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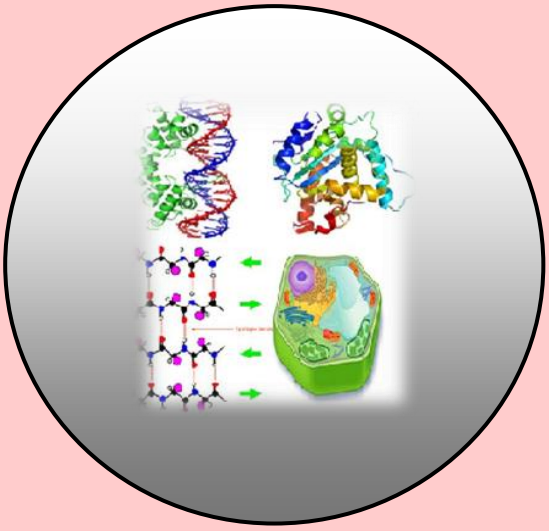

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Role of Plant based Medicines in the Post-traumatic Stress Disorder

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ABSTRACT
Post-traumatic stress disorder develops after experiencing traumatic incidents. In this disorder, feelings of phobia, anxiety and helplessness develop and progress. General symptoms of the disorder are flashbacks and nightmares, repulsive memories such as noises, objects reminding the traumatic events, hyperexcitability, high irritability and avoiding things or events linked with traumatic experience. Post-traumatic stress disorder should be controlled and managed at the earliest stage otherwise it may progress into severe pain, substance abuse, sleep linked abnormalities, depression and immune system related disorders. Plant based medicines can be helpful in alleviating various symptoms linked with post-traumatic stress disorder and improving and balancing mood. Usually these medicines are without side effects. Plant based extracts have synergistic and balancing action, the harmful effects caused by one constituent are balanced and minimized by other components in the same extract. This is not the case with synthetic medicines which have unavoidable side effects. Additionally, synthetic medicines are not so much cost-effective as compared to plant based medicines. Therefore due to their almost negligible side effects, accessibility and comparatively low cost, herbal and ayurvedic medicines are more beneficial as compared to synthetic medicines. In the present paper role of plant based medicines in the post-traumatic stress disorder is reviewed.
Key words: Herbal Medicines, Post-Traumatic Stress Disorder, Side Effects, Synthetic Medicines and Trauma.

INTRODUCTION
Post-traumatic stress disorder
PTSD standing for the post-traumatic stress disorder, is fundamentally a syndrome of symptoms like depression, anxiety, nightmares, detachment from outside environment and situations, increase in anger response, negative effect on various vital health parameters like heart rate, breathing and altered sleep patterns (Coltrera et al., 2013), developing after very stressful traumatic experiences like accidents, physical torture including sexual abuse, wars, natural catastrophic events such as flood, fire etc. The frequency of people experiencing traumatic events and later on developing PTSD is about 25% and women amongst them are most badly affected. Usually first 3 months of the event is the time period within which symptoms of PTSD manifest themselves, but sometimes it takes longer periods for expression of symptoms.

Usually hypothalamus, pituitary gland and autonomic nervous system are the regions of the brain which are affected by the hormones released after stress encountered in PTSD.

The brain once stimulated, causes release of hormones which travel to the adrenal glands through blood circulatory system and further affect the release of hormones epinephrine, cortisol and norepinephrine (Coltrera et al., 2013). These hormones in excess concentration adversely affect important health parameters of concerned person's body such as blood pressure and suppression of immune system (Coltrera et al., 2013; Sarris et al., 2013).

Modern pharmacological system linked therapies for post-traumatic stress disorder

Many drugs used in the treatment of PTSD are antidepressants (Zoellner et al., 2003), anti-anxiety and dopamine-blocking agents (Sobonosky, 2014). But these drugs exert side effects like drowsiness, digestive problems, nausea and have sedating qualities and these drugs are costly (Salako et al., 2015).

Herbal medicine

Nature based methods of treatment such as plant medicines and herbal formulations may be a cost-effective treatment free from side effects as compared to modern pharmaceutical medications. Herbs are generally employed in various forms such as dried/ liquid extracts, mixed with tea or other beverages.

