NEUROPROTECTIVE ROLE OF A HERB BACOPA MONNIERI ON COLCHICINE INDUCED DEMENTIA IN WISTAR RATS

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Thesis Abstract

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ABSTRACT

Alzheimer’s disease (AD) is the most prevalent form of dementia in aged population. About 25-30 million people are suffering from AD worldwide, which is expected to increase 3 folds by 2040 due to increased life expectancy. It is characterized by progressive memory impairment and cognitive deficits along with confusion, impaired social judgment, language disturbance and agitation. The major pathological characteristic of AD brain is extracellular senile plaques composed of amyloid-β (Aβ) peptide and intra-neuronal neurofibrillary tangles containing hyper-phosphorylated tau protein. Antioxidants may prevent the onset of AD as high dietary intake of vitamin C and E has been reported to be associated with lower risk of the disease. Therefore, the present study was designed to evaluate the neuroprotective potential of *Bacopa monnieri* (BM), an Indian traditional medicinal plant effective against cognitive impairment, in colchicine-induced dementia. Keeping in view the above objective, male wistar rats weighing about 200-250 g were randomly segregated into four groups viz. control group, Bacopa group, Colchicine group, Colchicine + Bacopa group. Animals were intracerebroventricularly (i.c.v.) infused with drug solution (15 μg colchicine dissolved in 5 μl artificial cerebrospinal fluid). BM was given orally in the form of water suspension, starting a day after surgery at a dosage of 50 mg/kg body weight daily for a period of 15 days. Colchicine administration showed a significant decline in memory retention which was restored by the BM supplementation. However, there was found no alteration in the motor activity following colchicine administration. These findings demonstrated the biochemical alterations produced by colchicine administration and the beneficial effects of BM supplementation. It is evident that oxidative stress plays a crucial role in colchicine induced neurotoxicity. A consequence of oxidative stress, perturbation of lipid composition and membrane integrity, further lead to dysfunctioning of the membrane bound enzymes resulting in increased synaptosomal calcium levels. Moreover, elevated intracellular calcium levels in colchicine treated animals were found to be associated with activation of pro-inflammatory mediators resulting in neuronal death. BM supplementation restored the changes following colchicine administration. Impaired neurotransmitters in colchicine treated animals were restored by BM supplementation via preventing the oxidative injury, enhancing synthesis of biogenic amines and by modulating of metabolism of neurotransmitters in AD brain. It can be suggested that BM exerted multi targeted pharmacological actions by preventing the Aβ accumulation, modulating the metabolism of monoaminergic neurotransmitters, enhancing the acetylcholine
levels, inhibiting oxidative stress and inflammation in AD brain. The findings from the study may, at least in part, explain the nootropic action of BM demonstrated in experimental and clinical studies. Therefore, BM can have the therapeutic potential of being an effective and safe treatment for AD.

**Key Words:** Alzheimer’s Disease, Colchicine, *Bacopa monnieri*, Cognitive function, oxidative stress