Para-Methylated Benzene Sulfonamides as Potential CETP Inhibitors: Chemical Synthesis and *In Vitro* Validation

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Abstract

Cardiovascular disease, which includes heart attacks and strokes, is the major cause of illness and mortality on a global scale. Low density lipoprotein cholesterol is a substantial risk factor, whereas high-density lipoprotein reduces the risk of coronary heart disease. Cholesteryl ester transfer protein (CETP) is a hydrophobic glycoprotein that has a molecular weight of 53 kDa and 476 amino acids which plays an essential role in reverse cholesterol transport and the maintenance of cholesterol homeostasis, making it hopeful therapy option to treat complications of hyperlipidemia. In this study, we synthesized ten *para*-methylated benzene sulfonamides as prospective CETP inhibitors and characterized their chemical structures using ^{13}C-NMR, IR, ^{1}H-NMR, and mass spectrometry. It was found that substitution of sulfonamide phenyl ring with EWG (Cl, NO_2) gives better inhibitory activity on CETP than presence of EDG (CH_3). Furthermore, *p*-NO_2 substitution was discovered to have the highest inhibitory activity of 44% at 10 µM. Moreover, it was found that the presence of *p*-methyl lowers the activity of benzene

sulfonamides in comparison with *p*-trifluoromethyl substituted sulfonamides. Compounds **6d, 6g**, and **6j** show the highest inhibitory activity at 10μM concentration.