Targeting cartilage matrix with cationic liposomes for osteoarthritis treatment

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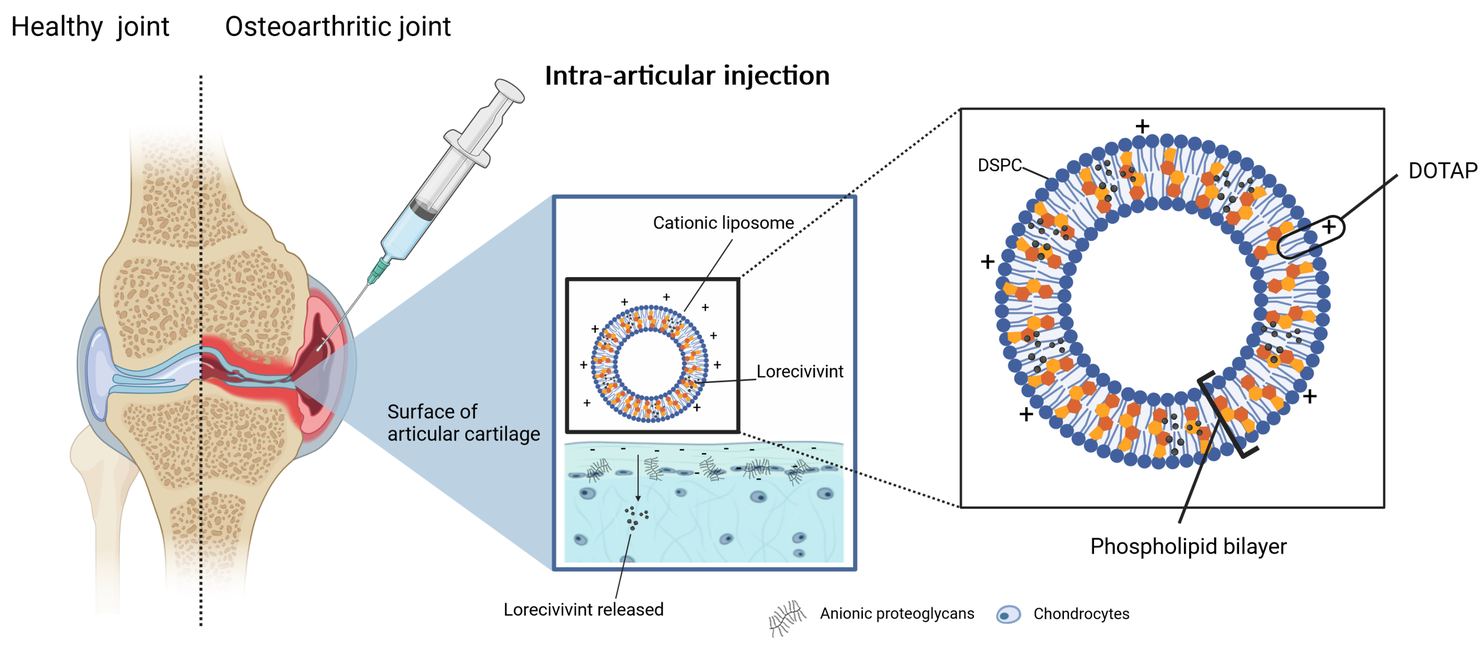
INTRODUCTION

Osteoarthritis (OA) is the most common degenerative joint disorder characterized by the progressive **deterioration of the articular cartilage**.

Disease-modifying osteoarthritis drugs (**DMOADs**) have emerged as a promising approach **to halt or slow doen OA progression** by targeting the mechanisms contributing to cartilage degradation. [1]

Lorecivivint (LOR), a promising hydrophobic DMOAD, can be encapsulated in liposomes to enhance its aqueous solubility.

