Phenanthridines: Design, Synthesis and Biological Evaluation as Potential DPP-IV Inhibitors

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ABSTRACT

Inhibition of dipeptidyl peptidase-IV (DPP-IV) enzyme prevents the inactivation of gastric inhibitory polypeptide (GIP) and glucagon-like peptide–1 (GLP-1). This increases circulating levels of active GLP-1 and GIP and stimulates insulin secretion, which results in lowering of glucose levels and improvement of the glycemic control in patients with type II diabetes. In this study, pharmacophore modeling and docking experiments were carried out and three novel 3,8-disubsituted-6-phenyl phenanthridines derivatives have been designed and synthesized guided by a previously reported molecular modeling data and scaffold- hopping strategy was adopted. Then, these compounds were evaluated for their ability to inhibit DPP-IV. The chemical structures of all synthesized compounds were confirmed by both IR and NMR. Most of the synthesized compounds were proven to have anti-DPP-IV activity where compound **5** displayed the best activity of 45.43% inhibition at 100 μM concentration. Results of this work might be helpful for further optimization to develop more potent DPP-IV inhibitors.