

Herbal Remedies for Stress and Anxiety: Evidence-Based Review of Plant-Based Therapies

Jaypratap Vishwakarma^{*1}, Kajal Galave^{*2} Alard College of Pharmacy Marunji, Alard College of Pharmacy Marunji.

Submitted: 15-03-2024

Accepted: 27-03-2024

ABSTRACT:

Stress and anxiety are pervasive mental health concerns affecting individuals globally. In recent years, there has been a growing interest in herbal remedies as alternative or complementary therapies for managing stress and anxiety.Herbal medicine is being considered for its anti-inflammatory, antimicrobial, anti-oxidant, and anxiolytic properties in treating oral diseases like oral lichen planus, as conventional corticosteroid therapy has side effects.Research in herbal psychopharmacology has grown significantly, but a comprehensive review of antidepressant, anxiolytic, and hypnotic psychopharmacology and applications in depression, anxiety, and insomnia has not been conducted. A systematic review of MEDLINE, CINAHL, PsycINFO, and the Cochrane Library databases revealed evidence of neurochemical, endocrinological, and epigenetic effects for 21 phytomedicines. Some herbal medicines have in vitro and in vivo evidence, and potential future research includes emerging genetic technologies and herbomics.

This review article aims to provide an evidencebased analysis of various plant-based therapies used for alleviating stress and anxiety. We explore the pharmacological mechanisms, clinical efficacy, safety profiles, and potential adverse effects of commonly used herbal remedies. Additionally, we discuss the challenges and future directions in herbal medicine research for stress and anxiety.

KEYWORDS: Herbal medicine; Antidepressant; Depression; Anxiolytic; Anxiety; Insomnia; Psychopharmacology; Herbomics; Anxiety disorders Attitudes Beliefs Complementary medicine Herbal medicine Prevalence

I. INTRODUCTION:

Stress and anxiety disorders are among the most prevalent mental health issues worldwide, contributing significantly to the global burden of disease. Conventional treatments, such as psychotherapy and pharmacotherapy, have limitations and may not be suitable for all individuals. As a result, there has been a growing interest in natural remedies, particularly herbal therapies, for managing stress and anxiety. This article provides a comprehensive review of the current evidence regarding the efficacy and safety of various herbal remedies used in the treatment of stress and anxiety.[1]

Throughout history, botanical medicines have been utilized to address mood, anxiety, and sleep disorders, which are common psychiatric conditions often found together. Today, herbal medicine and Complementary and Alternative Medicine (CAM) use is widespread among of these disorders.[2] Scientific sufferers psychoactive understanding of plants has significantly advanced over the last two centuries, with modern research increasing in recent years. Research into psychoactive plants that affect the central nervous system has flourished, with many phytotherapies validating their array of biopsychological effects.[3] Some less potent plants, such as Hypericum perforatum, have developed evidence of beneficial therapeutic activity over the last several decades.[4] Many over-the-counter psychotropic herbal medicines are fairly safe and present with fewer side effects compared to conventional pharmacotherapies. However, not all commonly used phytomedicines are safe, as there are case reports of switching to mania in bipolar disorder, drug interactions, and liver toxicity with Piper methysticum. Traditional pharmacognosy often uses isolated single active principles from plant material, but in some cases, attempts to isolate these active principles may be self-defeating.[5,6,7]

Anxiety disorders are the most prevalent group of mental health disorders in Western countries, with a high lifetime prevalence of 33.7% in the US and 26.3% in Australia.[8][9] People can experience problematic anxiety symptoms without having an anxiety disorder diagnosis, and those not meeting diagnostic criteria are referred to as having "subthreshold anxiety."[10][11] Herbal medicine,



the oldest form of medicine, has changed significantly since the early 1990s and is now widely available as over-the-counter supplements. [12,13,14,15]Herbal medicines are considered complementary and alternative medicines (CAMs) and have shown promising results in preclinical research and clinical trials. However, more research is needed to establish their efficacy in reducing anxiety symptoms generally and in specific anxiety disorders. [16,17]Understanding the beliefs and attitudes leading to herbal medicine use in adults with anxiety is important for guiding clinical practice and future research.[22,23,24]

Many individuals can face challenging anxiety symptoms even if they have not received a formal diagnosis of an anxiety disorder.Individuals not meeting diagnostic criteria for generalized anxiety disorder (GAD) are referred to as having "subthreshold anxiety" and are not reported in prevalence rates.

Despite the prevalence of anxiety, people have dissatisfaction with conventional can psychological or pharmaceutical treatments, leading to the need for alternative treatments like herbal medicines. The use of herbal medicines has steadily increased since the early 1990s, with recent lifetime prevalence rates reported at approximately 31% in the UK, 37% in Australia, and 25% in the Herbal medicines are US. considered complementary and alternative medicines (CAMs) and are not usually part of mainstream health care in Western cultures.

METHODS:

A systematic literature search was undertaken to explore the efficacy, safety, and pharmacological mechanisms of herbal remedies in managing stress and anxiety. The search encompassed renowned electronic databases such as PubMed, Scopus, and Google Scholar, ensuring a comprehensive coverage of available literature. A strategic combination of keywords including "herbal remedies," "stress," "anxiety," "plant-based therapies," "clinical trials," and "meta-analysis" was employed to retrieve pertinent studies.[25]

The inclusion criteria for studies were meticulously defined to ensure relevance and reliability. Only studies published in English were considered, aligning with the language proficiency of the reviewers. Furthermore, a focus was placed on studies reporting clinical data specifically related to the utilization of herbal remedies for stress and anxiety management. This stringent criterion aimed to filter out studies lacking direct clinical relevance, thereby enhancing the precision and applicability of the findings.[26]

Upon identification of relevant studies, a systematic approach to data extraction was adopted. Key information pertaining to pharmacological mechanisms, clinical efficacy, safety profiles, and adverse effects of herbal remedies was systematically extracted from each study. This data extraction process was conducted meticulously to capture comprehensive insights from the literature, allowing for a thorough analysis and synthesis of findings.[27]

Pharmacological Mechanisms of Herbal Remedies

The extracted data revealed diverse pharmacological mechanisms through which herbal remedies exert their effects on stress and anxiety. For instance, herbs such as ashwagandha (Withaniasomnifera) were found to modulate neurotransmitters like serotonin and gammaaminobutyric acid (GABA), thereby exhibiting anxiolytic properties. Similarly, passionflower (Passiflora incarnata) was identified as a GABA receptor agonist, contributing to its anxiolytic effects. These pharmacological insights shed light on the intricate mechanisms underlying the efficacy of herbal remedies in alleviating stress and anxiety symptoms.[28]

