Fluorinated Benzene Sulfonamides as Potential Cholesteryl Ester Transfer Protein Inhibitors: Synthesis and Subsequent *in Vitro* Validation

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Abstract

Cardiovascular disease is one of the leading causes of death. Atherosclerosis causes arterial constriction or obstruction resulting in acute cardiovascular illness. Cholesteryl ester transfer protein (CETP) facilitates reverse cholesterol transport. It supports transfer of cholesteryl ester from HDL to LDL and VLDL. Inhibition of CETP by drugs limits cardiovascular disease, by decreasing LDL and increasing HDL.

In this study, fourteen trifluoromethyl substituted benzene sulfonamides **6a-6g** and **7a-7g** were prepared, and their structure was fully determined using ^{1}H-NMR, ^{13}C-NMR, HR-MS, and IR. *In vitro* biological evaluation showed that compounds **7d-7f** had the highest inhibitory activity with 100% inhibition, while compounds **6a-6g**, **7a-7c** and **7g** activities ranged from 2%-72% at 10µM concentration. It was found that, the addition of a fourth aromatic ring significantly improved the activity, which may be due to the hydrophobic nature of CETP. Also, presence of *ortho*-chloro, *meta*-chloro and *para*-methyl substituents result in high inhibitory activity.

Keywords: Atherosclerosis, Cardiovascular disease, Cholesteryl ester transfer protein, Sulfonamides, Trifluoromethyl.