MICROFLUIDIC-MEDIATED SELF-ASSEMBLY OF PHOSPHOLIPIDS FOR THE DELIVERY OF BOVINE SERUM ALBUMIN AND TRYPSIN

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Background: Biologics play a major role in our current healthcare systems worldwide; for example, insulins and monoclonal antibodies; however, their use is restricted to parenteral delivery with a relatively uncontrolled release profile. Using a novel microfluidic-assisted method, the encapsulation of model biologics within phospholipids (e.g., liposomes), bovine serum albumin (BSA) and trypsin (TRP), have been successfully demonstrated in this study to portray a contemporary microfluidic method for biologic medical formulation.

Methods: Using various unmodified lipids (e.g., DMPC – Dimyristoylphosphatidylcholine, DPPC – Dipalmitoylphophatidylcholine, DSPC – Distearoylphosphatidylcholine, and DOPC – Dioleoylphosphatidylcholine), parameters such as lipid concentration, active pharmaceutical ingredient (API) concentration, total flow rate (TFR) and flow rate ratios (FRR) have been investigated to determine optimal conditions for loaded-liposome formation. To aid further in the characterisation of the liposomes produced, the carriers were subjected to atomic force microscopy (AFM), Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and high-performance liquid chromatography (HPLC) in order to capture the encapsulation efficiency and drug release.

Results: The current studies have shown encapsulation efficiencies greater than previously published data by methods such as sonication or film hydration, whilst maintaining very promising physicochemical properties. In addition, 28-day physical stability studies have been performed under various conditions to demonstrate the formulations' viability for expansive manufacturing. Aiming to maintain liposome diameters ≤500 nm throughout the study, the shorter chained lipids performed exceptionally at both 21°C and 5°C, suggesting towards their proclivity as suitable API carriers. Initial drug release studies have been measured over 72 hours to indicate the controlled release of the API *in vitro*, with a maximum release of *circa.* 80% release occurring within this duration from DMPC formulations. DSC measurements suggest minimal impact on the thermal stability of the liposomes upon encapsulation of the APIs and has been seen to slightly improve it in the cases of TRP-DMPC liposomes.

Conclusions: The results suggest the success of a novel microfluidic method in achieving the synthesis of biologic-loaded liposomes, as well as offering insight into areas for advancing the technique. Factors such as pH and temperature have been observed to influence factors including encapsulation efficiency and physical stability, which could be explored in further studies to help optimise the process.