

ABSTRACT

Ageing is characterized by biological decline in the body's ability to react to stress and cellular functions, which increases the risk of age related pathologies including neurodegenerative disorders especially Senile Dementia of Alzheimer's Type (SDAT). Current status of the treatment for age related neurodegeneration still remains a challenge; however, there are several evidences which suggest that age associated neurodegeneration can be prevented by various neuroprotective strategies; where the traditional system of medicine plays a vital role. Ayurveda is one such ancient system of medicine that provides preventive health care approach by utilizing single plant or formulation in order to provide promising therapeutic benefits.

Despite of the abundant textual and experience based evidences on the safety and efficacy of medicinal plants, there are limited studies that demonstrate the neuroprotective mechanism of action of these plants. In the present research work a polyherbal formulation containing the hydroalcoholic extracts of the three plants namely *Bacopa monnieri (L)*, *Dioscorea bulbifera (L)* and *Hippophae rhamnoides (L)* was investigated for its neuroprotective mechanism of action to promote healthy and successful brain ageing and to prevent further implications of SDAT using *in vitro*, *in vivo* and clinical studies.

Hydroalcoholic extracts of the three plants were combined to prepare a novel polyherbal formulation which was subjected to standardization and quality control analysis- including quantification of its major biomarkers components using HPLC. The formulation was evaluated for its *in vitro* antioxidant and neuroprotective activities. The antioxidant

potential of the polyherbal formulation was assessed using DPPH, OH radical scavenging and ferric thiocyanate assays in comparison to the respective standards. The neuroprotective activity of the formulation was evaluated on human neural cell line- IMR32 against stress induced exo-cytotoxicity using hydrogen peroxide.

The *in vivo* neuroprotective activity of the polyherbal formulation was evaluated using ageing brain model. 100, 200 and 300 mg/kg body weight of the formulation was used as dose for further experimentation in order to elucidate the neuroprotective mechanism of action for the promotion of successful ageing in aged rats.

Clinical study was conducted to evaluate the efficacy of the polyherbal formulation among aged and SDAT subjects through a randomized, double blinded, conventional and placebo controlled trial. The therapeutic effect of the formulation was evaluated by assessing various biochemical, immunological, oxidative stress and neuropsychological parameters.

The present study demonstrated that the polyherbal formulation showed a potent antioxidant activity by its ability to scavenge free radicals as noted by DPPH, ferric-thiocyanate and OH assays. Neuroprotective activity of the formulation prevented cell death and necrosis of IMR32 cells against H₂O₂ induced toxicity. A reduced intracellular ROS activity was observed in treated cells. Thus *in vitro* neuroprotective activity of polyherbal formulation may be attributed to its antioxidant property.

Results of the *in vivo* study demonstrated that the formulation prevented age related decline in cholinergic and monoaminergic neurotransmission with simultaneous regulation of acetylcholinesterase enzyme activity. The formulation further decreased the

levels of lipofuscin pigments and enhanced cognitive ability in aged rats. The *in vivo* efficacy of the formulation may be the converging effect of both antioxidant and neuroprotective activity of the formulation.

Clinical trial study conducted on the aged and SDAT subjects projected that subjects treated with polyherbal formulation showed enhancement in cognitive function and decline in inflammatory and oxidative stress markers.

The present research findings suggested that the synergistic action of biomarkers present in the polyherbal formulation was responsible for the neuroprotective effect in the *in- vitro*, *in vivo* and clinical studies. It improved the neural transmission and cognitive function in aged rats. Also its antioxidant, anti-inflammatory property may help in promoting healthy brain ageing and prevent age associated neurodegeneration in human subjects.

Keywords: *Ageing, SDAT, neurotransmitters, cognitive enhancement activity, oxidative stress, mitochondria, inflammation, polyherbal formulation.*

“Jivem saradah satam, Pasyem saradah satam”- (Rigveda) A LIFE OF 100 YEARS

WITH FUNCTIONING BRAIN AND SENSES