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| **Manufacturing & characterization of paclitaxel loaded liposomes by microfluidics** |
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| **Background:** Controlling the delivery of drug molecules can increase the concentration of the drug in chosen locations in the body and avoid unwanted effects, which is the optimum rationale for chemotherapy. Different types of nanoparticles (NPs) can be used for targeting drug delivery, such as metal, polymeric, and lipid NP. Lipid-based NPs, such as liposomes, were chosen for this project due to low toxicity and ability to carry hydrophilic or hydrophobic molecules. Liposomes are typically prepared by traditional methods (e.g., film hydration) with significant limitations, such as large diameter, high Polydispersity index (PDI), and unreproducible formulation. Microfluidics (MFs) is a novel method that excels other methods by offering control of the process parameters. Several parameters can critically impact the liposome properties, such as total flow rate (TFR), flow rate ratio (FRR), the composition of lipids, and surface modification. This project aims to use MFs to produce paclitaxel (PX) loaded liposomes with a diameter <200 nm, low PDI, high homogeneity, and good stability. Furthermore, the impact of using PEGylated lipids towards diameter, encapsulation efficiency (EE%), release profile, and stability, have also been investigated. |
| **Methods:** Both PEGylated (PEG) and conventional liposomes (CL) are fabricated by mixing the lipid phase of DPPC, cholesterol, and PX with the aqueous phase (e.g., PBS) by MFs. DSPE-PEG 2000 is added to the lipid phase for the PEG liposome. Different TFR and FRR have been used to fabricate empty CL, and an optimum ratio was determined for the fabrication of the PX-loaded liposomes. The lipid composition for PEG and CL formulations kept the same, 2:1 lipid to cholesterol. Different DPPC to DSPE-PEG2000 ratios were investigated. The NPs physicochemical characteristics were studied, by dynamic light scattering (DLS), Fourier transform infrared spectroscopy (FTIR) and atomic force microscopy (AFM). The dialysis tube method was used to study the drug EE% and release, which was analysed by HPLC. |
| **Results:**  Both CL and PEG liposomes show promising physiochemical characteristics with consistent, repeatable results. All the liposomal formulations have achieved the aimed diameter (<200 nm), and the PDI average was optimum (<0.3) with a neutral charge ζ-potential. The diameter of CL decreased after PX encapsulation from 168 ± 4 nm to 153 ± 10 nm. The diameter of the different ratios of the empty PEG liposomes was <150 ± 23 nm. The different ratios of PEG liposomes show different effects on PX encapsulation; some liposomes' diameter increased after encapsulation, and others decreased. Based on the results, the higher PEG lipid ratio leads to decreased liposome diameter after encapsulation from 137 ± 29 nm to 112 ± 14 nm. In contrast, the lower PEG lipid ratio increased the diameter from 144 ± 17 nm to 150 ± 40 nm. The EE% for the PEG and CL was above 90 %. For the CL, the release started after 24 h, which indicates delayed drug release, and the percentage of the drug release was 50 % after 72 h.​ For the PEG liposomes, the release started after 12 h for all the formulations and reach the highest drug release percentage (60%) after 72 h.  |
| **Conclusions:** Liposomes characteristics can be altered by changing parameters such as TFR, FRR, lipid composition, and PEG surface modification. The high-quality mixing of MFs and the ability to control the manufacturing method parameters can control the NP size, reduced the PDI, and increased the formulation reproducibility. |