Design, Synthesis, and Biological Evaluation of Benzophenone Hydrazone Derivatives as PI3Kα Inhibitors

By

Bara'a Ahmad Al-Azaideh

Supervisor

Dr. Dima A. Sabbah

Co-Supervisor

Prof. Ghassan Abu Sheikha

Abstract

Phosphoinositide 3-kinase α (PI3Kα) is a promising target for anticancer drug design. A series of *N*'-(diphenylmethylene)benzenesulfonohydrazide was synthesized and characterized using FT-IR and NMR (^{1}H and ^{13}C). Target compounds exhibited antiproliferative activity against human colon carcinoma (HCT-116) cell line. The *p*-tailored derivatives (*p*-NO_2 and *p*-CF_3) exhibited higher inhibitory activity inferring that electron-withdrawing group and/or hydrogen bond-acceptor guide/s ligand/PI3Kα complex formation on *p*-position. Contrarily, the inhibitory activity of *o*-motif confers that a hydrophobic pocket encloses the *o*-substituent. However, *m*-attachment implies that the steric effect boosts the binding interaction. The induced fit docking studies against PI3Kα illustrates that the series lodges PI3Kα binding pocket and suggests that aromatic interaction guides ligand/PI3Kα complex formation.