



A Brief Review on Herbal Medicinal Plants for Anxiety

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Date of Submission: 10-10-2021

Date of Acceptance: 22-10-2021

ABSTRACT:

Modern lifestyle is very stressful and millions of people follow an unhealthy lifestyle. In today's world the day to day activities are clumsy, confusing and hence annoying. This may give an invitation to lots of diseases and usage of medicines was automatically increased. From the beginning of human evaluation, plants have been used to relieve humans who are suffering with diseases. It has been documented that plants have been used for medicinal purposes from thousands of years. Today we are witnessing a great deal of public interest in use of herbal remedies and have become increasingly popular. Natural bioactive compounds, called phytochemicals, are derived from various parts of medicinal plants are used to combat various diseases. The prevalence and comorbidity of psychiatric disorders such as anxiety is very common. These well-known forms of psychiatric disorders have been affecting many people from all around the world. Herb alone, as well as herbal formula, is commonly prescribed for the therapies of mental illnesses. Since various adverse events of western medication exist, the number of people who use herbs to benefit their health is increasing. Over the past decades, the exploration in the area of herbal psychopharmacology has received much attention. This review has been performed to further explore the different herbal medicines for treating anxiety.

KEYWORDS: Herbal remedies, Phytochemicals, Comorbidity, Herbal psychopharmacology

INTRODUCTION:

In modern society, people suffer from various psychiatric disorders, especially depression, anxiety and insomnia. As one of the most prevalent forms of mental illness, depressive disorders have a huge influence on individuals and society. Anxiety is another common symptom of many psychiatric disorders in the community and other medical disorders. In fact, in humans, it is a common

emotion intimately associated with proper fear and probably functions as a mechanism to adapt the environment psychologically. Worldwide, one in five people meet with clinical criteria of anxiety disorder at least once in their lives. The study of anxiety has developed into a key area of psychopharmacological research during this decade [1].

Usually, Anxiety is a term used to describe experiences of normal people when they face threat, danger, or when stressed. When people become anxious, they typically feel upset, uncomfortable, and tense. Anxiety is a persistent feeling of dread, apprehension and impending disaster, or tension and uneasiness [2]. These psychiatric disorders not only affect individual's work and daily life, but also decrease their quality of life, and perceived well-being. To our knowledge about the present situation, the number of people with mental illness of anxiety is rapidly increasing across the world. Therefore, searching for more effective treatments for anxiety should be an important consideration.

Evidence-based options for treatment of anxiety disorders are limited. Pharmacological therapy is currently the most commonly used treatment for anxiety disorders. Although many drugs appear to have an important role in cases of most severe mental illness, many complaints that the drugs are not effective for all patients and incur diverse adverse events, as well as tolerance (if used for a long time). Numerous studies have demonstrated that the use of complementary and alternative medicine (CAM) among psychiatric disorders, especially depression and anxiety is a common phenomenon. Many literatures indicated the importance of CAM for the treatment of mental illnesses. Meanwhile, herbal medicine is the most commonly used form of complementary and alternative medicine therapies [3].

Herbal medicine is a popular complementary and alternative medicine (CAM)

used throughout the world. Herbal medicines are used to treat a range of health concerns, including common mental health problems such as anxiety. The prevalence of herbal medicine use has been reported to be as high as 21% in patients with anxiety disorders. The barriers (such as adverse drug reaction, tolerance etc.) to conventional treatment may be a factor causing people to consider herbal medicines as an alternative, or as a complement to evidence-based treatments to further relieve symptoms. Other clinical groups (e.g., cancer patients) and general population samples have been found to use herbal medicines because they are dissatisfied with their conventional treatments. However, this usage has yet to be explored in adults experiencing anxiety^[4].

Today, as many people favor herbal medicine over synthetic medicine, the separate industries are developing and growing day by day. Advantages of Herbal Medicine Herbal medicine is cost effective and less expensive than the medicines bought from an allopathic pharmacy. Another merit of herbal medicine is that it can be bought without a prescription. They are available in any health store. Herbal medicine and remedies are more effective than allopathic medicine for certain ailments. The chemical medicine prescribed by a pharmacist could have certain negative side effects. However, many of the herbal medicines and remedies do not have negative side effects. Herbal medicine can also be effectively used for body's natural detoxification process^[4].

