DELOS nanovesicle-based thermoreversible hydrogels for subcutaneous drug delivery: a promising strategy for extended release

Marta Vinha Vieira[1,2], C. Castellar-Álvarez[1], A. Córdoba[1], S. Sala[1], N. Ventosa[1,2,3], E. González-Mira[2,3], L. Ferrer-Tasies[1]

[1] Nanomol Technologies S.L., 08193 Cerdanyola del Vallès, Spain
[2] Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), 08193 Cerdanyola del Vallès, Spain
[3] Centro de Investigación Biomédica en Red-Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), 28029 Madrid, Spain

1 Background and Aim

- The **subcutaneous route** has recently gained attention for its potential to facilitate **extended drug release**, particularly for **chronic** and **long-term disease** treatments [1].

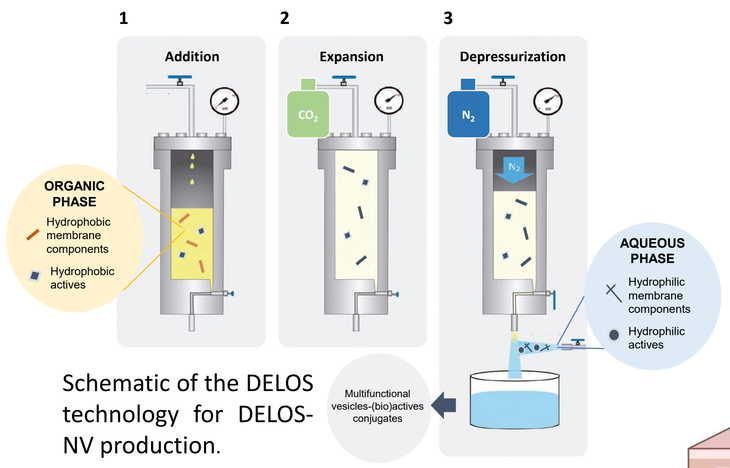
✓ Maintains therapeutic levels
✓ Reduces dosing frequency and side effects
✓ Suitable for biologics
✓ Improves patient's compliance

- Herein, we aimed to develop a **DELOS nanovesicle**-based **thermoreversible hydrogel** as a platform for **extended delivery** of active compounds.

2 DELOS Nanovesicles

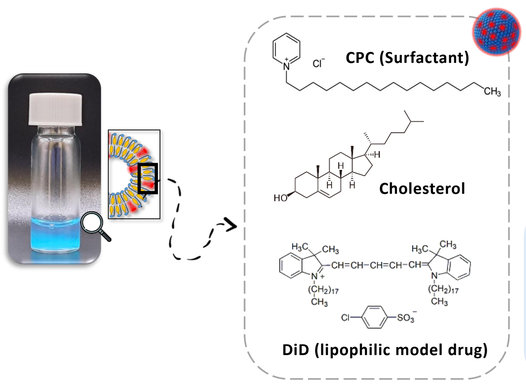
- DELOS-NV are **highly stable lipid-based unilamellar vesicles** formed by the self-assembly of **cholesterol** (Chol) and a quaternary ammonium **surfactant**, capable of **protecting and stabilizing** hydrophilic and lipophilic APIs [2].

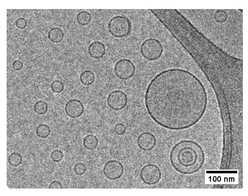
✓ Patented [3,4]
✓ Scalable
✓ Sustainable
✓ GMP available



Schematic of the DELOS technology for DELOS-NV production.

