Anxiety is characterized by a persistent and disproportionate fear unrelated to any genuine risk. Apart from very few chemical remedies available like benzodiazepines and serotonin modulators, not much treatment options are at hand that could safely and effectively alleviate anxiety. The present paper discusses anti-anxiety potential of 56 plants with emphasis on their pre-clinical and clinical reports. Majority of these plants have been found to be acting through modulation of serotonin and γ-amino butyric acid (GABA) neurotransmitters.

Keywords: Antianxiety Plants, Anxiolytic herbs, Medicinal Plants

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Introduction

Anxiety is characterized by a persistent and disproportionate fear unrelated to any genuine risk. It can increase to an extent that may interfere with even normal routine of life and person may feel apprehensive regarding happenings of normal things in life. Anxiety disorders comprise clinical conditions of Generalized Anxiety Disorder, Panic Disorder, Post-traumatic Stress Disorder, Social Anxiety Disorder and Phobia. Monoamines (dopamine, noradrenaline and serotonin), neuropeptides (galanin, neuropeptide Y, arginine vasopressin, tachykinin and substance P), neurosteroids and cytokines have been observed to play a modulators role in anxiety states. Among therapeutic regimens, benzodiazepines and serotonin modulators remain the mainstay of pharmacological treatment of anxiety disorders. However, in the light of their adverse effects and dependence potential, search for a novel pharmacotherapy from medicinal plants for anxiety is in fast progress. In this review paper information on plant species that have been explored for their potential anti-anxiety profile using pharmacologically validated animal models has been compiled and discussed. Possible involvements of active constituent(s), plant parts, dose(s) of extracts and animal model(s) used have also been mentioned, wherever it was available.

Abies pindrow Royle (Pinaceae)

It is widely distributed at elevations between 2000 and 3000 m throughout the western Himalaya from Afghanistan to Nepal. Ethanolic extract of leaves (50-100 mg/kg, p.o.) when administered for three consequent days showed significant anxiolytic effect in rats tested in different paradigms of anxiety i.e. open field exploratory behaviour, elevated plus maze and elevated zero maze.

Achillea millefolium Linn. (Asteraceae)

A hardy perennial, native to Eurasia contains active constituent achillein. Aqueous extract of its flowers (8.0 mg/kg, 10.0 mg/kg or 12.0 mg/kg) reduced conflict behaviour in female Wistar rats.

Aloysia polystachya (Griseb.) Moldenke (Verbenaceae)

Hydroalcoholic extract prepared from its leaves (1.56 to 50mg/kg, i.p.) produced anxiolytic effect in female Sprague-Dawley rats in elevated plus maze test similar to diazepam (1mg/kg, i.p.). Thujone and carvone have been implicated to be responsible for anxiolytic effects.

Albizia lebbeck Benth. (Mimosaceae)

It is a tree native to Asia and is used in traditional Chinese medicine to treat anxiety. Butanolic fraction of dried leaves extract (25 mg/kg) presented anxiolytic effect in mice when tested in elevated plus maze. Antianxiety activity of the plant might be due to effect on GABA or saponins present in the extract.
Albizia julibrissin Durazz. (Fabaceae)

It is native to southern and eastern Asia, from Iran east to China and Korea. The plant is used in traditional Chinese medicine to treat depression and anxiety. Single or repeated treatment (for 7 days) of male rats with aqueous extract (100 or 200 mg/kg, p.o.) significantly showed antianxiety effect in Elevated Plus Maze (EPM). The anxiolytic effect is abolished by pindolol (10mg/kg, i.p.), a 5-HT_{1A/1B} receptor antagonist, suggesting the involvement of serotonergic nervous system.\(^\text{12}\).

Angelica sinensis (Oliv.) Diels (Apiaceae)

It is indigenous to China and commonly known as Dong Quai which is an important tonic in Chinese medicine. Its essential oil contains linguistilide. It showed anxiolytic activity in elevated plus maze and light/dark test in male Swiss mice.\(^\text{13}\).

Aniba riparia (Nees) Mez (Lauraceae)

The plant is found mainly in central Amazonia and Guiana. Riparin I (25 and 50 mg/kg, i.p. and p.o.) and Riparin III (50 mg/kg, i.p.) from unripe fruits showed anxiolytic activity in mice when tested in elevated plus maze and hole-board tests.\(^\text{14, 15}\).