Plant metabolites found in plant based medicines used to treat psychiatric disorders, usually attach to neuromodulators receptors or modify the synthesis and functions of neurotransmitters. Their other mechanism of action is by stimulating or inhibiting central nervous system (CNS) activities and regulating or supporting functions of the endocrine system. Herbal medicines employed in the therapy of psychiatric disorders act as antidepressant (for treatment of depression), anxiolytic (inhibiting anxiety), nootropic (improving cognitive functions particularly memory, creativity or motivation), sedative (reducing brain activity, irritability or excitement and inducing sleep), hypnotic (related to sedatives; inducing sleep) and analgesic (controlling pain, reducing fever and decreasing inflammation). Herbal medicines also have adaptogenic function and they also serve as tonic. Adaptogenic action is modification of the neuro-endocrine system in a positive way, which later on optimizes adaptation of body to outside stress factors (Panossian, 2013). Important classes of herbal medicines and herbal formulations are given below:

Herbs

Different types of herbs are used in therapy of various symptoms linked with PTSD like stress, anxiety, depression etc.

Nervine Herbs

Nervine herbs are herbs exerting their action on the neurological system. Threre are 3 different categories of nervine herbs: (1) Nervine Tonic, (2) Nervine Relaxing, (3) Nervine Stimulants

Majority of nervine herbs have relaxing and mood boosting effect (but coffee and peppermint increase excitement and they are designated as nervine stimulants). They exert positive effect on sleep linked problems, worry, anxiety and they are beneficial for body pain (Ernsberger, 2015). Some nervine herbs used in treatment of various symptoms associated with PTSD are given below:

Lemon Balm

Lemon balm (*Melissa officinalis*), usually known as balm, common balm or balm mint is a herb of family Lamiaceae. Chamomile, valerian and lavender are other herbs that are employed in conjunction with lemon balm. Lemon balm has positive effect on calmness and alertness and reduces stress. It has also been reported to counter anxiety and improve sleep related disorders. Lemon balm increases GABA (gamma aminobutyric acid) function in the brain (Braun and Cohen, 2010; Cases et al., 2011; Yoo et al., 2011). GABA is a neurotransmitter that is responsible for interrupting impulses between nerve cells. This neurotransmitter provides calming (prevents hyperexcitability) and balancing effect by reducing stress and improving sleep. It has mood boosting effect on brain (Cryan and Kaupmann, 2005). Lemon balm can be used in liquid forms like in tea, tinctures or syrups, as lemon-balm mixed water or in cooking.

Adaptogens

Adaptogens exert a calming and energy enhancing effect without excess-stimulation. Various traditional medicinal systems have mention of use of adaptogens since early times. The adaptogenic action concept was floated initially by N.V. Lazarev in 1947.

This concept was assimilated in 1998 by American Agency for Food and Drug Administration (FDA) and European Medicines Agency (EMA), [Emea. European Medicines Agency, 2014 (http://www.ema.europa.eu/ema/), Vasileva and Getova, 2016]. Frequently employed adaptogens are Ashwagandha and Tulsi.

Ashwagandha

Ashwagandha (*Withania somnifera*, family Solanaceae), commonly known as winter cherry and Indian ginseng, is a herb possessing adaptogenic function. The root is the most frequently employed part of Ashwagandha. It is commonly employed after making powder. The powder can be used in solid form as capsule or tablet or by mixing it with foods, milk, teas and other beverages. *Withania somnifera* roots possess numerous important chemical components. The important ones are steroidal alkaloids and lactones (withanolides) (Rastogi and Mehrotra, 1998; Singh et al., 2006). Withanolides, withaferin A and withanolide D have been linked with most of the pharmacological actions of Ashwaganda (Singh et al., 2010).

