Review: Tinospora cordifolia in the Treatment of Depression

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Abstract:
Depression is a complex psychiatric disorder characterized by depressed mood, anhedonia, loss of energy and low self esteem. Nitric oxide (NO) is the smallest biologically active molecules which plays an important role in the intracellular signaling. NO negatively controls the levels of 5-HT. Inhibition of NO synthases (NOS) which are responsible for the production of NO; may exert antidepressants like action. Thus, NO is involved in the pathogenesis of depression and the agents which suppress the NO production exerts antidepressants like effect. Tinospora cordifolia commonly named as “Guduchi” belonging to family Menispermaceae; has been reported of its strong free radical scavenging properties against superoxide anion (O2•), hydroxyl radicals (OH), NO, and peroxynitrite anion (ONOO•). Thus the aim of the present manuscript is to demonstrate the role of NO in depression and how Tinospora cordifolia exerts beneficial effects in the patients of depression.

Keywords: Depression, Nitric Oxide, Tinospora cordifolia.

INTRODUCTION
Depression is a complex psychiatric disorder characterized by depressed mood, anhedonia, loss of energy and low self esteem. Dysregulation of monoaminergic neurotransmitters found to be involved in the etiology of depression. [1] The clinical characteristics of depression include mood changes, hopelessness, depressive episode, psychomotor retardation etc. [2] Stress, is an important risk factor for depression and the acute stressful life events have been found to be responsible for the onset of depression. [3] Serotonin (5-HT) and norepinephrine are primarily involved in regulation of mood and emotions and the alteration in the levels and transmission of these neurotransmitters is responsible for depression. Thus the lower levels of the 5-HT levels is linked with depression or may increase the vulnerability to depression. [4] Therefore the drugs which correct the alterations in the 5-HT signaling will be useful in the treatment of depression. SSRIs have been used in the treatment of the depression from the very long time, these drugs offers various advantages over the various other categories of the drugs used for the treatment of depression. But the treatment with the SSRIs increases the risk of suicides in the patients suffering from depression. Therefore there is a constant need of newer and safer antidepressants which are free from these life threatening adverse effects.

Nitric oxide (NO) is the smallest biologically active molecules which plays an important role in the intracellular signaling. NO serves as an unconventional messenger molecule in the nervous systems implicated in various cellular processes. [5] NO is synthesized from L-arginine by nitric oxide synthases (NOS). NO is produced by three cell-specific NOS isoforms that are classified according to the tissue or cell type in which they were first found: neuronal nitric oxide synthase (nNOS, NOS-I or Type I), expressed in most brain regions by small populations of neurons, typically GABAergic and also in skeletal, cardiac and smooth muscles; inducible nitric oxide synthase (iNOS, NOS-II or Type II), initially identified in macrophages and glia; and endothelial nitric oxide synthase (eNOS, NOS-III, NOS-3 or Type III), mainly described in endothelial cells. [6] Plasma nitrate concentrations were significantly higher in depressed patients, suggesting that the endogenous NO is involved in the pathogenesis of depression. NO activates soluble guanylyl cyclase, resulting in increase in cGMP levels. [7] cGMP would then activate cGMP-dependent kinase which further phosphorylates the 5-HT transporters and enhances the activity of 5-HT transporter. Thus cGMP mediated enhancement of the activity of 5-HT.
Tinospora cordifolia extracts reduced the cytokine production, mitogenicity, stimulation and activation of immune effector cells. Tinospora cordifolia extract exerts strong free radical scavenging properties against superoxide anion (O$_2^-$), hydroxyl radicals (OH), NO radical, and peroxynitrite anion (ONOO$^-$). Petroleum ether extract of Tinospora cordifolia produce antidepressant-like effect by interaction with $\alpha_1$-adrenceptors, dopamine D$_2$-receptors, serotonergic and GABA$_\alpha$ receptors, hence increasing the levels of norepinephrine, dopamine and serotonin; and decreasing the levels of GABA in brains of mice. Tinospora cordifolia extract also reduced the mouse whole brain MAO-A and MAO-B activities as compared to control. Tinospora cordifolia extract provides protection against oxidative stress, pro-inflammatory mediator release and redox signaling.

CONCLUSION

NO is involved in the pathogenesis of depression and the agents which suppress the NO production exerts antidepressants like effect. Tinospora cordifolia commonly named as Guduchi showed its strong free radical scavenging properties against superoxide anion (O$_2^-$), hydroxyl radicals (OH), NO, and peroxynitrite anion (ONOO$^-$). Tinospora cordifolia extract provides protection against oxidative stress, pro-inflammatory mediator release and redox signaling. Thus it has been concluded that the Tinospora cordifolia exerts beneficial effect in the depression through its NO scavenging activity.
REFERENCES

6. Montezumaa K, Biojoneb C, Lisboab SF, Cunhab FQ, Guimarãesb FS, Jocaa SRL. Inhibition of iNOS induces antidepressant-like effects in mice; Pharmacological and genetic evidence. Neuropharmacol 2012;62; 485e491
15. Dhingra D, Goyal PK. Evidences for the Involvement of Monoaminergic and GABAergic Systems in Antidepressant-like Activity of Tinospora cordifolia in Mice. Indian J Pharm Sci. 2008 Nov; 70(6); 761-7