Optimization of liposomal composition to efficiently encapsulate dexamethasone or dexamethasone phosphate and enable their sustained release

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1. INTRODUCTION

Liposomes can encapsulate an active ingredient (API) and selectively address it to its site of action while controlling its release, making them a good option to reach difficult targets such as inner ear hair cells in the treatment of sensorineural hearing loss. The development of a sustained release (SR) formulation would allow a stable concentration of API in the cochlea while reducing the number of administrations. This SR activity is determined by the lipid composition of the liposome. For example, the incorporation of saturated lipids (DPPC or DSPC) in the formulation, as well as the increase in the cholesterol (Chol) percentage, are described to stabilize the lipid bilayer and prolong the release. The addition of DSPE-PEG_{2000} can also improve the permeability of the liposome through the round window membrane (RWM), located between the middle and the inner ear. **The aim of this work is therefore to test the impact of different liposome formulations on the release of dexamethasone (Dexa) or dexamethasone sodium phosphate (DexaPO_4) used as APIs. These will be compared to identify the best therapeutic option.**

2. MATERIALS & METHODS

2.1 Liposomes composition and production

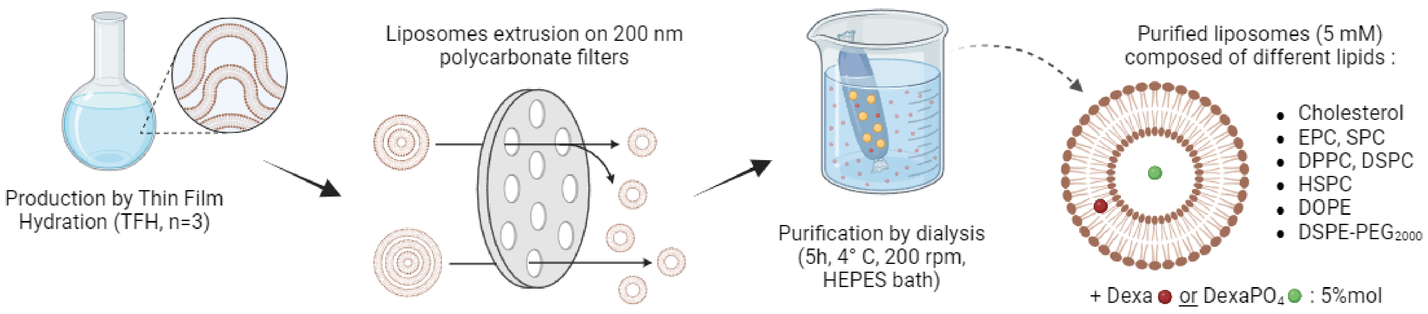

Figure 1. Production, extrusion and purification of liposomes composed of different types of lipids (Chol, EPC, SPC, DPPC, DSPC, HSPC, DOPE, DSPE-PEG_{2000}) [1].

2.2 Release test

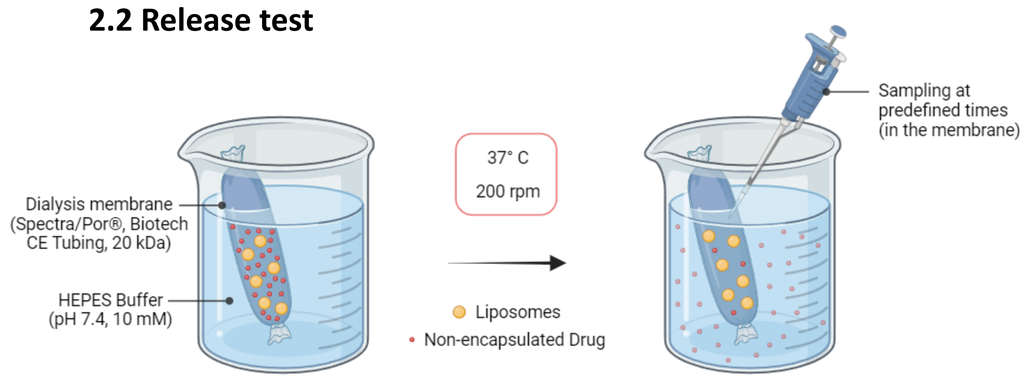

Figure 2. Release test based on a dialysis method [1].