Adaptogenic activity, stress control

Ashwagandha as a potent adaptogen, elevates energy levels. It is important in countering oxidative damage and thus protects cellular injury resulted by free radicals and improves cell mediated immunity (Sandhu et al., 2010; Mahima et al., 2012). *Withania somnifera* glycowithanolides have action similar to body's stress-reducing relaxation hormones, which decrease body's main stress hormone cortisol. Positive effect on activity of mitochondria, the power house of cell, results in improvement of energy levels (Pingali et al., 2014). Through optimization of the different neurological system functions, Ashwagandha exerts positive effect on the memory. It enhances vigour and vitality which are important factors contributing to good sexual life.

Anxiolytic action

Withania somnifera is useful for the treatment of anxiety, sleep related abnormalities, nervous exhaustion, and mild obsessive compulsive disorder (OCD). *Withania somnifera* action is similar to the neurotransmitter GABA (Sarris et al., 2011; Jahanbakhsh et al., 2016). GABA has been implicated in stress reduction and helpful in good sleep and countering sleep disorders. Glycowithanolides of *Withania somnifera* have actions similar to the benzodiazepine category of drug lorazepam for anti-anxiety treatment and the tricyclic class of anti-depressant drug imipramine for the therapy of depression in study on rats (Bhattacharya et al., 2000).

Neurodegenerative diseases

Through its anti-stress, anti-oxidant and inflammation-modifying mechanisms, *Withania somnifera* can be important in therapy of neurodegenerative disorders including Alzheimer's (Bhattacharya et al., 1995), Parkinson's disease (Nagashayana et al., 2000) and Huntington's disease (Praba et al., 2018).

Tulsi

Tulsi (*Ocimum sanctum*), named as holy basil is the "queen of herbs". Tulsi (family Lamiaceae) is an important part of Ayurvedic practice of medicine. Tulsi is significant in encountering symptoms of post-traumatic stress disorder. Leaves (dried or fresh) are the most useful part of Tulsi. Different forms in which Tulsi can be used are capsule or tablet, as powder, in liquid form, mixed with beverages such as tulsi-tea and it can be supplemented while cooking (Jamshidi and Cohen, 2017). Leaves of Tulsi possess different chemicals such as eugenol, ursolic acid, β-caryophyllene, linalool, and 1,8-cineole (Tewari and Gomathinayagam, 2014; Bernhardt et al., 2015). In three major Tulsi varieties, eugenol is the major bioactive compound common in each of these (Anand et al., 2016). Additionally, pharmacologically significant chemical constituents like methyl eugenol, rosmarinic acid, ocimene and germacrene are also found (Singh et al., 2015).

Tulsi has anti-anxiety and anti-depressant properties thus mimicking actions of diazepam and antidepressant drugs (Moinuddin et al., 2011; Pemminati et al., 2011). Tulsi has been reported to be beneficial for memory including ageing-induced memory loss and cognitive action (Joshi and Parle, 2006; Giridharan et al., 2011). In human studies, Tulsi has been reported to decrease different forms of stress, anxiety and depression (Cohen, 2014). Tulsi in high amount has been reported to exert stimulating effect on central nervous system and contributing to anti-stress activity. The effect was similar to antidepressant drug desipramine (Sakina et al., 1990). Tulsi is beneficial for sleep related disorders (insomnia) and fatigue (Saxena et al., 2011).

The plant has adaptogenic action also which may be a result of its capacity to stimulate immune system. Tulsi also has anti-oxidant properties (Godhwani et al., 1988).

Curcumin

Turmeric (*Curcuma longa*) belongs to the ginger family, Zingiberaceae, the roots of which are employed in cooking. The plant is a herb, rhizomatous and perennial and is native to the Indian subcontinent and Southeast Asia (Farkhondeh et al., 2016). Turmeric is employed as a flavouring food supplement and natural yellowing agent. Curcumin is the most bioactive component of turmeric. The dry rhizome of *C. longa* Linn. are the source of curcumin. Chemically curcumin (diferuloylmethane), abbreviated as CUR, is a flavonoid with formula of 1,7-Bis(4-hydroxy-3 methoxyphenyl)-1,6-heptadiene-3,5-dione (Sahu, 2016). Curcumin is beneficial for harmful effect of chronic stress on brain and it has been reported to reverse this brain change caused by stress (Xu et al., 2006). Turmeric has also anxiolytic (anti-anxiety) effect which may be due to alteration of serotonergic system (Lee and Lee, 2018). Serotonergic system is the system of nerve cells that employes serotonin as their neurotransmitter. Thus, curcumin may be employed as supplementary therapy for preventing anxiety symptoms encountered in PTSD (Lee and Lee, 2018). Curcumin has anti-depressant action and it is beneficial in other neuropsychiatric abnormalities such as major depressive disorder, obsessive-compulsive disorder (OCD) and bipolar disorder (Lopresti, 2017).

