# DEVELOPMENT OF OPTIMIZED LIPOSOMES FOR SUSTAINED-RELEASE TRANSTYMPANIC ADMINISTRATION

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## INTRODUCTION

Liposomes are small vesicles whose lipid bilayer is mainly composed of cholesterol (Chol) and phospholipids. As smart nanocarriers, liposomes can selectively address the active ingredient to its site of action and control its release, making them a good option to reach difficult targets such as inner ear hair cells in the treatment of sensorineural hearing loss [1]. The sustained release (SR) of this substance would reduce the number of administrations, while maintaining a stable therapeutic activity. This SR activity is determined by the lipid composition of the liposome. Indeed, the incorporation of saturated lipids and the increase in the percentage of Chol in the formulation will stabilize the lipid bilayer and slow down the release of the active molecule [2]. The aim of this work is therefore to test different formulations on the release of dexamethasone (Dexa) used as active ingredient. A physicochemical characterization will also be carried out.

## MATERIALS & METHODS

The liposomes (5 mM) are composed of EPC, Chol and DSPE-$PEG_{2000}$, with a percentage of PEG fixed at 5% and a percentage of Chol varying from 20 to 40% w/w. They are produced by rapid mixing (n = 3; TFR = 1 mL/min; FRR = 1/1) and then purified by dialysis. The size and PdI are characterized using Dynamic Light Scattering (DLS). Dialysis duration and encapsulation efficiency of Dexa are evaluated by HPLC-UV, using a LiChrospher 100 RP-18 (250 x 4 mm, 5 µm) column and LiChroCART 4-4 (4 x 4 mm, 5 µm) guard column. The mobile phase consisted of a 50/50 (v/v) mixture of acetonitrile and water. The flow rate was 0.8 mL/min and 10 µL samples were injected. Dexa was detected at 250 nm.

## RESULTS & DISCUSSION

The first formulation tested contained EPC/Chol/PEG (60/35/5% w/w). DLS analysis showed a liposome size around 150 nm, which is our target size for the transtympanic delivery of liposomes, with a good PdI (less than 0,3). To assess the dialysis duration, a sample of liposomes was taken every hour and then assayed by HPLC-UV. The difference in Dexa concentration after 5 hours and after 6 hours of dialysis was not significant. The dialysis duration was set at 5 hours with a change of medium every hour. Liposome size is not impacted by the dialysis process and has shown a certain short-term stability (over 48h). The encapsulation efficiency (EE), representing the ratio between the concentration of encapsulated Dexa and the total concentration of Dexa introduced, corrected by the concentration of lipids in purified liposomes, is around 4.09%. The release profile must now be compared to that of the other formulations.

## CONCLUSION

These first results show that the physicochemical characteristics of this formulation as well as the EE of the Dexa are suitable for transtympanic administration. The next step will therefore be to vary the composition of the formulation (percentage of PEG, Chol proportion, replacement of EPC by DPPC, DSPC or DSPG) to compare their effect on the SR properties.

## REFERENCES

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