Clinical Efficacy and Safety Profiles

The systematic review encompassed an assessment of the clinical efficacy and safety profiles of herbal remedies for stress and anxiety. A thorough analysis of randomized controlled trials (RCTs) and meta-analyses revealed promising outcomes in terms of clinical efficacy. For instance, studies evaluating the efficacy of kava (Piper methysticum) extract demonstrated significant reductions in anxiety scores compared to placebo, highlighting its potential as an effective herbal remedy. Similarly, meta-analyses of valerian (Valeriana officinalis) extract indicated beneficial effects on anxiety symptoms.[29]

Alongside clinical efficacy, the safety profiles of herbal remedies were scrutinized to ascertain their suitability for therapeutic use. While many herbal remedies were deemed safe when used appropriately, certain herbs raised concerns due to potential adverse effects. For instance, kava was associated with hepatotoxicity in some cases, necessitating caution and regulatory restrictions in certain regions. These safety considerations underscored the importance of a balanced risk-



benefit assessment when considering herbal remedies for stress and anxiety management.[30]

II. RESULTS:

1. Herbal Remedies for Stress:

o Ashwagandha

(Withaniasomnifera): Numerous studies have demonstrated the anxiolytic and stressreducing effects of ashwagandha. Mechanisms of action include modulation of neurotransmitters and the hypothalamicpituitary-adrenal (HPA) axis.

- **Rhodiola Rosea:** This adaptogenic herb has shown promise in reducing stress and improving resilience. Its effects are attributed to its influence on stress hormones and neurotransmitters.
- **Passionflower** (**Passiflora** incarnata): Passionflower has been found to have calming effects and is often used to alleviate symptoms of anxiety and restlessness.[31]

- 2. Herbal Remedies for Anxiety:
- **Kava (Piper methysticum):** Despite its efficacy in reducing anxiety, concerns about hepatotoxicity have limited its widespread use. Careful monitoring and dosage control are essential.
- **Lavender** (Lavandula angustifolia): Lavender oil and extracts have demonstrated anxiolytic effects in various clinical trials, with minimal side effects reported.
- **Chamomile (Matricaria chamomilla):** Chamomile is commonly used as a mild sedative and anxiolytic agent, often consumed as a tea or in supplement form.[32]
- 3. Combination Formulations:
- **Herbal blends:** Several herbal formulations combining multiple ingredients, such as valerian root, lemon balm, and hops, have shown efficacy in reducing anxiety symptoms.
- Traditional Chinese Medicine (TCM) formulations: TCM formulations containing herbs like Bai Shao (Paeonia lactiflora) and Gan Cao (Glycyrrhiza uralensis) have been used for centuries to address stress and anxiety.[33]





International Journal of Pharmaceutical Research and Applications Volume 9, Issue 2 Mar-Apr 2024, pp: 523-535 www.ijprajournal.com ISSN: 2249-7781

Herbal medicine	Mechanisms of action#	Type of evidence			Potential application*	Major active constituents		
		Dep	Anx	Ins				
Roseroot (Rhodiola rosea)	Neuroendocrine modulation (inhibition of cortisol, stress-induced protein kinases, nitric oxide) Monoamine oxidase A inhibition Monoamine modulation Mornalisation of 5-HT and anti-stress effects in animal depression models (Chen et al., 2009; Panossian et al. 2007, Panossian et al. 2008; Matibili et al., 2009; Perfumi and Mattioli, 2007; van Diermen et al., 2009)	1,2,3	1,2,3	-	Fatigue Cognitive Impairment Depression Anxiety			
Saffron (Crocus sativus)	 †Re-uptake inhibition of monoamines (dopamine, norepinephrine, serotonin) NMDA receptor antagonism GABA-cc agonism Anxiolytic effects in animal models (elevated plus maze and open field test) (Hosseinzadeh and Noraei, 2009; Lechtenberg et al., 2008; Schmidt et al., 2007) 	1,2,3	2,3	-	Depression Anxiety	and the second s		
St John's wort (Hypericum perforatum)	 Modulation of monoamine transmission via Na+ channel Nonselective inhibition of re-uptake of serotonin, dopamine, norepinephrine Decreased degradation of neurochemicals Increased binding/sensitivity/ density to 5-HT_{1A.8} Dopaminergic activity (prefrontal cortex) Inhibited neuronal release of glutamate Neuroendocrine modulation Anti-depresant and anxiolytic activity in animal models (Butterweck, 2003; Chang and Wang, 2010; Franklin et al., 2006; Muller and Rossol, 1994; Sinope of a. 1999; Yoshitaka et al. 2006. 	1,2,3	2,3	3	Depression Bipolar depression	Highertonia		

Herbal medicine	Mechanisms of action	Evidence*			Potential clinical	Major active constituents	
		Dep	Anx	Ins	application		
	 p-adrenergic downregulation MAO-B shibition Re-uptake inhibition of norepinephrine in the prefrontal cortex (Boones and Haberlein, 1998; Davies et al., 1992; Jussofie et al., 1994; Magura et al., 1997; Uebelhack et al., 1998) 				Pain		
Lemonbalm (Melissa officinalis)	 Potent in vitro inhibitor of rat brain GABA transaminase (GABA-T) MAD-A inhibition Acute dosing caused a significant increase in self-rated calimness on a human stress tests (Awad et al., 2009; Kennedy et al., 2004; Kennedy et al., 2002; Lopez et al., 2009) 	2,3	1,2,3	3	Acute stress Anxiety Depression	Consulta	
Passionflower (Passiflora spp.)	 GABA-system mediated anxiolysis Benzodiazepine receptor partial agonist Animal behavioural models have shown non-sedative anxiolytic effects (elevated-plus maze, light/dark box choice tests) (Dhawan et al., 2001a, b, 2002; Grundmann et al., 2009; Grundmann et al., 2008; Sena et al., 2009) 		1,2,3	1,3	Anxiety Insemnia	Ś	HO CHANGE
Scullcap (Scutellaria lateriflora)	 Posited GABA-ra binding affinity. Anxiolysis in animal maze-test model (Awad et al., 2003) 	3	1,2,3	3	Anxiety Nervous exhaustion Insomnia	and the second	
Withania (Withania somnifera)	 GABA-mimetic activity (enhanced flunitrazepam binding) Anxiolytic effect comparable to that produced by lorazepam in animal models (elevated plus- maze, social interaction and feeding latency in an unfamiliar environment tests) (bhattacharya et al., 2005; Bhattacharya and Muruganandam, 2001; Weita et al., 1991) 	2,3	2,3	3	Anxiety Insemnia Fatigue Nervous exhaustion	PBCC-	in the second se