Chemopreventive actions of curcumin

Curcumin also possesses anti-inflammatory and anti-oxidation action (Koh and Pan, 2018). Acetylcholinesterase (AChE) action strongly linked to oxidative stress, is decreased by curcumin. This action of curcumin supplements the treatment of neurological abnormalities (Akinyemi et al., 2017). AChE is the enzyme splitting cholinesterase and few other choline esters performing role of neurotransmitters. Neurological abnormalities like Alzheimer's disease can be treated by medicines reversibly blocking acetylcholinesterase (Julien et al., 2008). Curcumin has been observed to possess many functions related to neuroprotection including alleviation of traumatic brain damage by modifying Nrf2 signaling in microglia/macrophages (Dong et al., 2018). Nuclear factor (erythroid-derived 2)-like 2, abbreviated as NFE2L2 or Nrf2, is a transcription factor. It is basic leucine zipper (bZIP) protein controlling the expression of anti-oxidant proteins safeguarding against oxidative destruction resulting from injury and inflammation (Gold et al., 2012). Several drugs that stimulate the NFE2L2 pathway are being considered for treatment of diseases resulting by oxidative stress.

Berberine is helpful in curing drug abuse, in decreasing anxiety and treating neurological abnormalities in the rats (Lee et al., 2018). Plant Rhodiola (*Rhodiola rosea*) commonly called as Golden Root, is an important adaptogenic medicinal herb having beneficial effect on overall health. The reason for this activity may be perhaps due to the enhancement of serotonin in the mid-brain and hypothalamus regions of the brain by Rhodiola (Brown et al., 2002). It was observed that *R. rosea* L. is also important in treatment of symptoms of mild stress (Mattioli et al., 2009). *Rhodiola rosea* L. is also beneficial in curing neurological and various health problems like asthenic neuroses, hypotension, schizophrenia and in mitigating extreme physical and mental work and fatigue (Panossian and Wikman, 2010). Different classes of chemical components like phenylpropanoids, phenyletanoids derivatives, flavonoids and terpenes have been extracted form roots and rhizomes of *R. rosea* L. (Panossian et al., 2010). *R. rosea* has antidepressant activity and it is also helpful in encountering sleep linked and emotional problems. It has also been observed to significantly neutralize the side effects of tricyclic category of antidepressant drugs (Olsson et al., 2009). The plants like Kava Kava (*Piper methyscum*), Bacopa (*Bacopa monnieri*), Chamomile (*Chamaemelum nobile*), Ginkgo (*Ginkgo biloba*), Skullcap (*Scutellaria lateriflora*), Milk Thistle (*Silybum marianum*), Astragalus (*Astragalus membranaceus*), Passionflower (*Passiflora incarnata*), Valerian (*Valeriana officinalis*) and Gotu kola (*Centella asiatica*) have anti-anxiety function. *Aconitum* is employed for treating panic in a traumatic incident. Kava Kava has anti-depressant activity also but it has been reported to be affecting liver in a negative way [Harvard Women's Health Watch (HWHW), 2007; Sarris et al., 2013; Winston, 2014, Ernsberger, 2015]. Plants like Rosemary (*Rosmarinus officinalis*), American ginseng (*Panax quinquefolius*), Korean Ginseng (*Panax ginseng*), Schisandra (*Schisandra chinensis*) and Oat (*Avena sativa*) have anti-depressant function. Blueberries may be helpful in curing depression and suicidal urges encountered in PTSD.

