B-ASARONE ATTENUATES STREPTOZOTOCIN-INDUCED EXPERIMENTAL DEMENTIA IN RATS: POSSIBLE ROLE OF PHOSPHODIESTERASES AND CYCLIC NUCLEOTIDE SIGNALING

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In recent years, extract of Acorus calamus shown to inhibit phosphodiesterases (PDE) and β- asarone has been reported to be major active constituent. The purpose of the present study was to ascertain PDE inhibitory potential of β-asarone and to explore its therapeutic potential in sporadic Alzheimer's type dementia. In the current study, PDE inhibitory potential of β- asarone was determined using in vitro assay system. On the other hand, streptozotocin (STZ) was infused intracerebroventrically [bilaterally (3 mg/kg) ICV] to induce SAD in rats. Spatial and non-spatial memory was evaluated using Morris water maze and object recognition task in rats. Rats were treated with β-asarone (12.5, 25 and 50 mg/kg) from day 10 to 21 following 1st STZ infusion. On day 22 rats were sacrificed and the cortical and hippocampal brain regions were used to identify biochemical alterations. β-asarone produced significant PDE inhibition and the IC50 value was observed in the range of µg/ml. STZ infused rats showed significant learning and memory deficit which was linked with increase in oxidative stress (malondialdehyde and nitrite), compromised antioxidant defense (reduced glutathione), mitochondrial dysfunction (deficit in complex I and III activity) and pro-inflammatory cytokine levels. Significant decrease in both cAMP and cGMP levels were also observed in STZ-infused rats. β-Asarone dose dependently attenuated STZ-induced cognitive deficit, biochemical alterations and restored cyclic nucleotide levels. The observed results show important role of PDE inhibition and cyclic nucleotide signaling in the beneficial effects of β-asarone and suggest therapeutic potential of β-asarone in the management of cognitive disorders.