3. RESULTS

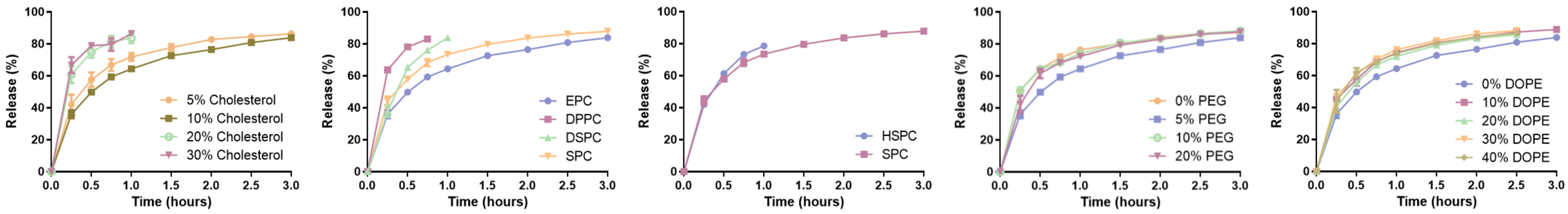

Figure 3. Optimization of lipid composition to sustain the release of **Dexa** encapsulated in liposomes.

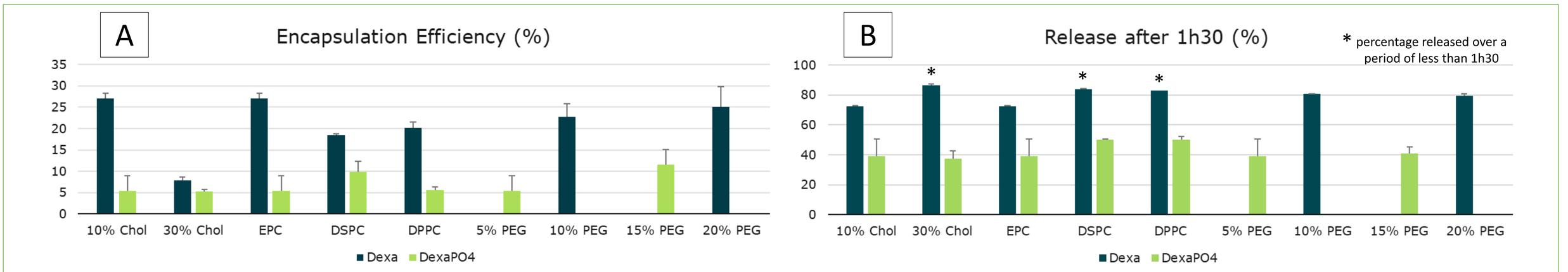

Figure 4. (A) Comparison of Dexa and DexaPO_4 encapsulation efficiencies for TFH-produced liposomes. (B) Comparison of the percentages of API (Dexa or DexaPO_4) released after 1h30 of release test (at 37° C and 200 rpm).

The percentage of Chol that led to the best encapsulation efficiency (EE) and release rate results is 10%, both for Dexa or DexaPO_4. Thus, Chol will be used at a low percentage due to its structural analogy with Dexa and their competitive effect for space in the bilayer. EPC is the lipid with the best EE and SR for both APIs, while saturated or hydrogenated lipids have no positive effect on these parameters. The percentage of DSPE-PEG_{2000} did not impact the release, but a higher percentage would increase the EE of Dexa and DexaPO_4. Adding DOPE to liposomes did not greatly affect EE and SR. In the next future, if DOPE shows interesting results on cell uptake, it could be added without affecting the kinetics. Overall, Dexa-liposomes have better EE and DexaPO_4-liposomes have better SR. The former seems more interesting to reach therapeutic concentrations.

4. CONCLUSION & PERSPECTIVES

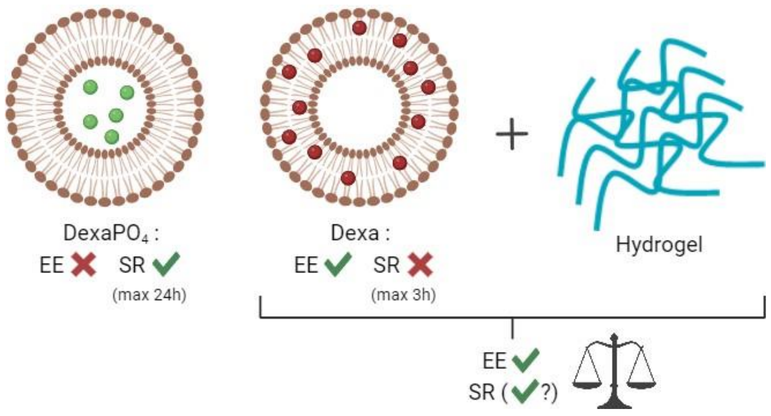

Figure 5. Dexa-liposomes will be dispersed in a hydrogel to improve the SR effect [1].

Impact of lipids

- Chol : should be used, but at low percentage
- EPC, SPC, DSPC, DPPC, HSPC, DOPE and DSPE-PEG_{2000} : negligible effect on EE and SR. These will be tested *in vitro* and depending on their biocompatibility with inner ear hair cells (HEI-OC1), the most appropriate components will be selected.

5. REFERENCES

[1] Created with BioRender.

6. ACKNOWLEDGMENTS

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