Herbs like Siberian ginseng (*Eleutherococcus senticosus*), Licorice (*Glycyrrhiza glabra)* and St. John's wort (*Hypericum perforatum*) can tackle extreme depression and other symptoms linked with PTSD (Winston, 2014; Ernsberger, 2015). The "omic" technique can be employed to explain mechanism of action and effects of herbal medicines, for checking their toxicity aspects genetically and supplementing towards their clinical validation studies. Proteomics study, included in omics technology can be used to study epigenetic modifications caused by herbal medicines on test subjects (Wong et al., 2004; Pennington et al., 2009, Vasileva and Getova, 2016). These studies throw light on the similarities in the mechanism of action of herbal medicines analyzed with conventional antidepressant drugs in the manner that both show same patterns of affecting transcription of genes and modulation of gene expression.

CONCLUSION

PTSD can be characterized by specific psychological abnormalities encountered. The nervines and/or adaptogenic herbs have been promising in the therapy of anxiety, nervous tension, sleep disorders and mental burnout symptoms linked with PTSD. Instead of single herb, often combinations of different herbs have been found to be more beneficial. Herbal formulations can be specifically manufactured according to individual's needs which are usually not the case with modern day pharmaceutical drugs used for encountering PTSD. These herbal plant based treatment options have no side effects as compared to modern pharmaceuticals. In future research should be focused on devising the appropriate combination of conventional antidepressants and plant based phytochemical compounds.

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REFERENCES

Akinyemi, A.J., Oboh, G., Fadaka, A.O., Olatunji, B.P. and Akomolafe, S. (2017). Curcumin administration suppress acetylcholinesterase gene expression in cadmium treated rats. *Neuro toxicol.,* 62: 75-79.

Anand, A., Jayaramaiah, R.H., Beedkar, S.D., Singh, P.A., Joshi, R.S., Mulani, F.A., Dholakia, B.B., Punekar S.A., Gade, W.N., Thulasiram, H.V. and Giri, A.P. (2016). Comparative functional characterization of eugenol synthase from four different *Ocimum* species: implications on eugenol accumulation. *Biochim. Biophys. Acta-Proteins and Proteomics*, 1864 (11): 1539-1547.

Bernhardt, B., Szabó, K. and Bernáth, J. (2015). Sources of variability in essential oil composition of *Ocimum americanum* and *Ocimum tenuiflorum*. *Acta Alimentaria*, 44 (1): 111-118.

Bhattacharya S.K., Bhattacharya A., Sairam K. and Ghosal S. (2000). Anxiolytic-antidepressant activity of *Withania somnifera* glycowithanolides: an experimental study. *Phytomed.*, 7(6): 463-469.

Bhattacharya S.K., Kumar A. and Ghosal S. (1995). Effects of glycowithanolides from *Withania somnifera* on an animal model of Alzheimer's disease and perturbed central cholinergic markers of cognition in rats. *Phytother. Res.*, 9(2): 110-113.

Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements: An Evidence-Based Guide. 3rd Edn., Vol. 1, Churchill Livingstone, Australia.

Brown, R.P., Gerbarg P.L. and Ramazanov, Z. (2002). *Rhodiola rosea*: a phytomedical overview. *Herbal Gram.*, 56: 40-52.

Cases, J., Ibarra, A., Feuillere, N., Roller, M. and Sukkar, S.G. (2011). Pilot trials of *Melissa officinalis* L. leaf extracts in the treatment of volunteers suffering from mild-to-moderate anxiety disorders and sleep disturbances. *Med. J. Nutrition Metab.*, 4(3): 211-218.

Cohen, M.M. (2014). Tulsi-*Ocimum sanctum*: a herb for all reasons. *J. Ayurveda Integrative Med.*, 5(4): 251-259.

Coltrera, F., Benson, H. and Casey, A. (2013). Stress management: approaches for preventing and reducing stress. Norwalk: Belvoir Media Group, LLC.

Cryan, J.F. and Kaupmann, K. (2005). Don't worry 'B' happy!: a role for GABA(B) receptors in anxiety and depression. *Trends Pharmacol. Sci.*, 26(1): 36-43.

