Preparation of nanoliposomes and nanocrystals using microfluidic strategies

[Poster]

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Preparation of nanoliposomes and nanocrystals using microfluidic strategies

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1. Introduction

- Nanocrystals (NC) and nanoparticles (NP) are used in pharmaceutical industries as they offer improved performance of active ingredients, stability, controlled delivery, increased comfort and reduction in overall drug content. It is also used in other industries such as food, cosmetics and other nanotechnology applications.
- Microfluidic devices (MFD) offer better control of different parameters such as size of NP, particle size distribution, reaction conditions, reduced residence time, etc.
- Encapsulated drug NP in liposomes are helpful in targeted delivery for cases of drugs with poor water solubility.
- Liposomes are spherical vesicles, organised in one or several concentric phospholipidic bilayers with aqueous core inside.
- Poor water-soluble drugs such as Hydrocortisone (HC) and Rapamycin (RAP) pose problems, such as the exact amount of the active ingredient to be delivered to the cells in most need of these drugs in the body, as such, encapsulated drugs using liposomes are already being used in some cancer therapies (Myocet, Duanoxome, Doxi, Paclitaxel, Docetaxel, Etoposide, Hydroxytamoxifen, Doxorubicin, etc.)
- The aim is to produce drug NP in microfluidic and membrane devices, and encapsulate in such a way that they could be delivered and released to the appropriate site in the human body.

2. Experimental set up

Experiments were carried out in fabricated glass capillary microfluidic devices, to synthesise hydrocortisone nanosuspensions and modified ethanol injection method to produce liposomes. Figures 1 and 2 is the schematic diagram of the microfluidic device and the synthesis of the hydrocortisone nanoparticles in the device respectively, while Figure 3 is the schematic diagram of the modified ethanol injection method.

3. Nanocrystals formation

HC is completely soluble in sodium, but the solubility in pure water at 298K is very low, which means that the HC solubility in ethanol/water mixture should have a very narrow range for pure water to be useable for pure ethanol. For crystallisation of HC, to occur, a sub-saturation, the operating line must be above the solubility line, e.g., in the super-saturated region of Figure 4. The yield of nanocrystal would be rather low if acetoehol is used as solvent. In order to obtain a reasonable yield of drug nanocrystals, HC was dissolved in a mixture of ethanol and water, rather than just pure ethanol.

4. Nanocrystal characterisation

XRPD profiles of processed and unprocessed HC were analysed. Peaks observed in Figure 7 corresponds to the profiles of the pure unprocessed and processed samples of HC as compared to the ICDD database for HC. This peak reduced for the processed drug which indicates the encapsulation of the drug in the polymer and stabilizers.

5. Nanoliposome characterisation

The counter-current MFD produced smaller sized nanoliposomes due to the micromixing occurring in the smaller round capillary. The concentration of the HC used in the samples was 7mg/ml while the concentration of the stabilisers hydroxypropyl methyl cellulose (HPMC) was 0.2g/ml and processed sample of HC with and without the stabilizers.

Conclusions
- Nozzle diameter of MFD affect the size of nanocrystals produced.
- Concentration of phospholipid, flux, membrane pore size and rotational speed of paddle all affect the size of nanoliposomes produced, and therefore size of drug nanoparticles can be modified based on these parameters.

Future Work
- Synthesis of nanoparticles using 3D-printed MFD.
- Encapsulation of various drug nanoparticles produced and study of the release rates of encapsulated drugs.
- Synthesis of liposomes using continuous phase systems.

REFERENCES

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