- **DELOS-NV membrane composition in this work:**

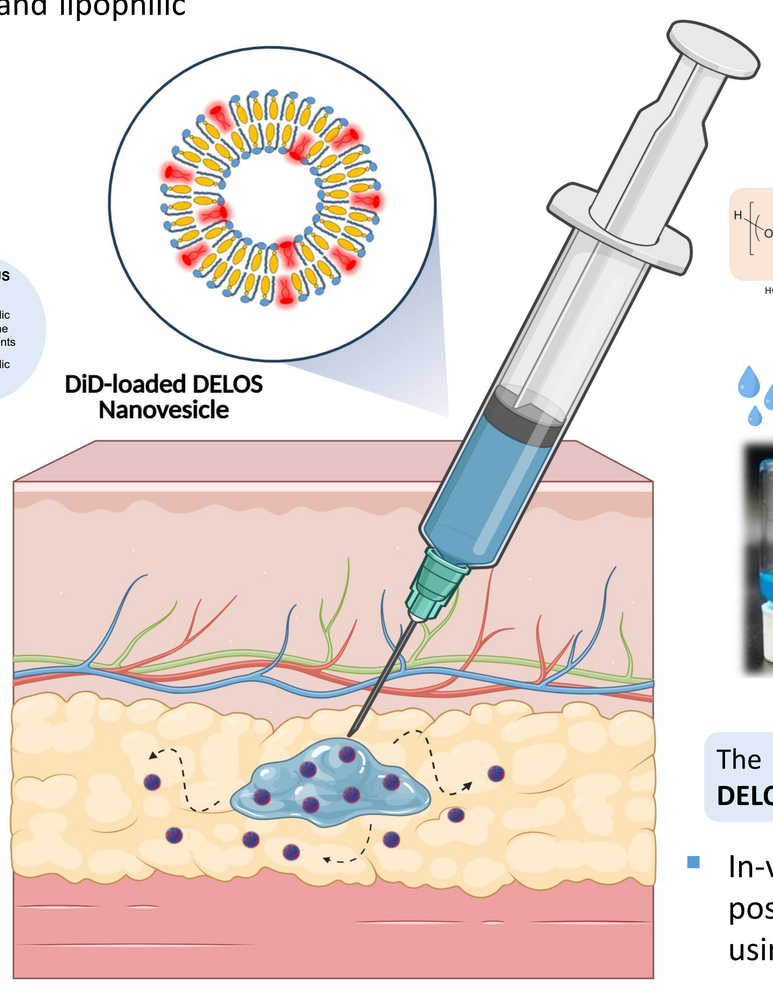




DiD-loaded DELOS-NV showed a **uniform nanometric** size (< 100 nm; PDI 0.2)

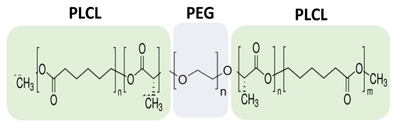
3 Thermoreversible hydrogel

- **Thermoreversible hydrogels** form **in-situ subcutaneous depots** via micellar self-assembly at **body temperature**.

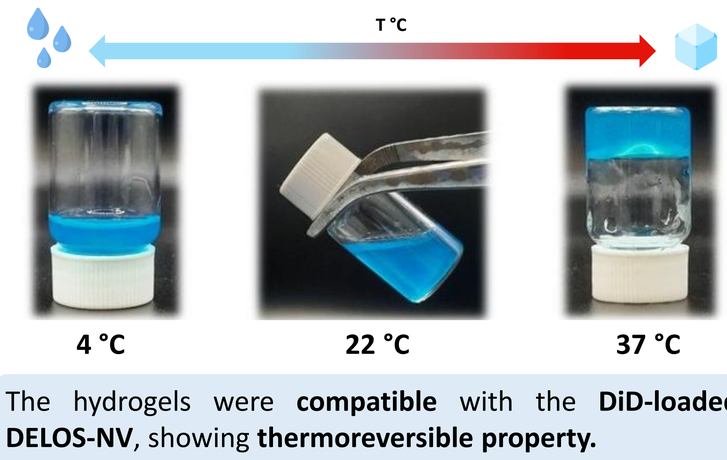


- To modulate drug release, **two triblock copolymers** were tested at **25%** and **30%** concentrations:

- LA:GA 75:25 Mw: 1600:1500:1600



- CL:LA 60:40 Mw: 1700:1500:1700



The hydrogels were **compatible** with the **DiD-loaded DELOS-NV**, showing **thermoreversible property.**

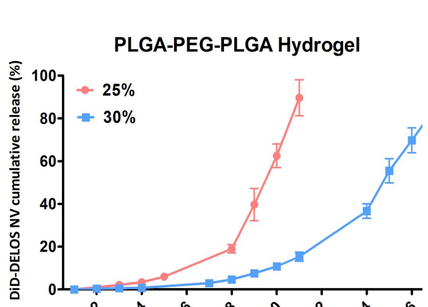
- In-vitro release of DiD-loaded DELOS-NV and their post-release integrity were assessed in PBS (pH 7.4) using a membraneless method.

