Elasticity-Driven Nanoparticle Penetration Across Hydrogel Barriers

Chathuri Isurika Sodimanage[1], Agnes-Valencia Weiß[1], Marc Schneider[1]

[1] Department of Pharmacy, Biopharmaceutics and Pharmaceutical Technology, PharmaScienceHub (PSH), Saarland University, 66123 Saarbrücken, Germany

UNIVERSITÄT DES SAARLANDES

TALENTS

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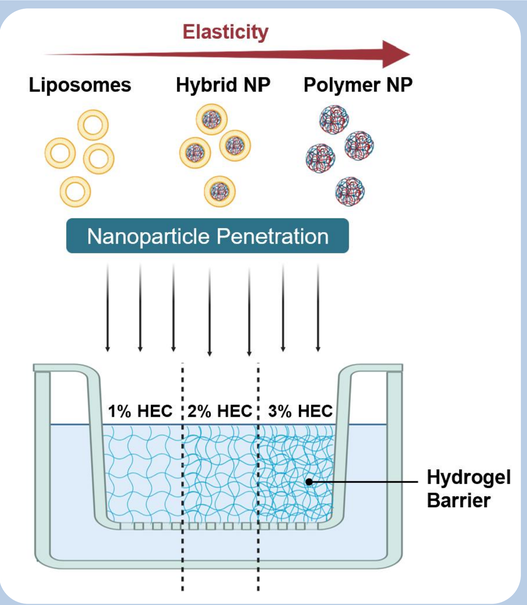
Introduction

Overcoming biological hydrogel barriers remains a significant challenge in drug delivery. Recently, nanoparticle elasticity has gained attention as a crucial physicochemical property influencing bio-barrier penetration. However, investigating elasticity-driven penetration behavior across dynamic biological environments remains a complex task [1]. As an initial approach to address this challenge, the current work investigates penetration behaviour of elasticity-modified nanoparticles across a mucus-mimicking hydroxyethyl cellulose (HEC) hydrogel. Specifically, the study evaluates three distinct types of nanoparticles namely liposomes, lipid–polymer hybrid nanoparticles composed of phospholipids and poly(lactic-co-glycolic acid) (PLGA), and bare PLGA polymeric nanoparticles.