HERBAL MEDICINAL PLANTS USED FOR ANXIETY –

1. *Nigella sativa* –



Figure no. 1 *Nigella sativa* plant, seed and oil

Nigella sativa (also called as black seed or kalonji) is a well-known herbal medicinal plant belonging to family Ranunculaceae used extensively all over the world. The *Nigella sativa* had gained extreme demand in historic culture of the medicines such as Unani and Tibb, Ayurveda and Siddha for alternative therapies of different diseases and ailments including antidiabetic, anticancer, hepatoprotective, anxiety etc. It is an emanating miraculous herb with an upscale historical and secular background. *Nigella sativa* seeds and oils have a prolong history of folklore utilization in variety of dietary and medicinal systems. This is found that majority of the

therapeutic effects of *Nigella sativa* are because of existence of thymoquinone (30-48%) which is a major bioactive compound of volatile oil. The other active compounds are thymohydroquinone, dithymoquinone, p-cymene (7%-15%), carvacrol (6%-12%), 4-terpineol (2%-7%), t-anethol (1%-4%), sesquiterpene longifolene (1%-8%), α -pinene and thymol etc^[5]. Among the constituents present, thymoquinone is reported to produced antianxiety effect by modulating GABA level similar to diazepam. When NSO was consumed recurrently to the animals, an increase in the brain levels of 5-HT was observed which indicate its anxiolytic effect^[6,7].

2. Ginkgo Biloba-



Figure no.2 Ginkgo Biloba

Ginkgo biloba, the oldest plant existing in the world for over 200 million years, is a famous Chinese herb employed frequently in the world to treat anxiety. It belongs from the family Ginkgoaceae. This herb is first documented in a Chinese book about 2800BC and the herb is also considered as a component of the Ayurvedic elixir soma.

As we know, drugs aiming to produce or increase the serotonin have been gaining much attention as possible anxiolytic candidates in searching for drugs that could be a substitute to the benzodiazepines. Extracts of Ginkgo biloba, are capable of suppressing the agglutination of thrombocyte and thus indirectly antagonizing the serotonin activity, besides their elevating effect upon the velocity of blood flow. Extract of Ginkgo biloba leaves are widely and frequently used to ameliorate the clinical manifestations related to

anxiety, producing removable suppressing effects on monoamine oxidase in rat brain, thus exhibiting the pharmacological activities of this natural product against anxiety. Taking into account the good compatibility, the drug is of particular anxiolytic value not only for senile people, but also for younger workers, as it reduces the tendency for addiction and decrease side effects on the cognitive function^[8].

3. Ashwagandha –

Ashwagandha or *Withaniasomnifera* is among a group of herbs called 'adaptogens'. Adaptogens affect systems and hormones in the body that regulate a person's stress response. Ashwagandha has a long history of use in traditional Indian, or Ayurvedic, medicine. Ashwagandha is a small shrub belonging to the Solanaceae family. It is prolifically grown in



Figure no. 3 Ashwagandha plant and roots

dry regions of South Asia, Central Asia, and Africa, and is regularly used in Ayurveda, an ancient Hindu system of medicine. Over 50 chemical constituents have been identified in the various parts of the ashwagandha plant with the major chemical constituents including steroidal

alkaloids and lactones, collectively known as withanolides^[9].

A small 2019 clinical trial investigated the efficacy of ashwagandha for stress and anxiety. In this 60-day, randomized, double-blind, placebo-controlled study the stress-relieving and

pharmacological activity of an ashwagandha extract was investigated in stressed (to induce anxiety) and healthy adults. Sixty adults were randomly allocated to take either a placebo or 240 mg of a standardized ashwagandha extract (Shoden) once daily. The outcomes were measured using the Hamilton Anxiety Rating Scale (HAM-A). Based on the HAM-A, anxiety levels reduced by 41% in participants taking ashwagandha, which compared favorably to the 24% reduction experienced in participants taking a placebo^[10].

These findings suggest that ashwagandha's anxiety-relieving effects may occur via its moderating effect on the hypothalamus-pituitary-

adrenal (HPA) axis. Ashwagandha temporarily impairs the HPA axis activity. Generally, activated HPA increases the secretion of cortisol and DHEA (Dehydroepiandrosterone) as a physiological response to stress. Postexcitation homeostasis is attained naturally through a negative feedback system. However, depression and anxiety hinder the HPA axis normal function, and increases cortisol secretion. Ashwagandha may reduce the cortisol level and restore normal function of the HPA axis^[10]. Apart from its modulatory activity on the HPA axis, ashwagandha can also modulate GABAergic and serotonergic activities, and therefore can aid in reducing anxiety^[11].

