Development of a Polymeric Nanoparticle Formulation for Phosphatidylinositol 3-Kinase Alpha (PI3Kα) Inhibitors as a Potential Anticancer Nanomedicine

By

Sundos Fouad Aliyeh

Supervisor

Dr. Suhair Sunoqrot

Co-supervisor

Dr. Dima Sabbah

Al-Zaytoonah University of Jordan, 2022

Abstract

N-(2-fluorphenyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (R19) is a newly synthesized phosphatidylinositol 3-kinase alpha (PI3Kα) inhibitor with promising activity against tumor cells. The purpose of this study was to develop a polymeric nanoparticle (NP) formulation for R19 to address its poor aqueous solubility. NPs were prepared by nanoprecipitation using two different polymers; Pluronic P123 and D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) in different ratios. Pluronic P123 was selected to improve solubility while TPGS was used for its cytotoxic activity. Physicochemical characterization of the NPs showed approximately 60% loading efficiency with around 100nm particle size, high monodispersity, and almost neutral surface charge. The NPs demonstrated a biphasic drug release profile with sustained release up to 96h. Furthermore, NPs containing TPGS enhanced R19's potency against breast cancer cells *in vitro* with IC_{50} reaching 1.8-4.3μM compared to free R19 which had an IC_{50} of 14.7-17.0μM. Our findings show a promising anticancer nanomedicine for the treatment of different cancer forms including breast cancer.

Keywords: Nanomedicine, breast cancer, PI3Kα, polymeric nanoparticles, Pluronic P123, TPGS