Doc. Ref. EMEA/HMPC/102655/2007. Emea. European Medicines Agency. 2014; (May). http://www.ema.europa.eu/ema/

Dong, W., Yang, B., Wang, L., Li, B., Guo, X., Zhang, M., Jiang, Z., Fu, J., Pi, J., Guan, D. and Zhao, R. (2018). Curcumin plays neuroprotective roles against traumatic brain injury partly via Nrf2 signaling. *Toxicol. Applied Pharmacol*., 346: 28-36.

Ernsberger, M.M. (2015). Drug-Free alternatives for post-traumatic stress disorder (PTSD). *Med. Aromat. Plants*, S2: 001.

Farkhondeh, T., Samarghandian, S. and Samini. F. (2016). Antidotal effects of curcumin against neurotoxic agents: an updated review. *Asian Pacific J. Tropical Med.*, 9(10): 947-953.

Giridharan, V.V., Thandavarayan R.A., Mani, V., Ashok Dundapa, T., Watanabe, K. and Konishi, T. (2011). *Ocimum sanctum* Linn. leaf extracts inhibit acetylcholinesterase and improve cognition in rats with experimentally induced dementia. *J. Med. Food*, 14(9): 912-919.

Godhwani, S., Godhwani, J.L. and Vyas, D.S. (1988). *Ocimum sanctum*: A preliminary study evaluating its immunoregulatory profile in albino rats. *J. Ethnopharmacol.*, 24(2-3): 193-198.

Gold, R., Kappos, L., Arnold, D.L., Bar-Or A., Giovannoni, G., Selmaj, K., Tornatore, C., Sweetser, M.T., Yang, M., Sheikh, S.I. and Dawson, K.T. (2012). Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. *The New England J. Med.*, 367(12): 1098-1107.

Harvard Women's Health Watch (HWHW) (2007). Herbs and supplements for anxiety: Kava, inositol may help.

Jahanbakhsh, S.P., Manteghi, A.A., Emami, S.A., Mahyari, S., Gholampour, B., Mohammadpour, A.H., Sahebkar, A. (2016). Evaluation of the efficacy of *Withania somnifera* (Ashwagandha) root extract in patients with obsessive-compulsive disorder: A randomized double-blind placebo-controlled trial. *Complementary Therap. Med.*, 27: 25-29.

Jamshidi, N. and Cohen, M.M. (2017). The clinical efficacy and safety of Tulsi in humans: A systematic review of the literature. *Evid. Based Complement. Alternat. Med.*, Vol. 2017, Article ID 9217567, pp. 1-13.

Joshi, H. and Parle, M. (2006). Cholinergic basis of memory improving effect of *Ocimum tenuiflorum* Linn. *Indian J. Pharm. Sci.*, 68(3): 364-365.

Julien, R.M., Advokat, C.D. and Comaty, J.E. (2008). A Primer of Drug Action: A Comprehensive Guide to the Action, Uses and Side Effects of Psychoactive Drugs. 11th Edition. Worth Publishers, New York, p. 50.

Koh, Y.C. and Pan, M.H. (2018). Review on discovery and development of novel phytochemicals which can be used in functional foods. *Curr. Res. Nutr. Food Sci.*, 6(2): 241-262.

Lazarev, N.V. (1947). 7th All-Union Congr. Physiol., Biochem., Pharmacol. Medgiz, Moscow, p. 579.

Lee B. and Lee H. (2018). Systemic administration of curcumin affect anxiety-related behaviors in a rat model of posttraumatic stress disorder via activation of serotonergic systems. *Evid.-Based Complement. Alternat. Med.*, vol. 2018, Article ID 9041309, pp.1-12.

Lee, B., Shim, I., Lee, H. and Hahm, D.H. (2018). Berberine alleviates symptoms of anxiety by enhancing dopamine expression in rats with post-traumatic stress disorder. *Korean J. Physiol. Pharmacol.*, 22(2): 183-192.

Lopresti, A.L. (2017). Curcumin for neuropsychiatric disorders: a review of *in vitro,* animal and human studies.*J. Psychopharmacol.*, 31(3): 287-302.