4. Lavender –



Figure no.4 Lavender flower and oil

Lavender is a flowering plant belonging to the mint family. Lavender is traditionally alleged to have a variety of therapeutic and curative properties. There is growing evidence suggesting that lavender oil may be an effective medicament in treatment of several neurological disorders. Several animal and human investigations suggest anxiolytic, mood stabilizer, sedative, analgesic, and anticonvulsive and neuroprotective properties for lavender. The main constituents of lavender are linalool, linalyl acetate, 1,8-cineole B-ocimene, terpinen-4-ol, and camphor. However, the relative level of each of these constituents varies in different species^[12].

Lavender was used in the treatment of anxiety disorders and related conditions. Lavender

oil aromatherapy has been given to the patient who having stress and thereby give relief from the symptoms of anxiety. Oral administration of lavender oil modulates GABAergic neurotransmission, especially on GABA_A receptors, and enhance inhibitory tone of the nervous system. Cholinergic system is also suggested to play the role in antianxiety activity. Lavender oil also give relief from anxiety by using the lavender in following ways -

- making tea from the leaves
- using the oil in aromatherapy
- mixing the essential oil into a base oil for massage
- adding the oil or flowers to baths^[12]

5. Passionflower –



Figure no.5 Passionflower

It is a rich source of vitamins A, C, B1, and B2, as well as calcium, phosphorus, and iron. Passionflower or *Passiflora* is a family of plants with around 550 different species. Some studies show that a particular species, *Passiflora incarnata*, may be effective in treating anxiety. The species is native to South America, Australia, and South East Asia, and today is cultivated to source raw material for pharmaceutical use. Maltol has been proposed as an active component, which may actually be formed during heat-extraction processes of passionflower. A study found that a commercial passionflower extract binds to central nervous system receptors sites for GABA-A and GABA-B,

in addition to glycine, N-methyl-D-aspartate and quisqualate receptors, and chloride ion channel receptors. Passionflower extract is a dose-dependent competitive inhibitor of in vitro binding at central benzodiazepine sites, and inhibits binding at alpha-2 adrenoceptors^[13].

6. Kava –

Kava (*Piper methysticum*) is a plant-based medicine, which has been previously shown to reduce anxiety. It is largely used to treat Generalized Anxiety Disorder (GAD). A study of total of 75 participants with GAD and no comorbid mood disorder were enrolled in a



Figure no. 6 Kava plant

6-week double-blind trial of an aqueous extract of kava (120/240 mg of kavalactones per day depending on response) versus placebo. F-Aminobutyric acid (GABA) and noradrenaline transporter polymorphisms were also analyzed as potential pharmacogenetic markers of response. Reduction in anxiety was measured using the Hamilton Anxiety Rating Scale (HAMA) as the primary outcome. Results revealed a significant

reduction in anxiety for the kava group compared with the placebo group^[14].

The therapeutic effect of kava is based on the six major lipophilic kavalactones, of which kawain and dihydrokawain have the strongest anxiolytic activity. Limbic structures of the brain have previously been suggested as the principal site of kavalactone action. Kavalactones exert their anxiolytic effect through an array of

neurobiological activity, primarily from modulation of gamma-aminobutyric acid (GABA) receptors via blockade of voltage-gated sodium ion channels, reduced excitatory neurotransmitter release via blockade of calcium ion channels, and enhanced ligand binding to GABA type A receptors. Other neurochemical effects include reversible inhibition of monoamine oxidase B, inhibition of cyclo-oxygenase, and reduced neuronal reuptake of dopa-mine and prefrontal cortex noradrenalin. This noradrenergic effect differentiates the central

bio-behavioural effects of kava from those of alcohol and benzodiazepines, while the combination of GABA modulation and increased noradrenergic activation contributes to feelings of physical relaxation with increased hedonic tone, with no deleterious effects on cognition^[15].

Kava are sold on the internet and in health food stores, including loose powders and tea bags used to make warm drinks, liquid extract added to water and other cool beverages, and capsules that are taken as dietary supplements^[15].

7. Galphimia glauca–



Figure no.7 Galphimia glauca

Galphimia glauca (Cav.) Kuntze is an important endemic plant species, which possesses many medicinal properties and for its sedative, anxiolytic, anticonvulsant, antiasthmatic and antiallergic properties. The therapeutic properties of this plant are mainly due to the presence of diverse bioactive compounds such as flavonoids, triterpenoids, and phenolics. The methanolic extract derived from the aerial parts of the plant was used to evaluate the anxiolytic effect caused by the presence of one of the bioactive constituents galphimine B. Additionally, further analysis revealed that this nor-secotriterpene compound could be exerting this anxiolytic effect due to an inhibition in dopaminergic activity along with possible interactions with the serotonergic system.