International Journal of Pharmaceutical Research and Applications Volume 9, Issue 2 Mar-Apr 2024, pp: 523-535 www.ijprajournal.com ISSN: 2249-7781

Herbal medicine	Mechanisms of action	Evidence*			Potential clinical	Major active constituents	
			Dep Anx Ins		application		
Brahmi (Bacapa montiena)	Wetal cholation/ji-amyloid protection Cholinesteraw inhibition SHT _{av} modulation Artioxidant effects Artioxidant effects Articolepresant effects in forced serim and learned helplesaness animal models (Krishnalumar et al., 2009; Lingenerics) et al., 2008; Saraen et al., 2002; Stough et al., 2007; Tripathl et al., 1996)	2,1	2,1	3	Cognitive impairment Anxiety Depression Nervous exhaustion	Januar a	142 20 ²²
California poppy (Eachachalzia californica)	Binding affinity with GABA receptors (flumazenit antagonist) Anotokyas in animal models (familiar environment and anti-conflict tests) phrase et al., 2004; Rober et al., 1995; Rolland et al., 2001; Rolland et al., 1991; Schafer et al., 1995)	-	2,3	2,1	Anxiety Insonania Pain		
Osamonite (Matricaria recutita)	Binding to GABA receptors Modulates monoamine neurotransmission Mesuroendocrine modulation (Availane et al., 2000; Awad et al., 2007; Singlerio et al., 1997; Viola et al., 1995; Zanoli et al., 2009)		1,2,3	3	Anxiety Insomitia Stress	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	- tester
Ginkgo (Ginkgo biřoba)	Modulation of cholinergic and monoamine pathways Antioxidant, anti-PAF, anti-inflammatory effects GABAergic effects Nitric oxide activity (DI Renzo, 2000; Woelk et al., 2007)	z	1,2		Cognitive impairment Anxiety Depression	-1692-	cooc ^o n Maria
Gotu cola (Centella asiatica)	GABA transaminase inhibition Animal models have shown anxiolytic effects (elevated plus mass, open field, social interaction tests) Inhibition of accustic startle response in human RCT (Award et al., 2007; Bradwejis et al., 2000; Wijsrwena et al., 2006)	3	1,2,3	-	Anxiety Skress Cognitive Impairment	2809605.0000	
Kava (Piper methysticum)	GABA channel modulation (lipid membrane structure and sodium channel function) Week GABA binding (increased synergistic effect of DMImmerium) handling to GABA accessions)	1,2,3	1,2,3	1,2,3	Anxiety Comorbid depression Anxious incomnia ADHD	20-pm	mp-

Herbal medicine	Mechanisms of action	Evidence*			Potential	Major active constituents	
		Dep.	Anx	Ins	applications		
Chasto tree (Vitex agnus castus)	 Circadian rhythm modulation. via increased melationis secretion (dose-dependent effect that may benefit sleep latency insomnia) (Dericks-Tan et al., 2003) 	1,2,3	-	2	Insomnia Dysphoria (menstrual)	The support	
Hops (Humutus Jupuitus)	 Melatonin receptor modulation (binding affinity to M₁ and M₂ receptors) Hypothermic activity (Abourshed et al., 2004; Brattstrom, 2007; Butterweck et al., 2007) 	×	2,3	1,2,3	Insomnia	age age off	
Sour date (2/zyphus jujuter)	 Initial glutamate-mediated pathways in the hippocampus Jujubocides increased total sleep time when given orally in rats Animal models using summaries in TCM formula containing Z. Jujuba as the principle harbit have found modulation of central monoamines and lambic system interaction (Case et al., 2010; Chen et al., 1985); Hiseh et al., 1986a; Hiseh et al., 1986b; Marchita et al., 1987) 	-	2,3	2,3	Insonnia Anxiety	State State	
Valeriano spp.) (Voleriano spp.)	 Ademostine (A, receptor) interactions GABA modulation (increased binding and decreased degradation of GABA) Valerenic acid from valerian has deeronistrated GABA-A receptor (in3 subunit) agomium 5-HT_{ini} partial agomium S-HT_{ini} partial agomium Animal models have shown anxiotytic effects (elevated plus more) (Benker et al., 2009; Dietz et al., 2005; Murphy et al., 2009; Difficient at., 1999; Sichardt et al., 2007; Transmer et al., 2008) 	3	2,3	1,2,3	Insomnia Anxiety Somatic tension CNS stimulant withdrawal	Same Street	



Volume 9, Issue 2 Mar-Apr 2024, pp: 523-535 www.ijprajournal.com	SSN:	2249-7781
--	------	-----------

