## College of Health and Pharmacy

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# DEVELOPMENT OF FOLATE RECEPTOR TARGETED PLGA-PEG NANOPARTICLES FOR DELIVERY OF GENISTEIN IN OVARIAN CANCER

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Genistein (GEN) is a natural isoflavone possessing anticancer activity against different types of cancers. Its use in clinical practice is limited due to its low water solubility, rapid metabolism and excretion, lack of cancer cell targeting, and poor bioavailability. One of the approaches to overcome the above limitations is targeted nano delivery to the affected site. Folic acid (FA), a water-soluble vitamin B, is required in the production of new cells and is essential for both tumor and normal cells. The folic acid receptor (folate receptor, FR) is over-expressed in more than 90% of ovarian cancer cells. In the present study, we investigated PEGylated poly(lactide-co-glycolide) nanoparticles conjugated with folic acid (PLGA-PEG-FA NPs) for targeted delivery of genistein to ovarian cancer cells. PLGA-PEG and PLGA-PEG-FA polymer conjugates were synthesized and characterized. Nanoprecipitation method was utilized for the fabrication NPs of PLGA, PLGA-PEG, and PLGA-PEG-FA. The prepared GEN containing PLGA-PEG and PLGA-PEG-FA NPs were small (104.17±1.61 and 125.41±3.11 nm, respectively) and exhibited sustained release of GEN for around 6 days. In comparison to the non-targeted PLGA-PEG NPs, FA decorated PLGA-PEG-FA NPs showed increased cellular uptake in FR overexpressing SKOV-3 ovarian cancer cells. The GEN containing PLGA-PEG-FA NPs showed superior anticancer activity than non-targeted PLGA NPs and PLGA-PEG NPs in the SKOV-3 ovarian cancer cells. The $IC_{50}$ of GEN, GEN encapsulated NPs of PLGA, PLGA-PEG and PLGA-PEG-FA in the SKOV-3 cells were 51.48, 26.70, 23.43 and 11.98 µg/ml, respectively. The GEN containing PLGA-PEG-FA showed superior anticancer activity than the non-targeted NPs in SKOV-3 ovarian cancer cells. Folate-targeted PLGA nanoparticles could be further developed for potential target-specific delivery of GEN in the treatment of ovarian cancer.