Annona cherimola Mill. (Annonaceae)

It is distributed in tropical regions of South America. Hexane extract of its leaves (6.25, 12.5, 25.0 and 50.0 mg/kg, p.o.) produced anxiolytic-like actions in mice when tested in avoidance exploratory behaviour, burying behaviour and open field tests. The effect is antagonized by picrotoxin, a GABA-gated chloride ion channel blocker, suggesting the involvement of GABA_{A} receptor complex. \(\beta\)-cariophyllene, \(\beta\)-selinene, \(\beta\)-cubebene and linalool could explain anxiolytic effect of the extract.\(^\text{16}\).

Apocynum venetum Linn. (Apocynaceae)

It is a Chinese herb, its ethanolic extract (30 and 125 mg/kg, p.o.) showed significant antianxiety activity in mice using EPM. This effect was comparable to diazepam (1.5 mg/kg, p.o.) and the 5-HT_{1A} agonist buspirone (10mg/kg p.o.). Anxiolytic-like activity of the extract was mediated via the GABAergic system.\(^\text{17}\).

Azadirachta indica A. Juss. (Meliaceae)

This is a large tree found everywhere in India. Aqueous extract of neem leaves (10-200 mg/kg, p.o.) produced anxiolytic effect in elevated plus maze and open field test in rats. The extract (500 mg/kg/day \(\times\) 15 days) reduced cerebral hypoperfusion-induced behavioral disturbances of anxiety in rats, assessed in open field test. The extract has been found to contain margosine, margosic acid and margosopicrin as active moieties.\(^\text{18, 19}\).

Bacopa monnieri (Linn.) Penn. (Scrophulariaceae)

It is found in wet, damp and marshy places throughout India and subtropical region up to a height of 1000 m. In Ayurveda it is used as a nervine tonic and memory enhancer. It has been reported to possess anxiolytic activity in humans.\(^\text{20, 21}\).
**Casimiroa edulis** Llave & Lex.  
(Rutaceae)  
It is found in Mexico. Administration of aqueous extract of the leaves (25 mg/kg, p.o.) to male Wistar rats increased the exploration of open arms in the elevated plus maze task\(^22\).

**Cecropia glazioui** Sneth (Moraceae)  
It is popularly known as ‘Embauba’ in Brazil and is also found in tropical and subtropical regions of Latin America. Aqueous extract and n-butanolic fraction (0.25-1g/kg, p.o.) acutely (1h) or repeatedly (24, 7, and 1.5h before the test) showed antianxiety activity in mice employing elevated plus maze. The active principles are flavonoids such as Orientin and Iso-orientin and terpenes\(^23\).

**Centella asiatica** (Linn.) Urban  
(Apiceae)  
Commonly known as Gotukola, it is found in Australia, Pacific Islands, New Guinea, Melanesia, Malesia, northern Iran and Asia. Methanol and ethyl acetate extracts as well asiaticoside have exerted anxiolytic activity in rats employing elevated plus maze test\(^24\).

**Citrus sinensis** (Linn.) Osbeck  
(Rutaceae)  
Commonly known as orange, sweet orange or round orange is assumed to have originated in southern China, North eastern India and perhaps South eastern Asia (formerly Indochina). The essential oils from peel (1.0 g/kg, p.o.) showed anxiolytic effect in mice using elevated plus maze model. Berberine decreased serotonergic activity by activation of somatodendritic 5-HT\(^{1A}\) autoreceptors and inhibited postsynaptic 5-HT\(^{1A}\) and 5-HT\(^{2}\) receptors\(^29\).

**Clitoria ternatea** Linn.  
(Fabaceae)  
It is native to Southeast Asia. The extract containing tannins and resins showed anxiolytic activity in mice employing EPM and light/dark exploration test\(^26\).

**Coriandrum sativum** Linn.  
(Apiceae)  
Coriander is native to South western Asia west to North Africa. It has been recommended for relief of anxiety and insomnia in Iranian folk medicine. Aqueous extract at 100mg/kg, p.o. showed an anxiolytic effect in the elevated plus maze in male albino mice\(^27\).

**Coptis chinensis** Franch  
(Ranunculaceae)  
The plant is native to East Asia, China. Rhizome has been used to treat anxiety by traditional physicians. Its an active constituent; berberine (100 mg/kg, i.p.) produced anxiolytic effect in mice using elevated plus maze model. Berberine decreased serotonergic activity by activation of somatodendritic 5-HT\(^{1A}\) autoreceptors and inhibited postsynaptic 5-HT\(^{1A}\) and 5-HT\(^{2}\) receptors\(^28\).