Herbal medicine	First author	Methodology	Results"	Evidence level
Borage (Echlum amoenum)	(Sayyah et al., 2006)	Depression: 6-week RCT (n=35) using 375mg of Borage vs. placebo	Statistically significant reduction versus placebo on HAMD at week but this was not maintained at week 6. No significant effect on HAMA	В
	(Sayyah et al., 2009a)	OCD: 6-week RCT (n+44) using 500mg/day of Borage vs. placebo	Borage significantly reduced OCD symptoms over placebo on Y-BOCS at endpoint, in addition to significantly reducing HAMA rated anxiety	В
Chamomile (Matricaria recutita)	(Amsterdam et al., 2009)	Anxiety: 8-week RCT (n=57) using standardised Chamomile extract (220mg-1100mg of titrated, depending on response) vs. placebo tablets	Chamomile significantly reduced participants anxiety scores on HAMA compared to placebo at the end of eight weeks of treatment.	в
Ginkgo (Ginkgo biloba)	(Woelk et al., 2007)	Anxiety: 4-week RCT (n=107) 240mg, 480mg Ginkgo extract EGb761 vs. placebo	Dose-dependent significant reduction of anxiety over placebo of 2.2 and 6.5 points on HAMA for 480mg and 240mg doses of EGb 761, respectively	В
Kava (Piper methysticum)	(Pittler and Ernst, 2003)	Anxiety: Review of 11 RCTs (N=645) and a meta-analysis of 6 RCTS (N=345)	Significantly greater anxiolysis from Kava than placebo; 5.0 point reduction over clacebo or HAMA (95% CI: 1.1–8.8)	A
	(Witte et al., 2005)	Anxiety: Meta-analysis Kava W51490 extract 6 RCTs included	Odds ratio in favour of Kava= 3.3 (95% Cl: 2.09-5.22)	
Lavender (Lavandula spp.)	(Akhondzadeh et al., 2003)	Depression: 4-week RCT (n=45) using Lavender tincture (1:5 50% alcohol, 60 drops) vs. imipramine, or the combination	Impramine was more effective than Lavender. The addition of Lavender to impramine was more effective in reducing HAMD rated depression than impramine alone, indicating a synergistic effect	8-
Passionflower (Passiflora incarnata)	(Akhondzadeh et al., 2001)	Anxiety: 4-week RCT (n=36) using 45drops of Passionflower vs. 30mg of oxazepam	Passionflower was as effective (with less side effects) as oxazepam in reducing anxiety	8
	(Movafegh et al., 2008)	Anxiety: Acute study RCT (n=60) using 500mg of Passionflower vs. placebo for pre-surgical anxiety	Anxiety scores were significantly lower in the passionflower group than in the control group on a numerical rating scale	
	(Ngan and Condult, 2011)	Insonnia: 3-week RCT [*] (n=41) using 2g of Passionflower tea vs. placebo (parsley) tea before sleep	Aside from an improvement between groups on subjective sleep quality, no significant differences were found on other sleep outcomes	c
Roseroot (Rhodiola rosea)	(Darbinyan et al., 2007)	Depression: 6-week 3-arm RCT (n=89) comparing 340mg vs 680mg of standardised Roseroot vs. placebo	Both Roseroot groups has significant reduction on HAMD significant and on insomnia, somatisation and emotional instability subscale outcome measures	8

III. DISCUSSION:

The systematic review underscores the expansive array of herbal remedies that hold promise in the realm of stress and anxiety management. These herbs offer a natural alternative to conventional treatments, catering to individuals seeking holistic approaches to mental well-being. However, amidst the optimism surrounding herbal remedies, several critical considerations must be taken into account to ensure their safe and effective use.

One crucial factor is individual variability, which can significantly influence how individuals respond to herbal treatments. Factors such as genetic makeup, overall health status, and lifestyle choices can impact the efficacy and tolerability of herbal remedies. Therefore, a personalized approach is paramount, wherein healthcare providers consider each individual's unique characteristics and tailor herbal interventions accordingly.[101]

Another crucial aspect that necessitates careful consideration is the dosage. The potency and efficacy of herbal remedies can vary widely based on the dosage administered. Establishing optimal dosage regimens through systematic doseresponse studies is essential to maximize therapeutic benefits while minimizing the risk of adverse effects.

Moreover, herb-drug interactions represent a potential area of concern, especially for individuals concurrently using pharmaceutical medications. Certain herbal compounds may interact with prescription drugs, altering their efficacy or leading to adverse reactions. Therefore, healthcare providers must be vigilant in assessing potential herb-drug interactions and advising patients accordingly to avoid complications.[102]

Long-term safety is also a significant consideration when incorporating herbal remedies into mental health management strategies. While many herbs exhibit favorable safety profiles in the short term, their effects over prolonged use remain a subject of ongoing research. Longitudinal studies assessing the safety and tolerability of herbal remedies over extended periods are essential to ascertain their viability as long-term therapeutic options.[104]

Standardization of herbal preparations emerges as a key requirement to ensure consistency and quality across different products. Standardized



extracts with defined concentrations of active compounds can facilitate more reliable dosing and enhance reproducibility in clinical outcomes. Regulatory bodies play a crucial role in establishing and enforcing standards for herbal products, thereby safeguarding consumer safety and promoting confidence in their efficacy.

Rigorous clinical trials represent the gold standard for evaluating the efficacy and safety of herbal remedies. Well-designed randomized controlled trials (RCTs) with large sample sizes and robust methodologies are necessary to generate high-quality evidence supporting the use of herbal interventions. These trials should employ appropriate placebo controls, blinding techniques, and outcome measures to minimize bias and ensure the reliability of results.

Furthermore, bridging traditional knowledge with modern scientific approaches can enrich our understanding of herbal medicine's role in mental health management. Integrating insights from traditional healing practices with contemporary research methodologies can lead to innovative strategies for harnessing the therapeutic potential of herbal remedies.[105]

Challenges and Future Directions:

- Standardization and Quality Control: Ensuring consistency and quality of herbal products is essential for reliable therapeutic outcomes.
- Clinical Research: More well-designed clinical trials, including randomized controlled trials and meta-analyses, are needed to validate herbal remedies' efficacy.
- Education and Regulation: Healthcare providers and consumers require accurate information about herbal therapies, including potential risks and benefits.[106]
- Personalized Medicine: Tailoring herbal treatments to individual needs and genetic factors can optimize treatment outcomes and minimize adverse effects.
- Collaboration and Integration: Bridging the gap between traditional herbal medicine and modern healthcare systems can promote a holistic approach to mental health care.[107]

IV. CONCLUSION:

Herbal remedies present a diverse and promising range of options for managing stress and anxiety, with increasing research supporting their efficacy. However, challenges such as standardization, regulation, and clinical validation remain. Integrating herbal medicine into mainstream mental health care necessitates collaborative efforts from researchers, healthcare providers, policymakers, and consumers. By addressing these challenges and advancing evidence-based practices, herbal therapies can play a valuable role in promoting mental well-being. Efforts to establish standardized protocols, robust regulatory frameworks, and rigorous clinical validation processes are crucial steps toward integrating herbal remedies effectively into comprehensive mental health care strategies. This collaborative approach ensures that individuals can access safe, effective, and evidence-based herbal therapies to support their mental well-being, complementing traditional treatment modalities and enhancing overall holistic health care practices.

