

Neuroprotective effects of vildagliptin, a dipeptidyl peptidase-4 inhibitor against streptozotocin induced Alzheimer's disease

Jayasankar Kosaraju
JSS College of Pharmacy, India

Adults with Type 2 diabetes (T2D) at later stages are at higher risk of developing Alzheimer's disease (AD). Recent studies report similarities in molecular mechanisms that underlie the respective degenerative developments in both T2D and AD. Pharmacological interventions with agents such as dipeptidyl peptidase-4 (DPP-4) inhibitors that increase the levels of glucagon-like peptide-1 (GLP-1) and ameliorate T2D have also become promising candidates as disease modifying agents in the treatment of AD. In addition, endogenous GLP-1 levels decrease amyloid precursor protein and amyloid beta (A β) peptide in AD. The present study investigates the efficacy of vildagliptin, a DPP-4 inhibitor in a streptozotocin (STZ) induced rat model of sporadic AD. Three months following induction of AD by intracerebral injection of STZ, animals were orally administered with vildagliptin (2.5, 5 and 10 mg/kg) for 30 days. Dose-dependent and time course effects of vildagliptin on memory retention were investigated during the course of treatment. Following treatment the animals were sacrificed and brain tissues were used to evaluate effects of vildagliptin on hippocampal and cortical GLP-1 levels, A β burden, tau phosphorylation and inflammatory markers. The results reveal a dose and time-dependent improvements in memory retention and dose-dependent attenuation of A β , tau phosphorylation and inflammatory markers and increased levels of GLP-1. These robust therapeutic effects of vildagliptin, mediated through DPP-4 inhibition, demonstrate a unique mechanism for A β and tau clearance by increasing GLP-1 levels and reverse the behavioral deficits and pathology observed in AD.

Biography

Jayasankar Kosaraju is a research scholar doing his doctoral program on therapeutics of Alzheimer's disease. His project was funded by Council of Scientific and Industrial Research (New Delhi, India). Recently his paper got accepted for publication in Neuropharmacology journal. He has presented papers at different national and international conferences and once got a best poster award. Other than Alzheimer's disease he is also working on Parkinson's disease and discovering the relation between pharmaceutical used for diabetes in neurodegenerative disorders.

jayasankar87@hotmail.com