Novel Meta-Methoxy Aromatic Sulfonamides: Synthesis, Characterization, and Biological Evaluation as Cholesteryl Ester Transfer Protein Inhibitors

By

Tamara Ibrahim Al Husban

Supervisor

Prof. Reema Abu Khalaf

Al-Zaytoonah University of Jordan, 2024

Abstract

Worldwide, the main causes of death are hyperlipidemia, atherosclerosis, coronary heart diseases, and stroke. Inhibition of cholesteryl ester transfer protein (CETP) is a possible strategy to raise high-density lipoprotein cholesterol while lowering low-density lipoprotein cholesterol.

Herein, synthesis and *in vitro* biological evaluation of the CETP inhibitory activity of seven *meta*-methoxy substituted sulfonamides **6a**-**6g** were carried out. Compound **6a** exhibited the best CETP inhibition of 50.5% at 10μM concentration. Interistingly, compound

6a has no substitution at the sulfonamido-phenyl ring which leads to the abscence of steric shield effect from substitution.

Generally, it was found that the presence of methoxy group at the *meta* position of the thiophenyl ring of the synthesized sulfonamides reduced the CETP inhibitory potential in comparison with other previously studied *meta*-chloro, *meta*-fluoro, and *meta*-trifluoromethyl substituted analogues.

Keywords: Atherosclerosis, Cholesteryl ester transfer protein, Inhibitors, Methoxy, Sulfonamides.