Synthesis, Characterization, and In-Vitro Validation of New Meta-Chlorinated Diaryl Sulfonamides as Potential Inhibitors of Cholesteryl Ester Transfer Protein

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Abstract

Hyperlipidemia is characterized by an abnormally elevated level of serum cholesterol, triglycerides, or both. The relationship between an elevated level of LDL and cardiovascular diseases is well-established. Cholesteryl ester transfer protein (CETP) is an enzyme responsible for moving cholesterol esters and triglycerides between LDL, VLDL, and HDL. CETP inhibition leads to a reduction in cardiovascular disease by raising HDL and minimizing LDL.

In this study, ten *meta*-chlorinated substituted benzene sulfonamides **6a-6j** were synthesized, and completely characterized by IR, ^{1}H-NMR, ^{13}C-NMR and HR-MS. Based on *in vitro* biological evaluation, compounds **6e**, **6i** and **6j** demonstrated the strongest inhibitory action against CETP with 100% inhibition, while other compounds **6a-6d** and **6f-6h** inhibitory activity ranged from 47.5% to 96.5% at 10µM concentration. It was found that the presence of meta-chloro moiety elevates the activity of these derivatives when compared to the unsubstituted analogues.

Keywords: Atherosclerosis, Cardiovascular disease, Cholesteryl ester transfer protein, Meta-chlorinated, Sulfonamides.