Synthesis and Biological Evaluation of Substituted Benzylamino Benzamide Derivatives as Potential CETP Inhibitors

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Abstract

Dyslipidemia is an abnormal lipid profile that is associated with many common diseases such as coronary heart disease (CHD), and atherosclerosis. Cholesteryl ester transfer protein (CETP) is a hydrophobic plasma glycoprotein that is responsible for transfer of cholesteryl ester (CE) from high density lipoprotein (HDL) atheroprotective particle to the proatherogenic very low density lipoprotein (VLDL), and low density lipoprotein (LDL) particles. In this work synthesis of eight potential CETP inhibitors (**9a-9h**) was done, with full characterization using infrared (IR) and nuclear magnetic resonance (NMR). *In vitro* study showed that most of these compounds have

appreciable CETP inhibitory activity. Compound **9b** showed the highest inhibitory activity against CETP with an IC_{50} of 15 nM. **9b** was thus selected for *in vivo* study on a hamster model. The *in vivo* study revealed that **9b** treated animals showed a significant increase in HDL concentration by 85% and a decrease in LDL concentration by 44%, and the HDL/TC ratio was significantly increased by 56%. In conclusion, successful synthesis and spectroscopic characterization of eight novel CETP inhibitors (**9a-9h**) was achieved and additional future *in vivo* studies are required to further understand pharmacokinetic and toxicity profiles of this new class of CETP inhibitors.