Development of Miriplatin-loaded Nanoparticles against Non-small Cell Lung Cancer

Lung cancer claims the highest mortality and the second-most new cases among all oncological diseases. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all newly diagnosed lung cancers. Although platinum-based drugs are standard first-line chemotherapy for stage IIIB/IV NSCLC, accumulating reports have shown the failure of conventional platinum-based regimens due to drug resistance. Miriplatin is a lipophilic anti-cancer drug that has been approved in Japan for transcatheter arterial chemoembolization treatment of hepatocellular carcinoma. Lipid-based nanoparticles such as liposomes, micelles, and solid lipid nanoparticles (SLNs) can encapsulate anti-cancer drugs to improve their water solubility and bioavailability.

In this study, we formulated miriplatin into novel ultrasmall dots and various SLNs by film-hydration and tested their physicochemical properties and anti-cancer activity against NSCLC cells in culture.

The dots were smaller (~10 nm) and more homogeneous (PDI~0.2), whereas SLNs of different compositions were much larger (~120 nm) and more heterogeneous (PDI~0.4). The images by transmission electron microscopy displayed their sizes and morphology that were consistent with the size and PDI measurements by Zetasizer. Inductively coupled plasma emission spectrometry studies have shown high platinum recovery (>80%) in both ultrasmall dots and SLNs. A three-dimensional multicellular spheroid model of A549-iRFP cells was used for *in vitro* evaluation of anti-cancer activity against NSCLC. The dots and selected SLNs showed significantly stronger activity than free miriplatin, and similar anti-cancer activity to cisplatin which is the first-line chemotherapy drug against NSCLC.

Thus, the reported lipid-based nano-formulations represent a promising delivery system for miriplatin against NSCLC.