Synthesis and Biological Evaluation of Aromatic Sulfonamides as Novel Cholesteryl Ester Transfer Protein Inhibitors

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Abstract

The number of cases of lipid disorders has risen dramatically around the world as a result of poor dietary habits, hereditary risk factors, or other diseases or medicines. Cholesteryl ester transfer protein (CETP) is a 476 amino acid lipophilic glycoprotein that helps transport cholesteryl esters and phospholipids from proatherogenic LDL and VLDL to atheroprotective HDL. It is mostly secreted into the plasma from the liver. CETP inhibition increases HDL cholesterol, lowering LDL cholesterol and triglycerides, rendering it a promising therapy option for hyperlipidemia and its comorbidities.

In this research, 14 sulfonamide derivatives **8a**-**8g** and **9a**-**9g** were synthesized and completely identified using ^{1}H-NMR, ^{13}C-NMR, IR and MS. These compounds were exposed to *in vitro* biological evaluation tests and showed inhibitory activities ranging from 15.6-100% at 10 μM concentration. Sulfonamide derivatives were established to be successful scaffold as possible CETP inhibitors. Compounds with four aromatic rings bearing either *m*-CH_3 (**9c**) or *p*-Cl (**9g**) were the most effective compounds among their analogs and showed 100% CETP inhibition at 10 μM, while the most active compound was **8c** bearing three aromatic rings and *m*-CH_3 with an IC_{50} of 0.124 μM.

Keywords: CETP, HDL, Hyperlipidemia, LDL, Sulfonamides.