

Development of DPP-IV inhibitors for the treatment of Type 2 Diabetes

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Type 2 diabetes mellitus is a worldwide chronic disorder which is characterised by insulin resistance and high blood glucose levels (1). The treatment of type 2 diabetes involves the use of traditional oral antidiabetic agents, such as sulphonylurea or glibenclamide, metformin, and/or insulin (2). However, incidence of the disease is increasing in many parts of the world which means novel antidiabetic agents are needed.

Recently, new types of oral antidiabetic agents that inhibit DPP-IV have been developed and one has been approved for medical use. Collaboration between Strathclyde Innovations in Drug Research (SIDR) and the Drug Discovery Portal (DDP) using a combination of virtual and high throughput screening identified a novel hit (AM11) against DPP-IV. The aim of this project was to modify AM11 to see if inhibition against DPP-IV could be improved.

Compounds with a range of activities against DPP-IV were prepared, but all had comparable or lower activity than AM11. Docking studies were performed to explain the structure-activity relationship profiles of the different libraries prepared.