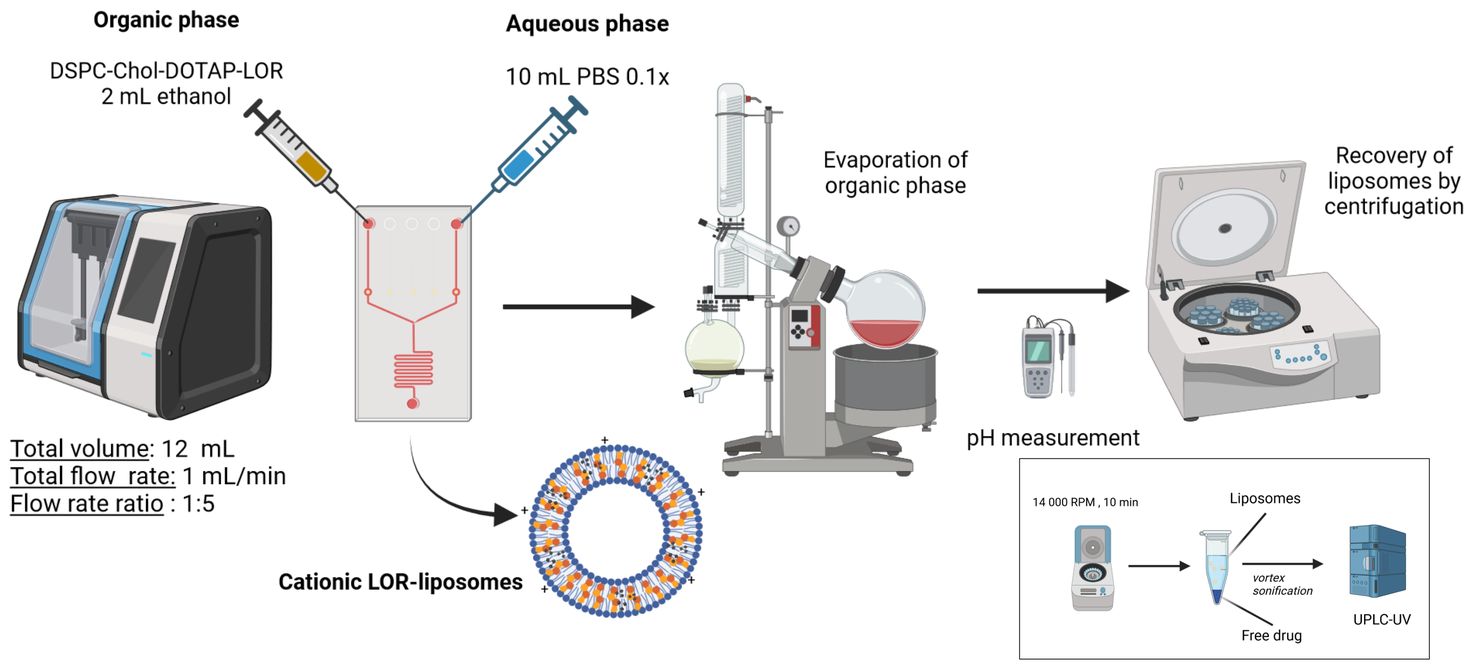


AIMS

DSPC-Chol-DOTAP-enriched cationic liposomes were designed to:
(i) **increase LOR water solubility**, (ii) **ensure a slow drug release**, and (iii) **target cartilage's anionic glycosaminoglycans (GAGs)** to increase cartilage uptake.