Materials & Methods

Method of Preparation

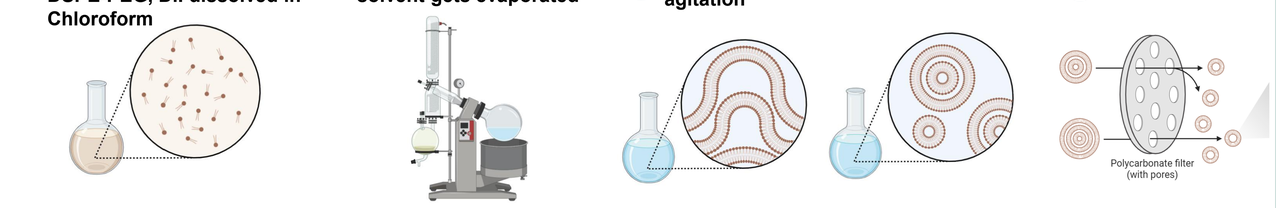
Liposomes -Thin Film Hydration

1 **Phospholipid, Cholesterol, DSPE-PEG, DiI dissolved in Chloroform**

2 **Rotovap the mixture until solvent gets evaporated**

3 **Hydrate the lipid film with PBS under agitation**

4 **Extrusion**



DiI-1,1'-Dioctadecyl-3,3,3',3'-Tetramethylindocarbocyanine Perchlorate

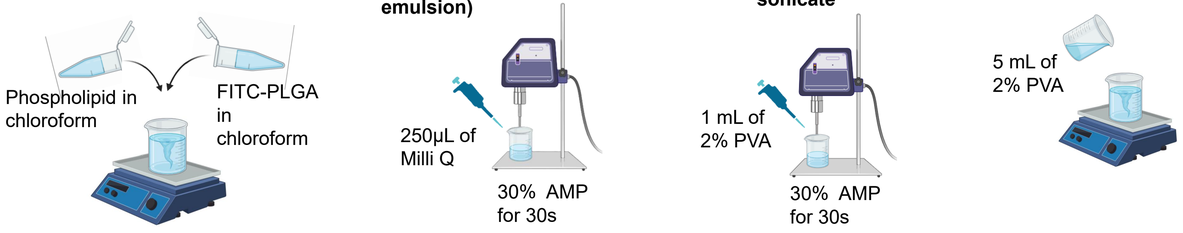
Hybrid NP – Nanoemulsion

1 **Mix Phospholipid and PLGA**

2 **Add 250 µL of Milli Q and sonicate (to form W/O emulsion)**

3 **Immediately add 2% PVA and sonicate**

4 **Add more PVA and Stire overnight**



FITC - Fluorescein Isothiocyanate

PLGA NP - Nanoprecipitation

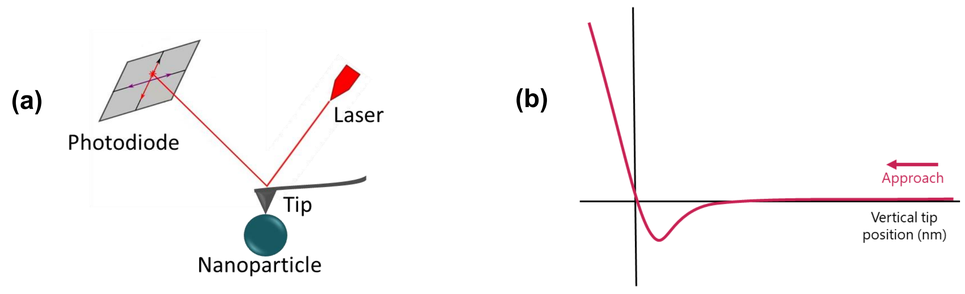
1 **Mixing organic phase and aqueous phase**

2 **Overnight stirring to remove organic phase**

3 **Centrifugation (3 washing cycles)**

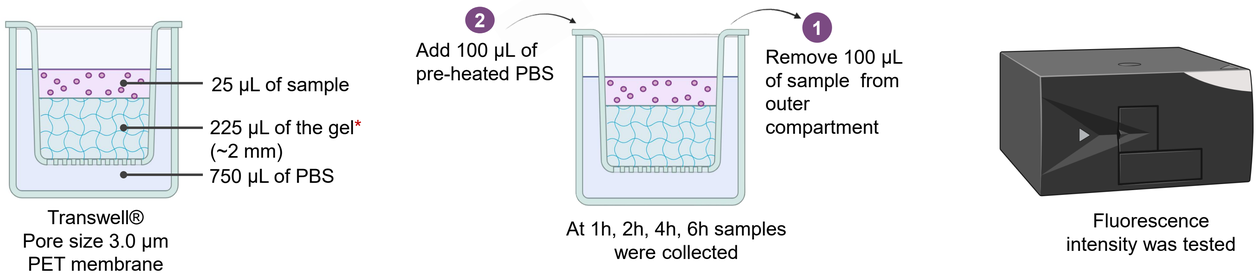
Elasticity measurement of Nanoparticles

- The elasticity of the resulting nanoparticles was measured using atomic force microscopy (AFM) in liquid media



***(a)** Schematic representation of the nanoindentation measurement using AFM and **(b)** the corresponding force-distance curve*

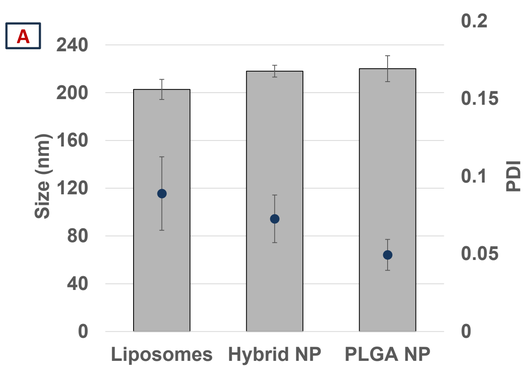
In vitro Penetration Assay



*Three concentrations of the HEC hydrogel (1%, 2% and 3% w/v) were tested, and phosphate-buffered saline (PBS) was used as control.