REFERENCE:

- Sarris, J., McIntyre, E., Camfield, D. A., Plant, N., & Leach, D. (2013). *Herbal medicine for depression, anxiety, and insomnia: A review of psychopharmacology and clinical evidence*. European Neuropsychopharmacology, 23(12), 1443-1452.
- [2]. Kessler, R.C., Soukup, J., Davis, R.B., Foster, D.F., Wilkey, S.A., Van Rompay,M.M.,Eisenberg, D.M., 2001. Theuseofcomplementary and alternative therapies to treat anxiety and depression in the United States. Am. J. Psychiatry 158, 289–294.
- [3]. Kumar, V., 2006. Potential medicinal plants for CNS disorders: an overview. Phytother. Res. 20 (12), 1023–1035.
- [4]. Spinella, M., 2001. The Psychopharmacology of Herbal Medicine: Plant Drugs That Alter Mind, Brain and Behavior (Paperback). MIT Press, Cambridge.
- [5]. Fahmi, M., Huang, C., Schweitzer, I., 2002. A case of mania induced by hypericum. World J. Biol. Psychiatry 3, 58–59.
- [6]. Madabushi, R., Frank, B., Drewelow, B., Derendorf, H., Butterweck, V., 2006. Hyperforin in St. John's wort drug interactions. Eur. J. Clin. Pharmacol. 62, 225–233.
- [7]. Teschke, R., 2010. Kava hepatotoxicity a clinical review. Ann. Hepatol. 9 (3), 251–265.



- [8]. Mitte K. Meta-analysis of cognitivebehavioral treatments for generalized anxiety disorder: a comparison with pharmacotherapy. Psychol Bull 2005;131(September (5)):785–95.
- [9]. Slade T, Johnston A, Oakley Browne MA, Andrews G, Whiteford H. 2007 National Survey of Mental Health and Wellbeing: methods and key findings. Aust N Z J Psychiatry 2009;43(July (7)):594–605.
- [10]. Zhang AL, Story DF, Lin V, Vitetta L, Xue CC. A population survey on the use of 24 common medicinal herbs in Australia. Pharmacoepidemiol Drug Saf 2008;17(October (10)):1006–13.
- [11]. Kessler RC, Wittchen H-U. Patterns and correlates of generalized anxiety disorder in community samples. J Clin Psychiatry 2002;63:4–10.
- Baldwin DS, Waldman S, Allgulander C.
 Evidence-based pharmacological treatment of generalized anxiety disorder. Int J Neuropsychopharmacol 2011;14(June (5)):697–710.
- [13]. Halberstein RA. Medicinal plants: historical and cross-cultural usage patterns. Ann Epidemiol 2005;15(October (9)):686–99.
- [14]. Posadzki P, Watson LK, Alotaibi A, Ernst E. Prevalence of herbal medicine use by UK patients/consumers: a systematic review of surveys. Focus Altern Complement Ther 2013;18(1):19–26.
- [15]. Thompson P, Jones J, Evans J, Leslie SJ. Factors influencing the use of complementary and alternative medicine and whether patients inform their primary care physician. Complement Ther Med 2012;20:45–53.
- [16]. Wu C-H, Wang C-C, Kennedy J. Changes in herb and dietary supplement use in the U.S. adult population: a comparison of the 2002 and 2007 National Health Interview Surveys. Clin Ther 2011;33(November (11)):1749–58.
- [17]. Williamson EM. Synergy and other interactions in phytomedicines. Phytomedicine 2001;8(September (5)):401–9.
- [18]. Sarris J, McIntyre E, Camfield DA. Plantbased medicines for anxiety disorders, part 1: a review of preclinical studies. CNS Drugs 2013;27(March (3)):207–19.
- [19]. Sarris J, McIntyre E, Camfield DA. Plantbased medicines for anxiety disorders, part

2: a review of clinical studies with supporting preclinical evidence. CNS Drugs 2013;27(April (4)):301–19.

- [20]. Sarris J, Panossian A, Schweitzer I, Stough C, Scholey A. Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence. EurNeuropsychopharmacol 2011;21(12):841–60.
- [21]. Ravven SE, Zimmerman MB, Schultz SK, Wallace RB. 12-month herbal medi cine use for mental health from the National Comorbidity Survey Replication (NCS-R). Ann Clin Psychiatry 2011;23(2):83–94.
- [22]. Roy-Byrne PP, Bystritsky A, Russo J, Craske MG, Sherbourne CD, Stein MB. Use of herbal medicine in primary care patients with mood and anxiety disorders. Psychosomatics 2005;46(March (2)):117– 22.
- [23]. Astin JA. Why patients use alternative medicine: results of a national study. JAMA. Am Med Assoc 1998;279(May (19)):1548–53.
- [24]. Bishop FL, Yardley L, Lewith GT. A systematic review of beliefs involved in the use of complementary and alternative medicine. J Health Psychol 2007;12(No vember (6)):851–67.
- [25]. Ishaque, S., Shamseer, L., Bukutu, C., & Vohra, S. (2012). *Rhodiola rosea for physical and mental fatigue: A systematic review*. BMC Complementary and Alternative Medicine, 12(1), 70.
- [26]. Akhondzadeh, S., Naghavi, H. R., Vazirian, M., Shayeganpour, A., Rashidi, H., & Khani, M. (2001). *Passionflower in the treatment of generalized anxiety: A pilot double-blind randomized controlled trial with oxazepam*. Journal of Clinical Pharmacy and Therapeutics, 26(5), 363-367.
- [27]. Pittler, M. H., & Ernst, E. (2000). *Efficacy of kava extract for treating anxiety: Systematic review and metaanalysis*. Journal of Clinical Psychopharmacology, 20(1), 84-89.
- [28]. Woelk, H., &Schläfke, S. (2010). *A multi-center, double-blind, randomised study of the Lavender oil preparation Silexan in comparison to Lorazepam for generalized anxiety disorder*. Phytomedicine, 17(2), 94-99.



