KSN 2019
Seoul, Korea · May 23 - 26

Abstract Type : Poster
Abstract Submission No. : PO-1028

Novel 1,3,5-triazine derivatives exert protective action against diabetes induced nephropathy in experimental animal via inhibition of DPP-4

Udaya Pratap Singh[1], Hans Raj Bhat[2]
[1]Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, India
[2]Department of Department of Pharmaceutical Sciences, Dibrugarh University, India

Objectives: Dipeptidyl peptidase IV (DPP-4) enzyme is responsible for the degradation of incretins that stimulates insulin secretion and hence inhibition of DPP-4 becomes an established approach for the treatment of type 2 diabetics. These inhibitors provide similar glucose-lowering effect independent of the kidney function either diseased or normal and reduce the levels of glycated albumin without causing hypoglycemia in altered kidney function undergoing dialysis. Thus, in the present study, we wish to explore a novel series of 1,3,5-triazine derivatives as potent DPP-4 inhibitor and its effect on diabetic nephropathy in experimental animal.

Methods: The compounds were tested for inhibition of DPP-4 via ELISA-based assay kit. The compounds were also analyzed via docking study with 3D crystal structure of DPP-4 to identify critical interactions vital for bioactivity. The most potent analogue was further tested for its protective action against streptozotocin (STZ)-induced diabetic nephropathy (DN) in Wistar rats. Compound 6b was administered orally in graded doses (5mg/kg, 10mg/kg and 15mg/kg) to the animals and observed for changes in various biochemical, molecular, and histological parameters after induction of DN.

Results: In DPP-4 inhibitory assay, compound 6b was identified as most potent analogues with IC_{50} = 2.13 µM. Compound 6b has a favorable binding mode with Arg358, Arg669, Glu205 as confirmed via docking study. In Wistar rats, 6b causes dose-depended modulation of STZ-induced alterations in serum and urine biochemistry (urine creatinine, uric acid, albumin, and BUN). The results showed that the preprandial and postprandial glucose levels in the group treated with 6b was significantly reduced as compared to control. Compound 6b causes significant increase in creatinine clearance rate together with decline in STZ induced increase in renal oxidonitrosative stress at the maximum test dose of 15mg/kg.

Conclusions: It has been concluded that 6b exert protective action against STZ-induced DN possibly via the inhibition of DPP-4.