Mahima, Rahal, A., Deb, R., Latheef, S.K., Samad, H.A., Tiwari, R., Verma, A.K., Kumar, A. and Dhama, K. (2012). Immunomodulatory and therapeutic potentials of herbal, traditional/indigenous and ethnoveterinary medicines. *Pak. J. Biol. Sci.*, 15(16): 754-774.

Mattioli, L., Funari, C. and Perfumi, M. (2009). Effects of *Rhodiola rosea* L. extract on behavioural and physiological alterations induced by chronic mild stress in female rats. *J. Psychopharmacol.* 23(2):130-142.

Moinuddin, G., Devi, K., Satish, H. and Khajuria, D.K. (2011). Comparative pharmacological evaluation of *Ocimum sanctum* and imipramine for antidepressant activity. *Lat. Am. J. Pharm.*, 30: 435-439.

Nagashayana, N., Sankarankutty, P., Nampoothiri, M.R., Mohan, P.K. and Mohanakumar, K.P. (2000). Association of L-DOPA with recovery following Ayurveda medication in Parkinson's disease. *J. Neurol. Sci.*, 176(2): 124-127.

Olsson, E.M., von Schéele B. and Panossian, A.G. (2009). A randomised, double-blind, placebo-controlled, parallel-group study of the standardised extract SHR-5 of the roots of *Rhodiola rosea* in the treatment of subjects with stress-related fatigue. *Planta Med.*, 75(2): 105-112.

Panossian, A. and Wikman, G. (2010). Effects of adaptogens on the central nervous system and the molecular mechanisms associated with their stress-protective activity. *Pharmaceut. (Basel)*, 3(1): 188-224.

Panossian, A., Wikman, G. and Sarris, J. (2010). Rosenroot (*Rhodiola rosea*): traditional use, chemical composition, pharmacology and clinical efficacy. *Phytomed.*, 17(7): 481-493.

Panossian, A.G. (2013). Adaptogens in mental and behavioral disorders. *Psychiatr. Clin. North Am.*, 36(1): 49–64.

Pemminati, S., Gopalakrishna, H.N., Venkatesh, V., Rai, A., Shetty, S., Vinod, A., Yugandhar, B. and Shenoy, A.K. (2011). Anxiolytic effect of acute administration of ursolic acid in rats. *Res. J. Pharm. Biol. Chem. Sci.*, 2(3): 431-437.

Pennington, K., Föcking, M., McManus C.A., Pariante C.M., Dunn, M.J. and Cotter, D.R. (2009). A proteomic investigation of similarities between conventional and herbal antidepressant treatments. *J. Psychopharmacol.*, 23(5): 520–530.

Pingali, U., Pilli, R. and Fatima, N. (2014). Effect of standardized aqueous extract of *Withania somnifera* on tests of cognitive and psychomotor performance in healthy human participants. *Pharmacognosy Res.*, 6(1): 12-18.

Praba, M.A., Venkataramaniah, C. and Kavitha, G. (2018). Neuroprotection of ethanolic extract of *Withania somnifera* and withanolide A in motor co-ordination on experimental Huntington's rat model. *Int. J. Pharmaceut. Sci. Res.*, 9(11): 4800-4804.

Rastogi, R.P. and Mehrotra, B.N. (1998). Compendium of Indian Medicinal Plants. 5th Edn., Vol. 6, Central Drug Research Institute, New Delhi, India, pp. 549.

Sahu, P.K. (2016). Design, structure activity relationship, cytotoxicity and evaluation of antioxidant activity of curcumin derivatives/analogues. *Eur. J. Med. Chem.*, 121: 510-516.

Sakina, M.R., Dandiya, P.C., Hamdard, M.E. and Hameed A. (1990). Preliminary psychopharmacological evaluation of *Ocimum sanctum* leaf extract. *J. Ethnopharmacol.*, 28(2): 143-150.

Salako, M.O., Perales, S., Rodriguez, R.M., Chavez, M.W. and Ndema C.E. (2015). Managing posttraumatic stress disorder in an outpatient setting. *US Pharm.*, 40(11): 53-57.