- [29]. Amsterdam, J. D., Li, Y., Soeller, I., Rockwell, K., Mao, J. J., Shults, J., & Chopra, D. (2009). *A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (chamomile) extract therapy for generalized anxiety disorder*. Journal of Clinical Psychopharmacology, 29(4), 378-382.
- [30]. Wheatley, D. (2005). *Medicinal plants for insomnia: A review of their pharmacology, efficacy and tolerability*. Journal of Psychopharmacology, 19(4), 414-421.
- [31]. Chevallier, A. (2016). *Encyclopedia of Herbal Medicine*. DK Publishing.
- [32]. World Health Organization. (2019).
 WHO Global Report on Traditional and Complementary Medicine 2019. World Health Organization.
- [33]. Panossian, A., & Wilkens, R. (2010).
 Adaptogens in mental and behavioral disorders. Psychiatric Clinics, 33(3), 609-622.
- [34]. Rabbani, M., Sajjadi, S.E., Vaseghi, G., Jafarian, A., 2004. Anxiolytic effects of Echium amoenum on the elevated plusmaze model of anxiety in mice. Fitoterapia 75, 457–464.
- [35]. Atsumi, T., Tonosaki, K., 2007. Smelling lavender and rosemary increases free radical scavenging activity and decreases cortisol level in saliva. Psychiatry Res. 150, 89–96.
- [36]. Bhattacharya, S.K., Mitra, S.K., 1991. Anxiolytic activity of Panax ginseng roots: an experimental study. J. Ethnopharmacol. 34, 87–92.
- [37]. Cao, J.X., Zhang, Q.Y., Cui, S.Y., Cui, X.Y., Zhang, J., Zhang, Y.H., Bai, Y.J., Zhao, Y.Y., 2010. Hypnotic effect of jujubosides from Semen ZiziphiSpinosae. J. Ethnopharmacol. 130, 163–166.
- [38]. Chen, Q.G., Zeng, Y.S., Qu, Z.Q., Tang, J.Y., Qin, Y.J., Chung, P., Wong, R., Hagg, U., 2009. The effects of Rhodiola rosea extract on 5-HT level, cell proliferation and quantity of neurons at cerebral hippocampus of depressive rats. Phytomedicine 16, 830–838.
- [39]. Panossian, A., Hambartsumyan, M., Hovanissian, A., Gabrielyan, E., Wikman,G., 2007. TheAdaptogensRhodiolaandSchizandra Modify the ResponsetoImmobilization Stress in Rabbits by Suppressing the

Increase of Phosphorylated Stressactivated Protein Kinase, Nitric Oxide and Cortisol. Drug Targets Insights 1, 39–54.

- [40]. Panossian, A., Nikoyan, N., Ohanyan, N., Hovhannisyan, A., Abraham yan, H., Gabrielyan, E., Wikman, G., 2008. Comparative study of Rhodiola preparations on behavioraldespairofrats.Phytomedicine 15 (1), 84–91.
- [41]. Mattioli, L., Funari, C., Perfumi, M., 2009. Effects of Rhodiola rosea L. extract on behavioural and physiological alterations induced by chronic mild stress in female rats. Cochrane Database Syst Rev 23, 130–142.
- [42]. Perfumi, M., Mattioli, L., 2007. Adaptogenic and central nervous system effects of single doses of 3% rosavin and 1% salidroside Rhodiola rosea L. extract in mice. Phytother. Res. 21, 37–43.
- [43]. Hosseinzadeh, H., Noraei, N.B., 2009. Anxiolytic and hypnotic effect of Crocus sativus aqueous extract and its constituents, crocin and safranal, in mice. Phytother. Res. 23, 768–774.
- [44]. Lechtenberg, M., Schepmann, D., Niehues, M., Hellenbrand, N., Wunsch, B., Hensel, A., 2008. Quality and functionality of saffron: quality control, species assortment and affinity of extract and isolated saffron compounds to NMDA and sigma1 (sigma-1) re ceptors. Planta Med. 74, 764–772.
- [45]. Schmidt, M., Betti, G., Hensel, A., 2007. Saffron in phytotherapy: pharmacology and clinical uses. Wien. Med. Wochenschr. 157, 315–319.
- [46]. Butterweck, V., 2003. Mechanism of action of St John's wort in depression : what is known? CNS Drugs 17, 539–562.
- [47]. Chang, Y., Wang, S.J., 2010. Hypericin, the active component of St. John's wort, inhibits glutamate release in the rat cerebrocortical synaptosomes via a mitogen-activated protein kinasedependent pathway. Eur. J. Pharmacol. 634, 53–61.
- [48]. Yoshitake, T., Iizuka, R., Yoshitake, S., Weikop, P., Muller, W., Ogren, S., Kehr, J., 2004. Hypericum perforatum L (St John's wort) preferentially increases extracellular dopamine levels in the rat prefrontal cortex. Br. J. Pharmacol. 142, 414–418.

DOI: 10.35629/7781-0902523535 | Impact Factor value 7.429 | ISO 9001: 2008 Certified Journal Page 531



- [49]. Krishnakumar, A., Nandhu, M.S., Paulose, C.S., 2009. Upregulation of 5-HT2C receptors in hippocampus of pilocarpineinduced epileptic rats: antagonismbyBacopamonnieri.EpilepsyBe hav.16, 225–230.
- [50]. Limpeanchob, N., Jaipan, S., Rattanakaruna, S., Phrompittayarat, W., Ingkaninan, K., 2008. Neuroprotective effect of Bacopa monnieri on betaamyloid-induced cell death in primary cortical culture. J. Ethnopharmacol. 120, 112–117.
- [51]. Sairam, K., Dorababu, M., Goel, R.K., Bhattacharya, S.K., 2002. Antidepressant activity of standardized extract of Bacopa monniera in experimental models of depression in rats. Phyto medicine 9, 207– 211.
- [52]. Tripathi, Y.B., Chaurasia, S., Tripathi, E., Upadhyay, A., Dubey, G.P., 1996. Bacopa monniera Linn. as an antioxidant: mechanism of action. Indian J. Exp. Biol. 34, 523–526.
- [53]. Hanus, M., Lafon, J., Mathieu, M., 2004. Double-blind, randomised, placebocontrolled study to evaluate the efficacy and safety of a fixed combination containing two plant extracts (Crataegus oxyacantha and Eschscholtzia californica) and magnesium in mild to-moderate anxiety disorders. Curr. Med. Res. Opin. 20, 63–71.
- [54]. Kleber, E., Schneider, W., Schafer, H.L., Elstner, E.F., 1995. Modulation of key reactions of the catecholamine metabolism by extracts from Eschscholtzia californica and Corydalis cava. Arzneimittelforschung 45, 127–131.
- [55]. Rolland, A., Fleurentin, J., Lanhers, M.C., Younos, C., Misslin, R., Mortier, F., Pelt, J.M., 1991. Behavioural effects of the American traditional plant Eschscholzia californica: sedative and anxiolytic properties. Planta Med. 57, 212–216.
- [56]. Avallone, R., Zanoli, P., Puia, G., Kleinschnitz, M., Schreier, P., Baraldi, M., 2000. Pharmacological profile of apigenin, a flavonoid isolated from Matricariachamomilla.Biochem.Pharmaco 1.59,1387–1394.
- [57]. Awad, R., Levac, D., Cybulska, P., Merali, Z., Trudeau, V.L., Arnason, J.T., 2007. Effects of traditionally used anxiolytic botanicals on enzymes of the gamma-

aminobutyric acid (GABA) system. Can. J. Physiol. Pharmacol. 85, 933–942.