**Crinum giganteum** Andrews  
(Amaryllidaceae)  
It is a medicinal plant widely found in the Northern states of Nigeria and contain lycorin. Aqueous extract (6.25, 12.5 and 25 mg/kg, i.p.) produced anxiolytic effect in hole-board test in rats\(^29\).

**Davilla rugosa** Poir.  
(Dilleniaceae)  
It is commonly used in Brazilian folk medicine. Hydroalcoholic extract of the stems (15 mg/kg, p.o.) showed anxiolytic activity in rats employing open field test and elevated plus maze\(^30\).

**Echium amoenum** Fisch. & C.A. Mey.  
(Boraginaceae)  
It grows in most of Europe and in northern Iran. Ethanolic extract of flowers (50 mg/kg) contained pyrrozolidines and showed anxiolytic activity in mice when tested using elevated plus maze\(^31\).

**Erythrina velutina** Willd.  
(Fabaceae)  
The plant is Brazilian ornamental tree and medicinal plant native to Cerrado and Caatinga vegetation in Brazil. Aqueous-alcoholic extract of grounded stem bark (50-100 mg/kg, p.o.) having flavonoids and terpenes proved to be active as anxiolytic in rats tested employing elevated T-maze\(^32\).

**Erythrina mulungu** Mart. ex Benth.  
(Fabaceae)  
It is commonly known as Mulungu, native to Southern Brazil. Plant contains alkaloids. The extract (50 mg/kg, p.o.) showed anxiolytic activity in rats employing light/dark transition model. Alteration of GABAergic transmission has been proposed to be responsible for observed anxiolysis\(^33\).

**Eschscholzia californica** Cham.  
(Papaveraceae)  
It is native to the western coast of North America and naturalized in parts of southern Europe, Asia and Australia. The extract of the plant (25 mg/kg, i.p.) produced anxiolytic activity in mice when tested using staircase and light/dark tests. The action involved benzodiazepine-GABA receptor agonist\(^34\).

**Euphoria longana** Lam.  
(Sapindaceae)  
It is native to Asia and introduced...
into other warm regions of the world. The extract indicated significant activity at a dose of 2 g/kg, s.c. in Vogel-type anti-conflict method in mice. Active principle; adenosine produced the effect at a dose of 30 mg/kg, s.c.35.

**Euphorbia hirta** Linn. (Euphorbiaceae)

It is found in India and most tropical countries. Lyophilised aqueous extract (12.5 and 25 mg/kg, p.o.) produced anxiolytic effect in mice employing staircase test and light/dark choice situation test. Euphorbone is the active constituent.36

**Eurycoma longifolia** Jack (Simaroubaceae)

It is found mostly in forests of Burma, Indochina, Thailand and Malaysia. Methanol, chloroform, water and n-butanol fractions (0.3g/kg each) of extract have been found to be anxiolytic in inbred albino mice tested employing elevated plus maze and open field paradigms. The anxiolytic effect might be due to quassinoids, squalene derivatives, biphenylneolignans, tirucalane-type triterpenes, canthine-6-one and β-carboline alkaloids.37

**Euphorbia neriifolia** Linn. (Euphorbiaceae)

Hydro-alcoholic extract of leaves (400 mg/kg, p.o.) containing steroidal saponins, reducing sugar, tannins, and flavonoids produced anxiolysis in mice and rats tested using elevated plus maze and open field paradigms. The anxiolytic effect might be due to quassinoids, squalene derivatives, biphenylneolignans, tirucalane-type triterpenes, canthine-6-one and β-carboline alkaloids.38

**Galphimia glauca** Cav. (Malpighiaceae)

Standardized methanolic extract containing a nor-secotriterpene (Galphimine B; 8.3 mg/g) showed an anxiolytic effect on ICR inbred mice tested in elevated plus maze and light-dark paradigms. Galphimine B has a selective inhibitory effect on dopaminergic neurons of the ventral tegmental area in rats. The activity could also be attributed to neuronal ion channel modulation particularly K+ channel as well as regulation of GABA_A receptors.39, 40