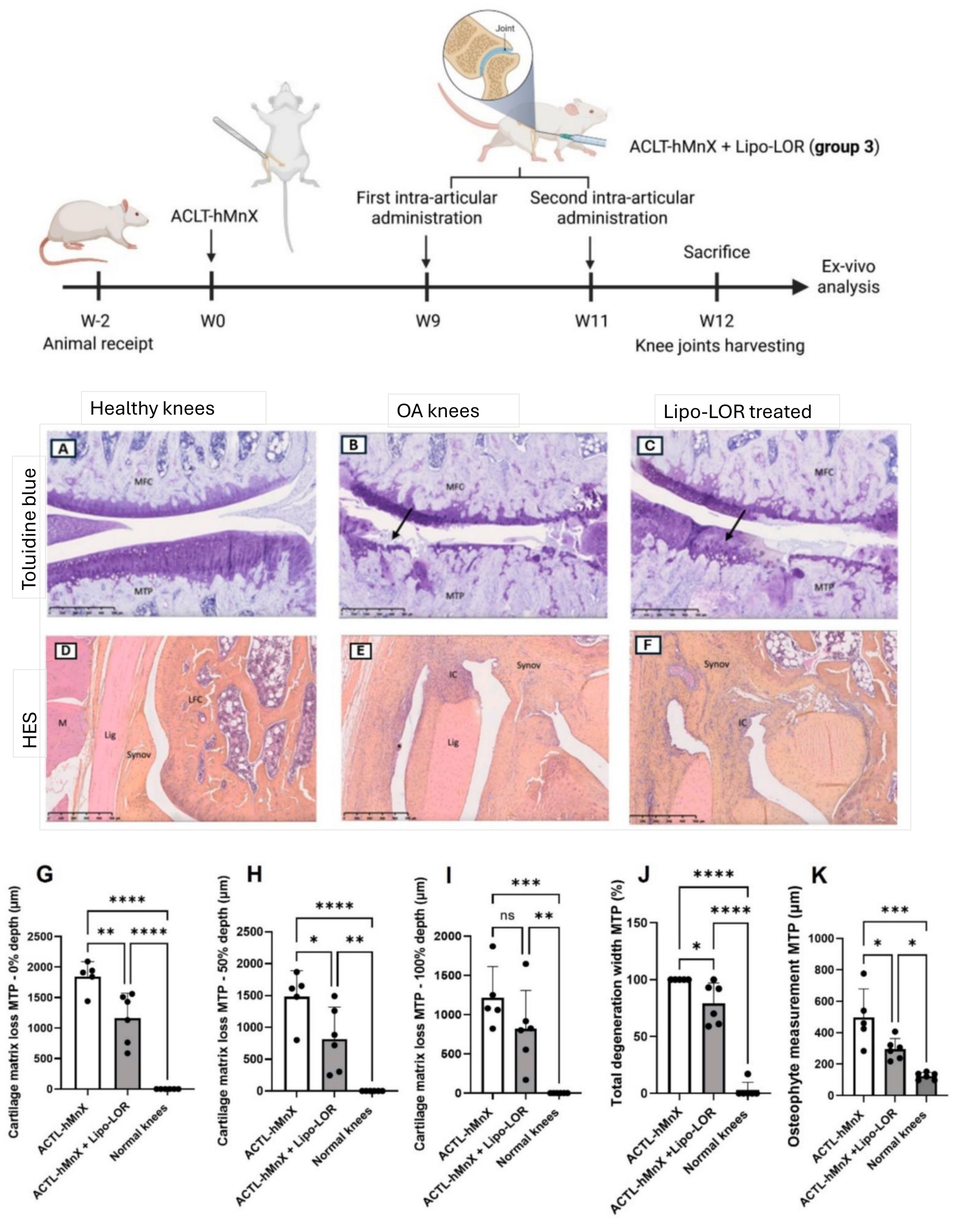
METHODS

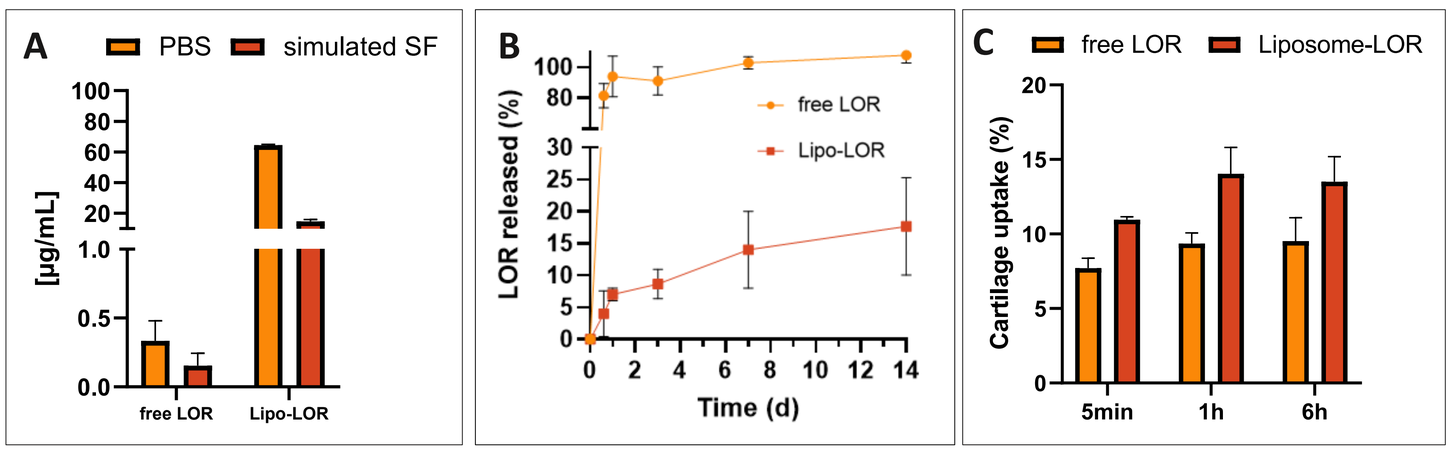
- **Microfuidic formulation** (NanoAssemblr Ignite™, Precision Nanosystem).
- **Encapsulation efficiency (EE)** : UPLC-UV.
- **Release study** in PBS, 14 days at 37°C.
- **Size** and **zeta potential** in H2O *vs* simulated synovial fluid (SF) by DLS (Zetasizer nano-ZS).
- **Ex-vivo cartilage uptake** using in bovine cartilage explants, PBS, 1min, 1 h, and 6 h.
- **In vivo pilot study i**n late-stage ACLT rat model.



RESULTS

- **Solubility** of LOR **increased** by 120x in PBS and 100x in SF **(A)**.
- Cationic liposomes showed a **slow LOR release** (18±8 % over 14 d, **B).**
- Liposomes **increased by 1.5-fold the uptake by cartilage** at 6h **(C)**.
- The **EE** of LOR was **48 %;** LOR-loaded liposomes of **145 nm** with **zeta potential** reversed from **+35.7 mV** in **PBS** to **-18.8 mV** in **SF.**
- In vivo, in a late-stage ACLT model of OA (histologies A-C), LOR-liposomes demonstrated **reduced cartilage loss** in the medial tibial plateau **(G-J)** a well as a **reduced osteophyte formation (K).**
- **No adverse effects** were observed in vivo, indicating a favorable **safety profile** of the cationic liposomal formulation.





ANOVA one-way & Tukey's, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

CONCLUSIONS

✓Cationic LOR-liposomes highly loaded with LOR, increasing its solubility in synovial fluid.
✓Enhanced incorporation of drug-loaded liposomes in cartilage explants.
✓In vivo preservation of some key cartilage features in an advanced OA model.

REFERENCES

[1] Morici L, et al. Int. J. Pharm. 2024
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