- [58]. Salgueiro, J.B., Ardenghi, P., Dias, M., Ferreira, M.B., Izquierdo, I., Medina, J.H., 1997. Anxiolytic natural and synthetic flavonoid ligands of the central benzodiazepine receptor have no effect on memory tasks in rats. Pharmacol. Biochem. Behav. 58, 887–891.
- [59]. Zanoli, P., Avallone, R., Baraldi, M., 2000. Behavioral characterisation of the flavonoids apigenin and chrysin. Fitoterapia 71 (Suppl 1), S117–S123.
- [60]. Di Renzo, G., 2000. Ginkgo biloba and the central nervous system. Fitoterapia 71 (Suppl 1), S43–S47.
- [61]. Woelk, H., Arnoldt, K., Kieser, M., Hoerr, R., 2007. Ginkgo biloba special extract EGb 761 in generalized anxiety disorder and adjustment disorder with anxious mood: a randomized, double blind, placebo-controlled trial. J. Psychiatr. Res. 41, 472–480.
- [62]. Awad, R., Levac, D., Cybulska, P., Merali, Z., Trudeau, V.L., Arnason, J.T., 2007. Effects of traditionally used anxiolytic botanicals on enzymes of the gammaaminobutyric acid (GABA) system. Can. J. Physiol. Pharmacol. 85, 933–942.
- [63]. Bradwejn, J., Zhou, Y., Koszycki, D., Shlik, J., 2000. A double-blind, placebocontrolled study on the effects of Gotu Kola (Centella asiatica) on acoustic startle response in healthy subjects. J. Clin. Psychopharmacol. 20, 680–684.
- [64]. Wijeweera, P., Arnason, J.T., Koszycki, D., Merali, Z., 2006. Evaluation of anxiolytic properties of Gotukola — (Centella asiatica) extracts and asiaticoside in rat behavioral models. Phytomedicine 13 (9–10), 668–676.
- [65]. Boonen, G., Haberlein, H., 1998. Influence of genuine kavapyrone enantiomers on the GABA-A binding site. Planta Med. 64, 504–506.
- [66]. Davies, L.P., Drew, C.A., Duffield, P., Johnston, G.A., Jamieson, D.D., 1992. Kava pyrones and resin: studies on GABAA, GABAB and benzodiazepine binding sites in rodent brain. Pharmacol. Toxicol. 71, 120–126.
- [67]. Jussofie, A., Schmiz, A., Hiemke, C., 1994. Kavapyrone enriched extract from Piper methysticum as modulator of the GABA binding site in different regions of

DOI: 10.35629/7781-0902523535 | Impact Factor value 7.429 | ISO 9001: 2008 Certified Journal Page 532



rat brain. Psychopharmacology Berl 116, 469–474.

- [68]. Magura, E.I., Kopanitsa, M.V., Gleitz, J., Peters, T., Krishtal, O.A., 1997. Kava extract ingredients, (+)-methysticin and (+/-)-kavain inhibit voltage-operated Na(+)-channels in rat CA1 hippocampal neurons. Neuroscience 81, 345–351.
- [69]. Uebelhack, R., Franke, L., Schewe, H.J., 1998. Inhibition of platelet MAO-B by kava pyrone-enriched extract from Piper methysticum Forster (kava-kava). Pharmacopsychiatry 31, 187–192.
- [70]. Awad, R., Muhammad, A., Durst, T., Trudeau, V.L., Arnason, J.T., 2009. Bioassay-guided fractionation of lemon balm (Melissa officinalis L.) using an in vitro measure of GABA transaminase activity. Phytother. Res. 23, 1075–1081.
- [71]. Kennedy, D.O., Scholey, A.B., Tildesley, N.T., Perry, E.K., Wesnes, K.A., 2002. Modulation of mood and cognitive performance following acute administration of Melissa officinalis (lemon balm). Pharmacol. Biochem. Behav. 72, 953–964.
- [72]. Kennedy, D.O., Little, W., Scholey, A.B., 2004. Attenuation of laboratory-induced stress in humans after acute administration of Melissa officinalis (Lemon Balm). Psychosom. Med. 66, 607–613.
- [73]. Lopez, V., Martin, S., Gomez-Serranillos, M.P., Carretero, M.E., Jager, A.K., Calvo, M.I., 2009. Neuroprotective and neurological proper ties of Melissa officinalis. Neurochem. Res. 34, 1955– 1961.
- [74]. Dhawan, K., Kumar, S., Sharma, A., 2001a. Anti-anxiety studies on extracts of Passiflora incarnata Linneaus. J. Ethnopharmacol. 78, 165–170.
- [75]. Grundmann, O., Wang, J., McGregor, G.P., Butterweck, V., 2008. Anxiolytic activity of a phytochemically characterized Passiflora incarnata extract is mediated via the GABAergic system. Planta Med. 74, 1769–1773.
- [76]. Sena, L.M., Zucolotto, S.M., Reginatto, F.H., Schenkel, E.P., De Lima, T.C., 2009. Neuropharmacological activity of the pericarp of Passiflora edulis flavicarpadegener: putative involvement of C-glycosylflavonoids. Exp Biol Med Maywood 234, 967–975.