Furthermore, the effect of galphimines A and E on anxiety was also evaluated; however, their action is less potent than that of galphimine B^[16].

The mechanism for this drug is based in its capacity to bind to molecular subunits (α and γ) of GABA_A (gamma amino butyric acid type A) receptors located in the neuronal membranes of the central nervous system, which allows the opening of chloride ion channels^[16]. The compound produced modifications in the neuron discharge rate of the ventral tegmental area (VTA). The effects produced by G-B are selective for the dopaminergic neurons which, besides not interacting with the GABAergic system, are capable of blocking the effects produced by glutamate on the NMDA ionotropic receptors^[17].

8. Valerian –



Figure no.8 Valerian plant

Valerian or *Valeriana officinalis* is a plant native to Europe and Asia. For many centuries, people have used the root to help treat sleep problems, anxiety, and depression. The root of valerian plant has been widely used to get rid from anxiety. Valerian root is available in the following forms of tea (soak 2 to 3 grams of dried herbal valerian root in 1 cup of hot water for 10 to 15 minutes), tablet (120 to 200 mg, three times per day), tincture. Valerian root seems to work best after taking it regularly for two or more weeks^[18].

Valerian root contains a number of compounds that may promote sleep and reduce anxiety. These include valerenic acid, isovaleric acid and a variety of antioxidants. This route is

work by increasing the levels of a chemical known as gamma aminobutyric acid (GABA) in the brain. GABA contributes to a calming effect in the body. Valerenic acid has been found to inhibit the breakdown of GABA in the brain, resulting in feelings of calmness and tranquility. Valerian root also contains the antioxidants hesperidin and linarin, which appear to have sedative and sleep-enhancing properties after relieving the anxiety symptoms. Many of these compounds may inhibit excessive activity in the amygdala, a part of the brain that processes fear and thus treat the anxiety^[18].

9. Cannabidiol –



Figure no.9 Cannabidiol

Cannabidiol (CBD), a *Cannabis sativa* constituent, is a pharmacologically broad-spectrum drug that in recent years has drawn increasing interest as a treatment for a range of neuropsychiatric disorders including anxiety. Cannabidiol (CBD) is one of the active ingredients of the cannabis plant. Cannabidiol (CBD) is a phyto-cannabinoid constituent of *Cannabis sativa* that lacks the psychoactive effects of Δ^9 -

tetrahydrocannabinol (THC). *Cannabis sativa*, a species of the *Cannabis* genus of flowering plants, is one of the most frequently used illicit recreational substances in Western culture. The 2 major phyto-cannabinoid constituents with central nervous system activity are THC, responsible for the euphoric and mind-altering effects, and CBD, which lacks these psychoactive effects^[19].

It has been investigated that potential mediators of CBD's anxiolytic action: CB1R, TRPV1 receptors, and 5-HT1A receptors. CB1R is an endocannabinoid receptor. The CB1R is an inhibitory Gi/o protein-coupled receptor that is mainly localized to nerve terminals, and is expressed on both γ -aminobutyric acid-ergic and glutamatergic neurons. CB1R activation has been suggested as a target for anxiolytic drug development. While CBD has affinity for the CB1R, it functions as an indirect agonist, potentially via augmentation of CB1R constitutive activity and give relief from anxiety. CB1R agonists have capacity also activate TRPV1 receptors when administered at high doses. CBD acts as a TRPV1 agonist at high concentrations, potentially by interfering with AEA inactivation (Anandamide which is an endocannabinoid) to produce anxiolytic effect. Also the 5-HT1A receptor (5-HT1AR) is an established anxiolytic target. Both pre- and postsynaptic 5-HT1ARs are coupled to various members of the Gi/o protein family. They are expressed on serotonergic neurons in the raphe, where they exert autoinhibitory function, and various other brain areas involved in fear and anxiety. Mechanisms underlying the anxiolytic effects of 5-HT1AR activation are complex, varying between both brain region, and pre- versus postsynaptic locus, and are not fully established. While in vitro studies suggest CBD acts as a direct 5-HT1AR agonist, in vivo studies are more consistent with CBD acting as an allosteric modulator, or facilitator of 5-HT1A signaling and thus act anxiolytic^[19].

