Liposomes for delivery of a novel chalcone analogue as a proposed treatment for triple negative breast cancer

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Background: Triple negative breast cancer (TNBC) accounts for almost 20% of all breast cancer cases, and is the most aggressive type of breast malignancies. Unfortunately, the treatment options of TNBC are limited, and the risk of relapse and metastasis to other organs are significant. In our laboratory, we have developed a range of chalcone analogues, including DK14 that proved to offer a powerful anticancer activity against different types of cancer including TNBC. Like many other potent anticancer drugs, DK14 has poor water-solubility, hindering its further development as a solution or a traditional suspension. Liposomes are established nanocarrier systems with evident safety, attributed to their similar constituents to mammalian biological membranes. Thus, DK14-liposomal formulations were prepared and subsequent physical characterization and biological studies were conducted.

Methods: DK14 liposomes were studied in terms of particle size and zeta potential, using dynamic light scattering and electrophoretic mobility, respectively, and the drug entrapment was determined using High Performance Liquid Chromatography (HPLC). DK14 liposomes were screened against TNBC cell lines using varying techniques such as cell viability, morphological examination, colony formation, migration assay, and gene expression analysis. Furthermore, the liposomes were studied in ovo using a chicken embryo model to evaluate the anti-angiogenic effect of DK14 liposomes versus the drug alone.

Results: Liposomes have a measured hydrodynamic size of 100-140 nm, and the polydispersity index was less than 0.3, with slightly negative zeta potential measurements. The drug entrapment efficiency was as high as 89%, indicating high affinity of DK14 to the liposomal bilayers. Our studies demonstrated that liposomal DK14 have inhibited the proliferation of TNBC cells with less effect on MCF-10A cells. The formulation has also induced apoptosis, evident by the morphological changes of the cancer cells, with apparently less effect on normal cells. Furthermore, DK14 in liposomes had higher selectivity towards the cancerous cells compared to the free drug. Moreover, the liposomal DK14 formulation has inhibited the migration of TNBC cells and colony formation, indicating their potential for inhibiting tumor growth and metastasis. Apoptosis was induced via deregulation of BAX/BCL-2/Caspase-3 pathway. DK14 liposomes have downregulated the PI3K/AKT/mTOR pathway. The in ovo experiment showed DK14 liposomes were able to inhibit angiogenesis of the CAM model.

Conclusions: DK14 liposomes were developed in the nano-size and have demonstrated a substantial anticancer activity against TNBC and have provoked apoptosis via the PI3K/AKT/mTOR pathway. Furthermore, the inhibited angiogenesis in chicken embryos suggests that in vivo studies are merited.