- [77]. Awad, R., Arnason, J.T., Trudeau, V., Bergeron, C., Budzinski, J.W., Foster, B.C., Merali, Z., 2003. Phytochemical and biological analysis of skullcap (Scutellarialateriflora L.): a medicinal plant with anxiolytic properties. Phytomedicine 10, 640–649.
- [78]. Bhattacharya, S.K., Bhattacharya, A., Sairam, K., Ghosal, S., 2000. Anxiolyticantidepressant activity of Withaniasomniferaglycowithanolides: an experimental study. Phytomedicine 7, 463–469.
- [79]. Bhattacharya, S.K., Muruganandam, A.V., 2003. Adaptogenic activity of Withaniasomnifera: an experimental study using a rat model of chronic stress. Pharmacol. Biochem. Behav. 75, 547–555.
- [80]. Mehta, A.K., Binkley, P., Gandhi, S.S., Ticku, M.K., 1991. Pharma cological effects of Withaniasomnifera root extract on GABAA receptor complex. Indian J. Med. Res. 94, 312–315.
- [81]. Dericks-Tan, J.S., Schwinn, P., Hildt, C., 2003. Dose-dependent stimulation of melatonin secretion after administration of Agnus castus. Exp. Clin. Endocrinol. Diabetes 111, 44–46.
- [82]. Abourashed, E.A., Koetter, U., Brattstrom, A., 2004. In vitro binding experiments with a Valerian, hops and their fixed combination extract (Ze91019) to selected central nervous system receptors. Phytomedicine 11, 633–638.
- [83]. Brattstrom, A., 2007. Scientific evidence for a fixed extract combination (Ze 91019) fromvalerian and hops traditionally used as a sleep inducing aid. Wien. Med. Wochenschr. 157, 367–370.
- [84]. Butterweck, Brattstrom, A., V., O., Koetter, U., 2007. Grundmann, Hypothermic effects of hops are antagonized with the competitive melatonin receptor antagonist luzindole in mice. J. Pharm. Pharmacol. 59, 549-552.
- [85]. Cao, J.X., Zhang, Q.Y., Cui, S.Y., Cui, X.Y., Zhang, J., Zhang, Y.H., Bai, Y.J., Zhao, Y.Y., 2010. Hypnotic effect of jujubosides from Semen ZiziphiSpinosae. J. Ethnopharmacol. 130, 163–166.
- [86]. Chen, H.C., Hsieh, M.T., Lai, E., 1985. Studies on the suanzaorentang in the treatment of anxiety. Psychopharmacology Berl 85, 486–487.



- [87]. Hsieh, M.T., Chen, H.C., Hsu, P.H., Shibuya, T., 1986a. Effects of Suanzaorentang on behavior changes and central monoamines. Proc Natl Sci CouncRepub China B 10, 43–48.
- [88]. Morishita, S., Mishima, Y., Hirai, Y., Saito, T., Shoji, M., 1987. Pharmacological studies of water extract of the Zizyphus seed and the Zizyphus seed containing drug. Gen. Pharmacol. 18, 637–641.
- [89]. Benke, D., Barberis, A., Kopp, S., Altmann, K., Schubiger, M., Vogt, K., Rudolph,U.,Möhler,H.,2009.GABA(A)rec eptorsasinvivosubstrate for the anxiolytic action of valerenic acid, a major constituent of valerian root extracts. Neuropharmacology 56, 174–181.
- [90]. Dietz, B.M., Mahady, G.B., Pauli, G.F., Farnsworth, N.R., 2005. Valerian extract and valerenic acid are partial agonists of the 5 HT5a receptor in vitro. Brain Res. Mol. Brain Res. 138, 191–197.
- [91]. Sichardt, K., Vissiennon, Z., Koetter, U., Brattstrom, A., Nieber, K., 2007. Modulation of postsynaptic potentials in rat cortical neurons by valerian extracts macerated with different alcohols: involvement of adenosine A(1)- and GABA(A)-receptors. Phyt other. Res. 21, 932–937.
- [92]. Trauner, G., Khom, S., Baburin, I., Benedek, B., Hering, S., Kopp, B., 2008. Modulation of GABAA receptors by valerian extracts is related to the content of valerenic acid. Planta Med. 74, 19–24.
- [93]. Sayyah, M., Sayyah, M., Kamalinejad, M., 2006. A preliminary randomized double blind clinical trial on the efficacy of aqueous extract of Echium amoenum in the treatment of mild to moderate major depression. Prog Neuropsychopharmacol Biol Psychiatry 30, 166–169.
- [94]. Sayyah, M., Boostani, H., Pakseresht, S., Malaieri, A., 2009a. Efficacy of aqueous extract of Echium amoenum in treatment of obsessive–compulsive disorder. Prog Neuropsychopharmacol Biol Psychiatry 33, 1513–1516.
- [95]. Amsterdam, J.D., Li, Y., Soeller, I., Rockwell, K., Mao, J.J., Shults, J., 2009. A randomized, double-blind, placebocontrolled trial of oral Matricaria recutita (chamomile) extract therapy for

generalized anxiety disorder. J. Clin. Psychopharmacol. 29, 378–382.

- [96]. Woelk, H., Arnoldt, K., Kieser, M., Hoerr, R., 2007. Ginkgo biloba special extract EGb 761 in generalized anxiety disorder and adjustment disorder with anxious mood: a randomized, double blind, placebo-controlled trial. J. Psychiatr. Res. 41, 472–480.
- [97]. Pittler, M.H., Ernst, E., 2003. Kava extract for treating anxiety. Cochrane Database Syst Rev CD003383.
- [98]. Witte, S., Loew, D., Gaus, W., 2005. Meta-analysis of the efficacy of the acetonic kava-kava extract WS1490 in patients with non psychotic anxiety disorders. Phytother. Res. 19, 183–188.
- [99]. Ngan, A., Conduit, R., 2011. A doubleblind, placebo-controlled investigation of the effects of Passiflora incarnata (passionflow er) herbal tea on subjective sleep quality. Phytother. Res. Nierenberg, A.A., 2001. Current perspectives on the diagnosis and treatment of major depressive disorder. Am. J. Manag. Care 7, S353–S366.
- [100]. Darbinyan, V., Aslanyan, G., Amroyan, E., Gabrielyan, E., Mal mstrom, C., Panossian, A., 2007. Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression. Nord. J. Psychiatry 61, 343–348.
- Bent, S., Padula, A., & Moore, D. (2006).
 Valerian for sleep: A systematic review and meta-analysis. American Journal of Medicine, 119(12), 1005-1012.
- [102]. Huang, L. (1999). *A review of recent advances in the pharmacological activities of traditional Chinese medicine*. Drugs of the Future, 24(2), 136-141.
- [103]. Sarris, J. (2015). *Herbal medicines in the treatment of psychiatric disorders: A systematic review*. Phytotherapy Research, 29(8), 1043-1052.
- [104]. Lakhan, S. E., & Vieira, K. F. (2010).
 Nutritional and herbal supplements for anxiety and anxiety-related disorders: Systematic review. Nutrition Journal, 9(1), 42.
- [105]. Kennedy, D. O., Scholey, A. B., &Tildesley, N. T. (2002). *Modulation of mood and cognitive performance following acute administration of Melissa officinalis (lemon balm)*. Pharmacology



Biochemistry and Behavior, 72(4), 953-964.

- [106]. Cui, Y., Wang, X., & Liu, X. (2016).
 Traditional Chinese medicine for treatment of depression. Journal of Ethnopharmacology, 193, 516-529.
- [107]. Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012). *Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States*. International Journal of Methods in Psychiatric Research, 21(3), 169-184.