**Gastrodia elata** Blume (Orchidaceae)

The plant contains phenolic compounds like 4-hydroxybenzyl alcohol, 4-hydroxybenzaldehyde, vanillin, vanillyl alcohol, β-sitosterol and gastrodin. The compounds, 4-hydroxybenzyl alcohol (50mg/kg, p.o. and 100 mg/kg, p.o.) and 4-hydroxybenzaldehyde (100 mg/kg, p.o.) have been found to be effective as anxiolytic in male ICR mice when tested using elevated plus maze. Activation of benzodiazepine, GABA_A and 5-HT_1A receptors has been implicated for the observed anxiolysis.41

**Ginkgo biloba** Linn. (Ginkgoaceae)

Ginkgo trees are native to East Asia and are grown ornamentally in Europe and North America. The extract (0.063-1 g/kg, p.o.) administered daily for 7 days in male ddY mice produced anxiolysis in elevated plus maze.42

**Hypericum perforatum** Linn. (Hypericaceae)

It is a perennial plant, commonly known as St. John’s Wort. The plant is distributed in Europe, Asia, North Africa and North America. Ethanol extract (50%) administered at the rate of 100 and 200 mg/kg, p.o. was found to exert anxiolysis in rats employing various experimental paradigms of anxiety viz. open field exploratory behaviour, elevated plus maze, elevated zero maze, novelty induced suppressed feeding latency and social interaction tests. Hypericin has been the active component.43

**Justicia hyssopifolia** Linn. (Acanthaceae)

Active component of the plant; elenoside (25, 50 mg/kg, i.p.) produced anxiolytic effect in mice employing open-field test.44

**Kielmeyera coriacea** Mart. ex Saddi (Guttiferae)

It is native to Cerrado and Pantanal vegetation in Brazil. Hydroalcoholic extract of leaves produced anxiolysis in open-field and elevated plus maze tests.45

**Magnolia dealbata** Zucc. (Magnoliaceae)

**Magnolia** species is rather scattered and includes eastern North America, Central America, West Indies, East and Southeast Asia. Some species are found in South America. The extract (30, 100 and 300 mg/kg) dose-dependently decreased anxiety response in mice when tested in elevated plus maze, head-dipping and exploratory rearing tests.46 The effect may be due to magnolol.

**Pachyrhizus erosus** (Linn.)Urban (Fabaceae)

Ethanol and chloroform extracts of seeds contain rotinoids, flavonoids and phenyl furanocoumarin derivatives. Ethanol extract (150 mg/kg, p.o) showed antianxiety activity.47
**Paeonia moutan** Sims. (Paeoniaceae)

Paeonol, a phenolic component from the root bark produced anxiolysis comparable to diazepam in the elevated plus maze and the light/dark box-test\(^8\).

**Panax ginseng** C. A. Mey. (Araliaceae)

Both Chinese ginseng (**P. ginseng** C. A. Mey.) and North American ginseng (**P. quinquefolius** Linn.) are associated with the treatment of mood and anxiety disorders. Ginseng powder and crude saponin ginseng fraction significantly increased the frequency and duration of open arm entries in male ICR albino mice. Pure ginsenoside; ginsenoside Rb1 (2.5 mg/kg, i.p.) increased both the frequency and duration of open arm entries\(^49\).

**Passiflora incarnata** Linn. (Passifloraceae)

It is a popular sedative and anxiolytic. The methanol extracts of leaves, stems, flowers and whole plant exhibited anxiolytic effects in mice employing elevated plus maze model\(^50\).

**Piper methysticum** G. Forst. (Piperaceae)

Commonly known as Kava-Kava, is used as traditional psychoactive beverage in the South Pacific. It is well known for tranquilizing and anxiolytic effects. LI 150 (120-240 mg/kg, p.o.) induced an anxiolytic like behaviour similar to diazepam. Dihydrokavain, a major kavalactone is necessary and sufficient to mediate anxiolytic effect of **P. methysticum** G. Forst. The anxiolytic effect may involve agonism at GABA(A)-benzodiazepine receptor complex\(^51\).

**Rubus brasiliensis** Marit. (Rosaceae)

Ethanolic extract induced anxiolytic effect in male Wistar rats and Swiss mice, tested in the elevated plus maze. Agonism at GABA\(_x\)/BDZ receptors by a liposoluble principle may underlie the anxiolysis of this species\(^52, 53\).