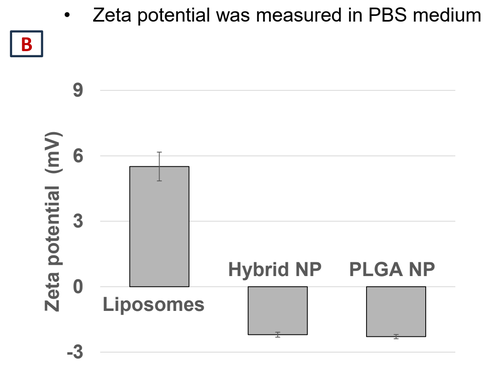
Results

Particle Size



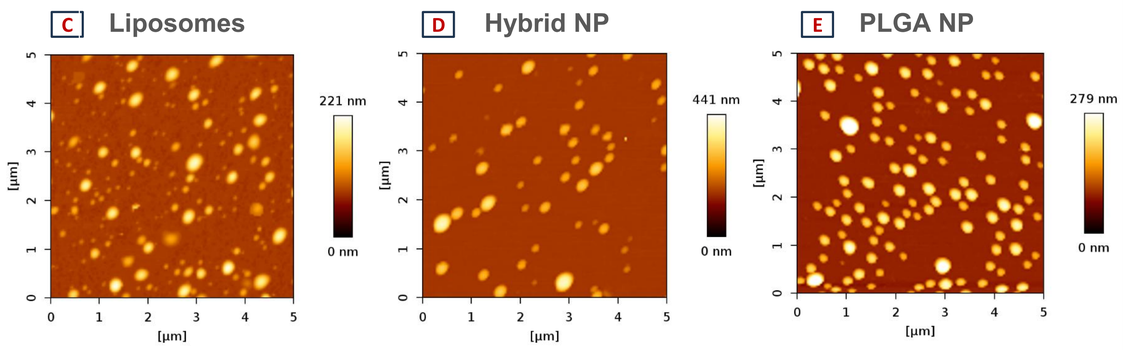
Zeta Potential

- Zeta potential was measured in PBS medium



A.** Size, Poly dispersity index (PDI), and **B.** Zeta potential of **Nanoparticles

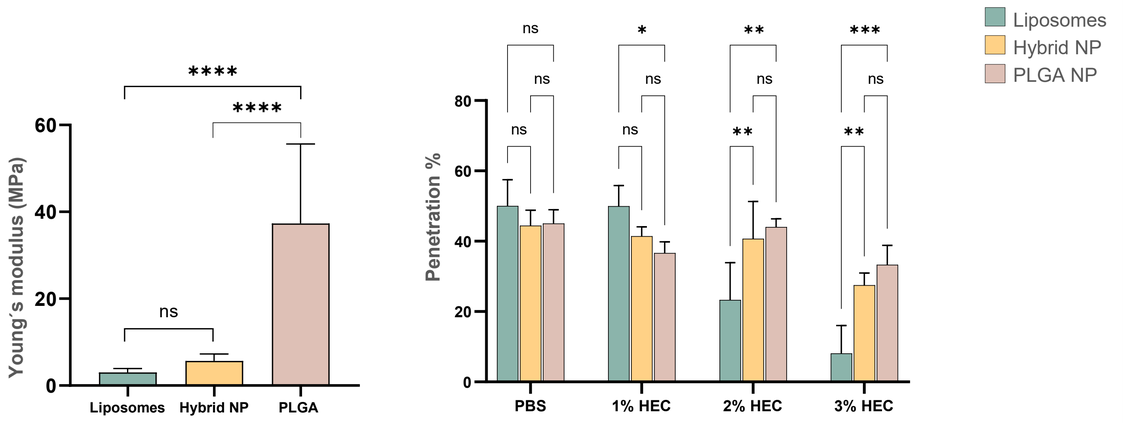
AFM imaging



*AFM images of **C.** Liposomes, **D.** Hybrid NP, and **E.** PLGA NP (Probe: MLCT, Pixels: 128 x 128, imaged in Milli-Q water at 25°C)*

F Elasticity

G Penetration Profile



***F.** Elasticity comparison of nanoparticles. Data are shown as the means ± SDs of 30 particles (ns, p>0.9999; ****p<0.0001) and **G.** Comparison of Liposomes, Hybrid NP and PLGA NP penetration in PBS and different HEC gel concentrations after 6 h. Data are shown as the means ± SDs (n=3) (ns, p>0.05;*p<0.01; **p<0.001; ***p<0.0001)*

Conclusion

- When the HEC gel concentration increases liposome penetration decreases drastically
- For PLGA NP and Hybrid NP, particle penetration is independent of the gel concentration

Outlook

- Test particle penetration behaviour in biological hydrogels

References

[1] C.I. Sodimanage, M. Schneider, The Role of Nanoparticle Elasticity on Biological Hydrogel Penetration, Pharmaceutics 2025, Vol. 17, Page 760 17 (2025) 760. https://doi.org/10.3390/PHARMACEUTICS17060760.

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This research was co-funded by the **Marie Skłodowska-Curie COFUND-Action of the European Commission** under the **Grant Agreement Number 101081463**. We also extend our gratitude to **Lipoid GmbH** for generously providing free phospholipid samples.

Images: Created with BioRender.com

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