Sandhu, J.S., Shah, B., Shenoy, S., Chauhan, S., Lavekar, G.S. and Padhi, M.M. (2010). Effects of *Withania somnifera* (Ashwagandha) and *Terminalia arjuna* (Arjuna) on physical performance and cardiorespiratory endurance in healthy young adults. *Int. J. Ayurveda Res.*, 1(3): 144-149.

Sarris, J., McIntyre, E. and Camfield, D.A. (2013). Plant-based medicines for anxiety disorders, part 2: a review of clinical studies with supporting preclinical evidence. *CNS Drugs*, 27(4): 301-319.

Sarris, J., Panossian, A., Schweitzer, I., Stough, C. and Scholey, A. (2011). Herbal medicine for depression, anxiety and insomnia: A review of psychopharmacology and clinical evidence. *Europ. Neuropsychopharmacol.*, 21(12): 841–860.

Saxena, R.C., Singh, R., Kumar, P., Negi, M.P.S., Saxena, V.S., Geetharani, P., Allan, J.J. and Venkateshvarlu, K. (2011). Efficacy of an extract of *Ocimum tenuiflorum* (OciBest) in the management of general stress: A double-blind, placebo-controlled study. *Evid. Based Complement. Alternat. Med.*, vol. 2012, Article ID 894509, pp. 1-7.

Singh, A.K., Varshney, R., Sharma, M., Agarwal, S.S. and Bansal, K.C. (2006). Regeneration of plants from alginate-encapsulated shoot tips of *Withania somnifera* (L.) Dunal, a medicinally important plant species. *J. Plant Physiol.*, 163(2): 220-223.

Singh, G., Sharma, P.K., Dudhe, R. and Singh, S. (2010). Biological activities of *Withania somnifera*. *Ann. Biol. Res.*, 1(3): 56-63.

Singh, P., Kalunke, R.M. and Giri, A.P. (2015). Towards comprehension of complex chemical evolution and diversification of terpene and phenylpropanoid pathways in *Ocimum* species. *RSC Adv.*, 5(129): 106886–106904.

Sobonosky, J.L. (2014). Overview and management of anxiety disorders. *US Pharm.*, 39(11): 56-62.

Tewari, B.B. and Gomathinayagam, S. (2014). A critical review on *Ocimum tenuiflorum*, *Carica papaya* and *Syzygium cumini*: the medicinal flora of Guyana. *Revista Boliviana de Química* (*Bolivian J. Chem.*), 31 (2): 28-41.

Vasileva, L. and Getova, D. (2016). Herbal medicines in the treatment of post-traumatic stress disorder: A review. *IOSR J. Pharm.*, 6(7): 34-38.

Winston, D. (2014). Differential treatment of depression with botanical and nutritional medicines.

Wong, M.L., O'Kirwan, F., Hannestad, J.P., Irizarry, K.J., Elashoff, D. and Licinio, J. (2004). St John's wort and imipramine-induced gene expression profiles identify cellular functions relevant to antidepressant action and novel pharmacogenetic candidates for the phenotype of antidepressant treatment response. *Mol. Psychiatry*, 9(3): 237-251.

Xu, Y., Ku, B., Tie, L., Yao, H., Jiang, W., Ma, X. and Li, X. (2006). Curcumin reverses the effects of chronic stress on behavior, the HPA axis, BDNF expression and phosphorylation of CREB. *Brain Res.*, 1122(1): 56-64.

Yoo, D.Y., Choi, J.H., Kim, W., Yoo, K.-Y., Lee, C.H., Yoon, Y.S., Won, M.-H. and Hwang, I.K. (2011). Effects of *Melissa officinalis* L. (Lemon Balm) extract on neurogenesis associated with serum corticosterone and GABA in the mouse dentate gyrus. *Neurochem. Res.*, 36(2): 250-257.

Zoellner, L.A., Feeny, N.C., Cochran, B. and Pruitt, L. (2003). Treatment choice for PTSD. *Behav. Res. Ther.*, 41(8): 879-886.

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