Chemical Synthesis and Biological Evaluation of Novel Ortho-Fluorinated Benzene Sulfonamides as Potential CETP Inhibitors

By

Lama Abdallah Al Jaradat

Supervisor

Prof. Dr. Reema Abu Khalaf

Al-Zaytoonah University of Jordan, 2022

Abstract

One of the primary causes of death is cardiovascular disease. Atherosclerosis produces artery constriction or obstruction, which can lead to a heart attack or stroke. Cholesteryl ester transfer protein (CETP) is a protein that aids reverse cholesterol transport. It promotes cholesteryl ester transfer from HDL to LDL and VLDL. Inhibition of CETP by drugs limits cardiovascular disease, by decreasing LDL and increasing HDL. In this study, ten *ortho*-fluoro substituted benzene sulfonamides **6a-6j** 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 compound **6d** have the highest inhibitory activity with 100% inhibition, while compounds **6a-6c** and **6e-6j** had activities ranged from 29% - 83% at 10µM concentration. Interestingly, it was observed that *para*– substituted derivatives (**6d**, **6g**, and **6j**) have greater CETP inhibitory activities than their *ortho*– and *meta*– analogues irrespective to the nature of substituent, i.e., CH_3, Cl, or NO_2.

Keywords: Atherosclerosis, Cardiovascular disease, Cholesteryl ester transfer protein, *Ortho*-fluoro, Sulfonamides.