REFERENCES

- [1]. Baldessarini RJ. Drug therapy of depression and anxiety disorders. Goodman and Gilman's The Pharmacological Basis of Therapeutics. Edited by Brunton LL, Lazo JS, Parker KL. New York, McGraw-Hill. 2006:429-60.
- [2]. Kaur S, Singh R. Role of different neurotransmitters in anxiety: a systemic review. International Journal of Pharmaceutical Sciences and Research. 2017 Feb 1;8(2):411.
- [3]. Hsu MC, Creedy D, Moyle W, Venturato L, Tsay SL, Ouyang WC. Use of complementary and alternative medicine among adult patients for depression in Taiwan. Journal of Affective Disorders. 2008 Dec 1;111(2-3):360-5.
- [4]. McIntyre E, Saliba AJ, Moran CC. Herbal medicine use in adults who experience anxiety: A qualitative exploration. International journal of qualitative studies on health and well-being. 2015 Jan 1;10(1):29275.
- [5]. Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, Damanhour ZA, Anwar F. A review on therapeutic potential of *Nigella sativa*: A miracle herb. Asian Pacific journal of tropical biomedicine. 2013 May 1;3(5):337-52.
- [6]. Perveen T, Haider S, Kanwal S, Haleem DJ. Repeated administration of *Nigella sativa* decreases 5-HT turnover and produces anxiolytic effects in rats. Pak J Pharm Sci. 2009 Apr 1;22(2):139-44.
- [7]. Gilhotra N, Dhingra D. Thymoquinone produced antianxiety-like effects in mice through modulation of GABA and NO levels. Pharmacological Reports. 2011 May 1;63(3):660-9.
- [8]. Liu L, Liu C, Wang Y, Wang P, Li Y, Li B. Herbal medicine for anxiety, depression and insomnia. Current neuropharmacology. 2015 Jul 1;13(4):481-93.
- [9]. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. African Journal of Traditional, Complementary and Alternative Medicines. 2011;8(5S).
- [10]. Lopresti AL, Smith SJ, Malvi H, Kodgule R. An investigation into the stress-relieving and pharmacological actions of an ashwagandha (*Withaniasomnifera*) extract: A randomized, double-blind, placebo-controlled study. Medicine. 2019 Sep;98(37).
- [11]. Candelario M, Cuellar E, Reyes-Ruiz JM, Darabedian N, Feimeng Z, Mileidi R, Russo-Neustadt A, Limon A. Direct evidence for GABAergic activity of *Withaniasomnifera* on mammalian ionotropic GABAA and GABA ρ receptors. Journal of ethnopharmacology. 2015 Aug 2;171:264-72.
- [12]. Koulivand PH, Khaleghi Ghadiri M, Gorji A. Lavender and the nervous system. Evidence-based complementary and alternative medicine. 2013 Oct;2013.
- [13]. Cott J. Medicinal plants and dietary supplements: Sources for innovative treatments or adjuncts. Psychopharmacology bulletin. 1995.



- [14]. Sarris J, Stough C, Bousman CA, Wahid ZT, Murray G, Teschke R, Savage KM, Dowell A, Ng C, Schweitzer I. Kava in the treatment of generalized anxiety disorder: a double-blind, randomized, placebo-controlled study. *Journal of clinical psychopharmacology*. 2013 Oct 1;33(5):643-8.
- [15]. Savage KM, Stough CK, Byrne GJ, Scholey A, Bousman C, Murphy J, Macdonald P, Suo C, Hughes M, Thomas S, Teschke R. Kava for the treatment of generalised anxiety disorder (K-GAD): study protocol for a randomised controlled trial. *Trials*. 2015 Dec;16(1):1-3.
- [16]. Sharma A, Angulo-Bejarano PI, Madariaga-Navarrete A, Oza G, Iqbal H, Cardoso-Taketa A, Luisa Villarreal M. Multidisciplinary investigations on Galphimia glauca: a Mexican medicinal plant with pharmacological potential. *Molecules*. 2018 Nov;23(11):2985.
- [17]. Romero-Cerecero O, Islas-Garduño AL, Zamilpa A, Pérez-García M, Tortoriello J. Therapeutic effectiveness of Galphimia glauca in young people with social anxiety disorder: A pilot study. *Evidence-Based Complementary and Alternative Medicine*. 2018 Jan 1;2018.
- [18]. Nunes A, Sousa M. Use of valerian in anxiety and sleep disorders: what is the best evidence?. *Acta medica portuguesa*. 2011;24:961-6.
- [19]. Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a potential treatment for anxiety disorders. *Neurotherapeutics*. 2015 Oct;12(4):825-36.