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Renoprotective along with antioxidant effect of dipeptidyl peptidase–IV inhibitors from flavonoids rich fraction of Terminalia Arjuna in diabetic nephropathy rats model

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Objectives: The most frequent cause of renal disease in the world is diabetic nephropathy (DN). Dipeptidyl peptidase–IV (DPP-IV) enzyme is most abundant in kidneys and elevated in DN. A novel approach to treat type 2 diabetes mellitus (T2DM) along with DN, based on incretin hormones glucagon-like peptide-1 (GLP-1) which regulated by DPP-IV. We hypothesized that DPP-IV inhibitors isolated from flavonoids rich fraction of *Terminalia Arjuna* (TA) will regulate DPP-IV activity as well as DN: *in-vivo; in-silico* and kidney histology

Methods: DPP-IV inhibitors from flavonoids rich fraction of TA in high sucrose diet along with dexamethasone induced T2DM was explored *in-vivo* in rat. Apart from serum glucose; DPP-IV and inhibition activity, HbA1c, Insulin were estimated. We also examined GLP-1, albuminuria, and antioxidant properties in kidney tissue along with histology. Molecular docking of flavonoids fraction (Gallic acid) of TA inhibitors with DPP-IV

Results: High sucrose diet with Dexamethasone administration (1 mg /kg BW 45 days) increased concentration of serum glucose, DPP-IV and albuminuria, cholesterol and renal LPO with increase in tissue antioxidant to scavenging free radicals generated by oxidative stress, but after some time antioxidants such as SOD, CAT, GSH was decreased. However, after administration of flavonoids fraction TA, DPP-IV inhibition activity increase in TA (67.5%), as compared to Sitagliptin (87.3%) with significant reduction in levels of glucose, albuminuria, TC, TG and with increased Insulin and GLP-1. Kidney histology showed some significant change as compared to diabetes control. Isolated Gallic acid depicts the conformer and affinity energy was – 5.3 and distance from RMSD i.b was 38.669. Sitagliptin depicted the conformer and affinity energy was – 8.9 and distance from RMSD i.b was 3.826

Conclusions: DPP-IV inhibitors isolated from TA are novel antidiabetic agents with renoprotective along with antioxidant properties. DPP-IV inhibition lower blood glucose by decreasing DPP-IV activity, albuminuria and increasing levels of GLP-1