Schiff's Bases: Synthesis, Characterization, *In Vitro* and *In Vivo* Biological Evaluation as DPP-IV Inhibitors

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Abstract

Absolute or relative insulin deficiency brings about hyperglycemia which represents one of the most popular chronic diseases called diabetes mellitus. Dipeptidyl peptidase IV (DPP-IV) inhibitors act by stopping the action of the enzyme, rapidly activating both incretins GIP and GLP-1, and improve glycemic control in type-2 diabetes. In the present study, ten schiff's bases **5a-f** and **9a-d** were synthesized and identified using ^{13}C-NMR, ^{1}H-NMR and IR. These compounds were biologically evaluated *in vitro* and exhibited DPP-IV inhibitory activities ranging from 2% - 25% at 100 µM concentration, where compound **9c** has the highest inhibition and the positive inhibitor sitagliptin has a % inhibition of 86.4.

It was found that presence of four rings, and fluoro-substitution in the structure enhances the inhibitory activity against the enzyme. Compound **9c** with the highest *in vitro* % inhibition was subjected to the *in vivo* glucose lowering test using vildagliptin as a positive inhibitor. Vildagliptin and **9c** showed significant reduction of blood glucose level of the treated mice after 30 minutes of glucose administration. Further structural modifications of compound **9c** can produce better DPP-IV inhibitors.

Keywords: Diabetes, DPP-IV inhibitors, hydrazone, incretins, schiff's base.