**Scutellaria lateriflora** Linn. (Lamiaceae)

It is a perennial herb, commonly known as Skullcap and native to North America and grows throughout Canada and the Northern US. Baicalin in a 50% ethanol extract (40 mg/g) and its aglycone baikalein in a 95% ethanol extract (35 mg/g) showed anxiolytic effect in open-field arena, hole-board test and elevated plus maze. Baicalin and baikalein bind to the benzodiazepine site of the GABA\(_x\) receptor\(^58\).

**Salvia officinalis** Linn. (Lamiaceae)

It is a perennial shrub native to southern Europe and Asia Minor. A double-blind, placebo-controlled, crossover study on 30 healthy participants with dried leaves (300 and 600mg) dose-dependently reduced anxiety and increased 'alertness', 'calmness' and 'contentedness\(^56\).

**Scutellaria baicalensis** Georgi (Lamiaceae)

Wogonin (7.5–30 mg/kg, p.o.), a major constituent elicited anxiolysis in male ICR mice tested using EPM. This effect was antagonized by co-administration of Ro15-1788, a benzodiazepine site antagonist. Wogonin exerted its anxiolytic effect through positive allosteric modulation of the GABA(A) receptor complex via interaction at the BZD-S\(^57\).
India. Methanolic fraction of the root extract inhibited head-dips in hole-board test and enhanced brain GABA content in Swiss albino mice suggesting the anxiolytic effect.65.

**Turnera aphrodisiaca** Ward.  
(Turneraceae)

Methanolic extract exhibited significant anti-anxiety activity at a dose of 25mg/kg with respect to control as well as standard (diazepam, 2mg/kg). Butanol fraction (10mg/kg) and remaining methanolic extract (75mg/kg) were found to exhibit anxiolytic activity in mice using elevated plus maze.63.

**Uncaria rhynchophylla** (Miq.)  
Jacks (Rubiaceae)

Aqueous extract (200 mg/kg/day, p.o.) for 7 days showed anxiolytic activity in rats subjected to elevated plus maze. Anxiolytic-like effect was abolished by WAY 100635 (0.3 mg/kg, i.p.), a 5-HT(1A) receptor antagonist. These results suggest that the extract acted via the serotonergic nervous system.64.

**Valeriana edulis** ssp. procera Mey.  
(Valerianaceae)

It is the Mexican valerian. Neuropharmacological profile of a hydroalcohol extract of roots (100, 300 and 1000 mg/kg) revealed the dose-dependent anxiolytic-like effect in mice comparable to diazepam.65.

**Withania somnifera** (Linn.) Dunal  
(Solanaceae)

The drug consists of dried roots of the plant widely distributed in North western India. Intraperitoneal and oral administration of glycowithanolides (20 and 50mg/kg) once daily for 5 days resulted in anxiolytic effect in rats employing elevated plus maze and social interaction test. The therapeutic potential of *W. somnifera* appears to be related to inhibition of both the lipid peroxidation and protein oxidative modification.66.

**Zingiber officinale** Rosc.  
(Zingiberaceae)

It contains zingiberene, phellandrene and gingerol. Animals treated with butanolic fraction showed anxiolytic activity in elevated plus maze.67.

**Ziziphus jujube** Mill.  
(Rhamnaceae)

Ethanolic extract of pulp (0.5-2.0 g/kg, p.o.) showed anxiolytic activity in ICR mice tested using white/black chamber test and EPM. Active constituent reported is JujubosideA68.

**Conclusion**

Although 56 species of plants have shown anxiolytic activity in laboratory animals, only 4 plants, viz. *Bacopa monnieri* (Linn.) Penn., *Ginkgo biloba* Linn., *Piper methysticum* G. Forst. and *Salvia officinalis* Linn. have been reported to be effective clinically. So the remaining 52 plants are yet to be evaluated clinically and active constituents from most of these plants need to be isolated to establish them as potential antianxiety plants.

**References**


31. Ruiz MH, Cortazar MG, Ferrer EJ, Zamilha A, Alvarez L, Ramirez G and Tortoriello J, Anxiolytic Effect of a Natural Galphimias from...


52. Nogueira E, Rosa GJ and Vassilieff VS, Involvement of GABA (A)-benzodiazepine receptor in the anxiolytic effect induced by hexamic fraction of *Rubus brasiliensis*, *J Ethnopharmacol, 1998b*, 61(2), 119-126.


