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| **Microfluidic Production of 7ACC2 Encapsulated Liposomes** |
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| **Background:**  Oxygen is a potent sensitiser to radiation treatment; therefore, increasing oxygen concentration within a tumour is believed to enhance the therapeutic effects of radiotherapy. The mitochondrial pyruvate carrier (MPC) represents a potential therapeutic target, as it links glycolysis with the TCA cycle, playing a crucial role in facilitating oxidative metabolism. Nanoparticles (NPs) have been at the forefront of research for improving delivery and efficacy of cancer therapeutics. The use of microfluidics (MF) to formulate lipid nanoparticles, is a novel approach, which provides precise control and manipulation of fluids, enabling the formulation of homogenous and reproducible liposomes with desirable size and charge characteristics. |
| **Methods:**  In this research, MFs was utilised to successfully encapsulate the MPC inhibitor drug 7ACC2. Liposomes were prepared using different phospholipids at a concentration of 1 mg mL-1, with variations in phospholipid:cholesterol (p:c) ratio, MFs total flow rate (TFR), and flow rate ratio (FRR), resulting into the manufacturing of NPs with different sizes, polydispersity, and zeta potential results. The NPs were characterised using a variety of physicochemical methods, including DLS, AFM and UV-Vis spectrophotometry for encapsulation efficiency and *in vitro* drug release. |
| **Results:**  DMPC and DPPC liposomes demonstrated the optimum characteristics for drug encapsulation. Lipid type and drug loading concentration had no significant effect on encapsulation efficiency. The drug release rate was faster for high drug loading concentrations (20 µM), with an initial burst release (50%) followed by steady drug release for up to 72 h (98%), and sustained release for up to 1 week. Stability studies showed that liposomes stored at 4°C maintained the most stable size of ~200 nm. Overall, the results suggest that DMPC and DPPC liposomes are suitable for 7ACC2 drug encapsulation, with potential applications in drug delivery. |
| **Conclusions:**  MF formulations, show promising capacity to formulate homogenous and reproducible 7ACC2 NPs. The high-quality ﻿mixing of MF combined with the ability to control the manufacturing method parameters such as FRR and TFR produced favourable liposome characteristics by controlling particle size, reducing PDI, and increasing particle homogeneity. |