SYNTHESIS AND BIOLOGICAL EVALUATION OF SUBSTITUTED FLUORINATED ALKYLOXY BENZYLAMINO BENZAMIDE AS POTENTIAL CETP INHIBITORS

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ABSTRACT

Hyperlipidaemia is one of the most common chronic diseases worldwide. Cholesteryl ester transfer protein (CETP) is a hydrophobic glycoprotein that facilitates the transfer of cholesteryl ester from the atheroprotective HDL to the proatherogenic LDL and VLDL.

In this work, synthesis and characterization of four fluorinated 3-benzylamino benzamides **8a**-**8d** that target CETP activity was carried out. Benzamide **8a** showed the highest CETP inhibitory activity with IC_{50} of 1.6 µM. The *in vitro* biological data shows that the presence of *p*-trifluoromethoxy group (as in **8a** and **8b**) enhances CETP inhibitory activity more than *m*-trifluoromethyl groups. The bulkiness of compounds **8c** and **8d** decreases their % inhibition. The IFD docking shows that compounds **8a**-**8d** accommodate the binding cleft of CETP and are enclosed by hydrophobic lining. Moreover, their scaffold matches five out of six pharmacophoric points. Further optimization of this core nucleus is required to improve CETP inhibitory activity and to better understand the structure-activity relationship.