, erysothrine	EPM, Light dark model	[23]

18.	Fennel	<i>Foeniculum vulgare</i> (Umbelliferae)	Essential oil	EPM, Staircase model, open field test	[24]
19.	Indian fumitory	<i>Fumaria indica</i> (Fumariaceae)	Protopine	EPM, Open field test, novelty induced feeding test	[25]
20.	Sweet tea vine	<i>Gynostemma pentaphyllum</i> (Cucurbitaceae)	Gypenoside, flavonoids	EPM, marble burying test	[26]
21.	Pennywort	<i>Hydrocotyle umbellata</i> (Araliaceae)	Triterpenes, essential oils, flavonoids, Saponins	EPM, marble burying test, open field test	[27]
22.	Warer willow	<i>Justicia gendarussa</i> (Acanthaceae)	Flavonoids, alkaloids, steroids, saponins	EPM, Light dark model	[28]
23.	Mango	<i>Mangifera indica</i> (Anacardiaceae)	Polyphenols, flavonoids, triterpinoids	EPM, staircase model	[29]
24.	Indian mulbery	<i>Morinda citrifolia</i> (Rubiaceae)	Scopoletin, rutin	Isolation induced aggression	[30]
25.	Tulsi	<i>Ocimum sanctum</i> (Lamiaceae)	Ursolic acid	EPM, Light dark model	[31]
26.	Indian sorrel	<i>Oxalis corniculata</i> (Oxalidaceae)	Flavonoids, tannins	EPM	[32]
27.	Passion flower	<i>Passiflora actinia</i> (Passifloraceae)	Beta carboline, Flavonoid ( Isovitexin)	EPM, Open field test	[33]
28.	Pomegranate	<i>Punica granatum</i> (puniaceae)	Flavonoids	EPM	[34]
29.	Indian madder	<i>Rubia cordifolia</i> (Rubiaceae)	Alkaloids, flavonoids, terpinoids	EPM, Open field test	[35]
30.	Black berry	<i>Rubus fruticosus</i> (Rosaceae)	Gallotannins, ellagitannins, flavonoids	Open field test, hole board apparatus	[36]
31.	Nimble bush	<i>Siparuna guianensis</i> (Siparunaceae)	Flavonoids, vicenin-2, essential oil	EPM	[37]
32.	Marigold	<i>Tagetes erecta</i> (Asteraceae)	Flavonoids	EPM, Light dark model	[38]
33.	Chebolic myrobalan	<i>Terminalia chebula</i> (Combretaceae)	Tannic acid, polyphenols	EPM	[39]
34.	Damiana	<i>Turnera aphrodisiaca</i> (Turneraceae)	Apigenin	Hole board apparatus, light dark model, mirrored chamber test	[40]
35.	Indian ipecac	<i>Tylophora indica</i> (Asclepiadaceae)	Tylophorine	EPM, Light dark model	[41]
36.	Dabra	<i>Uraria picta</i> (Fabaceae)	Flavonoids, triterpinoids	EPM	[42]
37.	Indian valerian	<i>Valeriana jatamansi</i> (Valerianaceae)	Borneol	EPM	[43]
38.	Chaste tree	<i>Vitex negundo</i> (Verbanaceae)	Volatile oil, flavonoids, terpenes	EPM, Light dark model	[44]
39.	Ashwagandha	<i>Withania somnifera</i> (solanaceae)	Sitoindosides vii-x, withaferin-A	EPM, ethanol withdrawal anxiety	[45]
40.	Blue star water lilly	<i>Nymphaea stellata</i> (Nymphaeaceae)	Alkaloids, saponins, flavonoids	Immobilization induced anxiety	[46]

**CONCLUSION**

The review has focused on some of the medicinal plants exhibiting anxiolytic activity. However use of specific medicinal plants for management of specific subtypes of anxiety disorder is yet to be substantiated.

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