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Qurecetin-metformin exert protection against diabetes mellitus induced nephropathy in experimental animal via inhibition of DPP-4

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Objectives: Dipeptidyl-peptidase IV inhibitors (DPP-4) have gain lot of popularity as anti-diabetic agents and now are extensively used the treatment of Type-2 diabetes patient with chronic renal dysfunction but also on patients with end stages renal disease on dialysis. DPP-4 inhibitors have potential to provide lowering glucose effect independent of the renal function either by decrease or reduction in the level of glycated albumin without inducing the hypoglycaemia effect in altered renal function with dialysis.Investigations have established that the DPP-4 exert renal protective effect by controlling the incidence of albuminuria. This workis an attempt to explore the qurecetin-metformin co-drug as potent DPP-4 inhibitor andits renal protective effects in animal model.

Methods: Qurecetin-metformin was tested for DPP-4 inhibitor via ELISA based assay kit. Qurecetin-metformin co-drug were also analysed via docking study with 3D crystal structure of DPP-4 to identify critical interactions vital for bioactivity. Albino rats were used for the DPP-4 inhibition model. The experimental animals were treated with STZ, with or without treatment of Quercetin-metformin. The oral administration of Qurecetin-metformin was performed daily over the 6 weeks.

Results: In DPP-4 inhibitory assay, Qurecetin-metformin was identified as most potential co-drugIC_{50}= 5.47 µM. Qurecetin-metformin combinations interacted with Glu205, Arg669 and Arg358 residue confirmed via docking study. Qurecetin-metformin co-drug was able to reduce the systolic blood pressure in rats in STZ induced nephropathy. This combination was also able to ameliorated the inflammatory cell infiltration, interstitial fibrosis and tubulointestitial injuryanimal tissue. Qurecetin-metformin showed the remarkably reduction in caspase-1 (42%), IL-1β (36%), NLRP3 (67%) and ASC (52%) in the kidney of STZ nephropathy rats. Additionally, with decrease in mRNA expression of IL-6 (63%).

Conclusions: The result of the current investigation suggests that the Qurecetin-metformin exert the protective effect against the STZ induced DN via inhibition of DPP-4.