DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF A NEW SERIES OF POTENTIAL CETP INHIBITORS.

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Abstract

Cholesterol ester transfer protein (CETP) transfers cholesteryl esters and triglycerides from high density lipoproteins (HDL) to low density lipoproteins (LDL). A deficiency of CETP activity is associated with an increase in HDL levels and a decrease in LDL levels; an antiatherogenic profile. Therefore, CETP is a promising target to treat atherogensis. In this work we identified 3- and 4- benzylamino benzamides as a novel scaffold for CETP inhibitors.

The three aromatic rings of the synthesized molecules were linked by an imine moiety (reduced to 2º amine) and amide functional group guided by a previous pharmacophore and QSAR model.

Compounds **(13)** and **(15)** are low active inhibitors. Interestingly, the lowest activity of **(14)** and **(16)** inferred that the scaffold of Q199 and S230 are not involved in H-bond with key binding moieties.

The 3-benzylamino-benzamide (**17**) was the most active compound. It suppressed CETP activity by 64% at 10 mM concentration.

We expected that the generated binding conformation of **(17)** increased the binding affinity. And, **(17)** might get deeper in the binding cleft and closer to H-bond binding residues. Also, we speculated that the binding groove accommodating the methyl moiety is tightly fit.

The bioassays suggested that compound **(17)** could be promising lead for further optimization.