4 In-vitro release

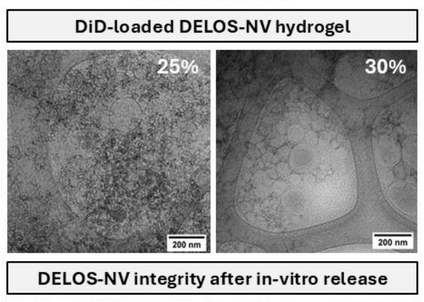
- **Polymer type** and **concentration** significantly **affect** release **kinetics**.

- **DELOS-NV** maintained **morphological integrity** post-release, confirming their **stability**.

PLGA-PEG-PLGA

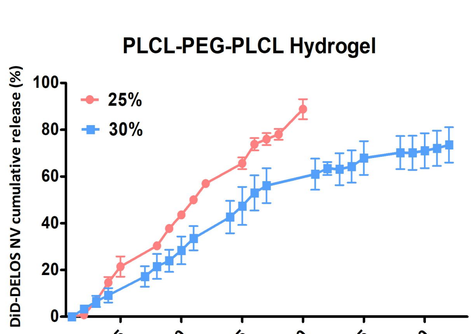


Biphasic release: slow onset, then rapid degradation-driven release.

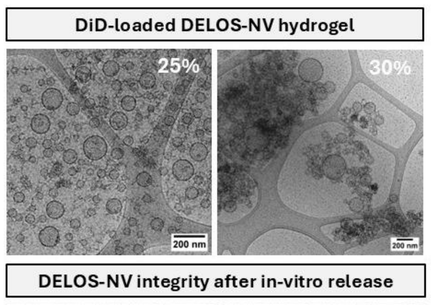


Cryo-TEM images of the PLGA-PEG-PLGA DiD-loaded DELOS-NV-based hydrogels and of the final release medium (integrity post-release).

PLCL-PEG-PLCL



Controlled and extended release up to **30 days.**



Cryo-TEM images of the PLCL-PEG-PLCL DiD-loaded DELOS-NV-based hydrogels and of the final release medium (integrity post-release).

5 Conclusions

- DELOS-NV-based hydrogels showed extended in-vitro release of an encapsulated lipophilic model compound.
- The release profile was tuneable based on polymer type and concentration.
- The platform shows strong potential for prolonged drug delivery, enhanced efficacy, and improved patient compliance in long-term treatments.

Hybrid hydrogel system for long-term therapies

✓ Improves patient treatment compliance
✓ Protects and stabilises sensitive drugs
✓ Use of eco-friendly, sustainable technology

References:

[1] KAR, A. et al. Wearable and implantable devices for drug delivery: Applications and challenges. *Biomaterials*, 283, 2022.
[2] FERRER-TASIES, L. et al. Quatsomes: Vesicles formed by self-assembly of sterols and quaternary ammonium surfactants. *Langmuir*, 29 (22), 6519–6528, 2013.
[3] VENTOSA, N. et al. (2005). Method for obtaining micro- and nano-disperse systems (Patent WO2006079889A1).
[4] CÓRDOBA, A. et al. (2024). Method for obtaining nano-disperse systems (Patent EP4382895).
[5] FERRER-TASIES, L.. … VINHA VIEIRA, M. et al. (2024). Stimulus-responsive gelable liquid composition comprising vesicles (Patent EP24382895).

Acknowledgements:

This poster is part of the GreenX3 project - funded by the European Union Horizon Europe MSCA Doctoral Network programme under EC Grant Agreement 101120061 and by UK Research and Innovation (UKRI) under the UK government's Horizon Europe funding guarantee [grant number EP/Y032039/1].