23

Impact of Lipid Composition on Liposome Stability and Cannabinoid Drug Encapsulation

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INTRODUCTION

Recent literature increasingly supports the therapeutic use of cannabinoids. They have been shown to be beneficial in the treatment of chronic pain, nausea and seizures.[1] Due to their poor solubility in water,[2] cannabinoids have difficulty entering the bloodstream and demonstrate low oral bioavailability. Lipid nanoparticles offer an effective alternative to improve pharmacokinetic and biodistribution profiles of drug payloads. Crucial considerations for these systems pertain to size and uniformity, which impact liposome circulation time and tissue penetration.

Microfluidic-based preparation of liposomes allows particle size tuning either by controlling instrument process parameters or by means of changing the lipid composition including the cholesterol content, phospholipid type and lipid to API ratio.

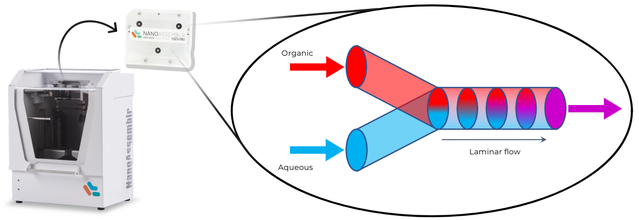
Cholesterol plays an important role in the physical properties of liposomes[3] as well as in tuning drug release profiles.[4] Saturated phospholipid species have more intermolecular interactions and can pack more densely which resuts in more rigid bilayers and consequently produce larger liposomes.

PURPOSE

To study the impact of phospholipid type (synthetic vs. natural, unsaturated vs saturated) and lipid components ratio on liposome drug retention, size, and stability using microfluidic techniques.

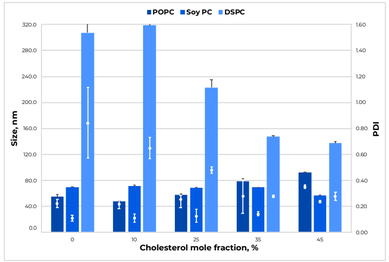
METHODS

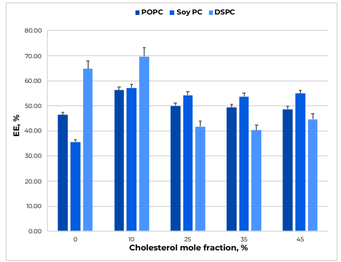
- Precision NanoSystems' NanoAssemblr Benchtop was used to formulate the nanoparticles.
- Lipids and THC were solubilized in ethanol (organic phase).
- Particles were dialyzed and then sized by DLS (Malvern Zetasizer).
- Dissolution profiles were obtained by the dialysis sac method.
- THC concentration in the release media was measured by ELISA.



RESULTS

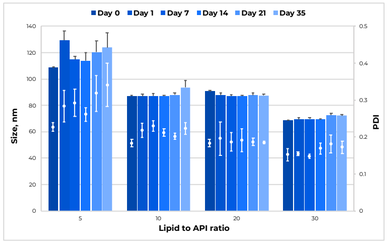
Lipid Composition Effect on Liposome Size and EE%

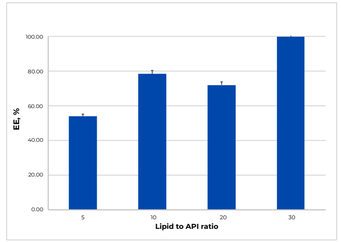




Lipid to API Ratio Effect on Liposome Size and EE%

POPC : Chol : DSPE-PEG = 77 : 20 : 3 mol%





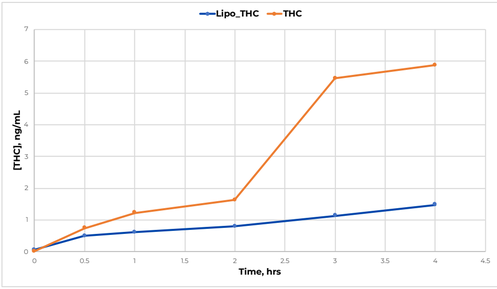
Formulation Parameters

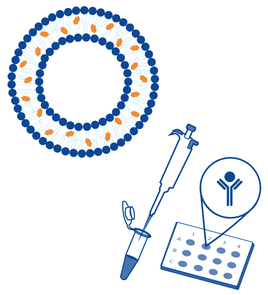
Lipid Composition	PC* : Chol : DSPE-PEG (97-x : x : 3 mol%) PC* = POPC, SoyPC, DSPC
Total Lipid Concentration	40 mg/mL
Organic Solvent	Ethanol
Aqueous Solvent	PBS pH 7.4
Total Flow Rate	12 mL/min
Flow Rate Ratio	1.5 : 1
Lipid to API Ratio	n : 1 - n indicated on the horizontal axis
Solvent Removal	Dialysis

Dissolution Parameters

Lipo_THC	PC : Chol : DSPE-PEG 72 : 25 : 3 mol% Lipid to API 10 : 1 Size 68.7 ± 0.7 nm [THC] = 1.24 mg/mL PBS
THC	[THC] = 1.24 mg/mL EtOH : H_2O 1:1
Conditions	37°C PBS pH = 7.4
Method	ELISA

Dissolution Results





CONCLUSIONS

- Particle size can be tuned with instrument parameters, FRR and TFR.
- Unsaturated lipids (POPC, Soy PC) produce smaller particles than saturated (DSPC).
- POPC liposome size increases with increasing cholesterol concentration.
- DSPC liposome size decreases with increasing cholesterol concentration.
- Soy PC liposome size is not significantly affected by cholesterol amounts.
- Higher lipid to API ratios result in higher EE%.
- Liposomes with higher cholesterol content are more stable upon storage.
- THC release profile can be tuned using liposomal formulation.

FUTURE WORK

- Apply the microfluidic approach to the preparation of cannabinoid solid lipid nanoparticles.
- Study the behaviour of different cannabinoids in various types of lipid-based nanoparticle formulations.

AFFILIATIONS

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