Transport of Gel-Filled Liposomes across a Blood-Brain Barrier Model

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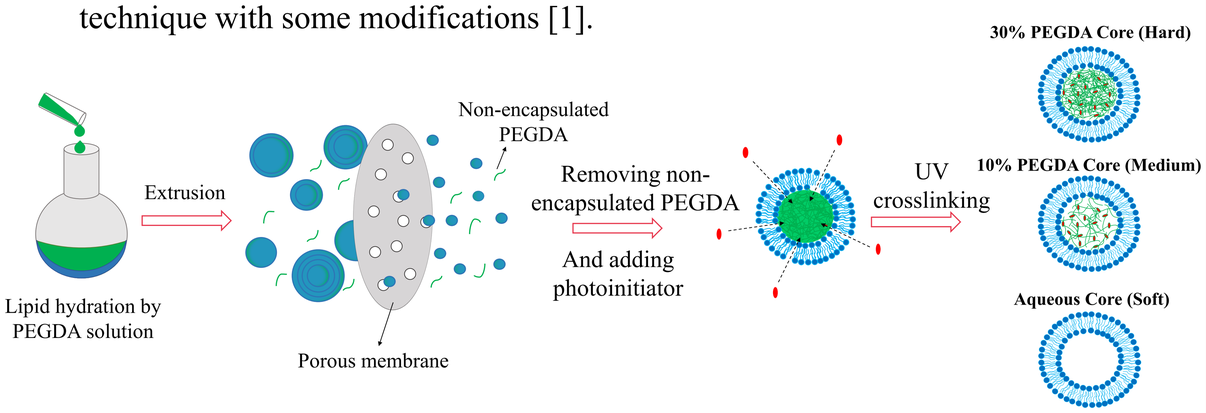
Background

- Nano-scale carriers have emerged as a promising platform for delivery of therapeutic molecules to diseased sites in the body. Despite significant progress in application of nanotechnology in medicine, the success of these nanocarriers in addressing brain diseases remains limited, mainly due to the limited transport across the blood-brain barrier.
- BBB is one of the most exclusive barriers in the body and nanocarrier's physicochemical properties (e.g. size, shape, and surface chemistry) are known as key factors for their transport across BBB.
- The impact of nanocarriers' rigidity on their transport across BBB has, however, not been studied independent of other physical and chemical characteristics.
- This study aims to unravel the role of particle rigidity, without changing other particle properties, in their BBB transport using an *in vitro* BBB model. Towards this goal, we utilize nanoliposomes to encapsulate hydrogels of various compositions and to form particles with different rigidity levels while maintaining the particle size, shape, and surface chemistry unchanged. The resultant nanoliposomes are characterized and examined for their transport across a transwell BBB model.

Materials and Method

- Hydrogel-filled nanoliposomes were prepared by encapsulating poly(ethylene glycol) diacrylate (PEDGA) in the lumen of liposomes using a previously reported technique with some modifications [1].



- The size and zeta potential of liposomes were assessed using dynamic light scattering and laser Doppler electrophoresis techniques, respectively.
- The Young's moduli of bulk PEGDA hydrogel at concentration of 10 and 30 v/v% were evaluated using uniaxial compression testing.
- The BBB model quality was evaluated by trans-endothelial electrical resistance (TEER) measurements. The gel-filled nanoliposomes were introduced onto the BBB model and their ability to cross this barrier was assessed by screening the particle concentration across the barrier.

Acknowledgement

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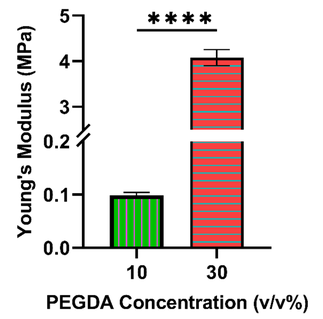
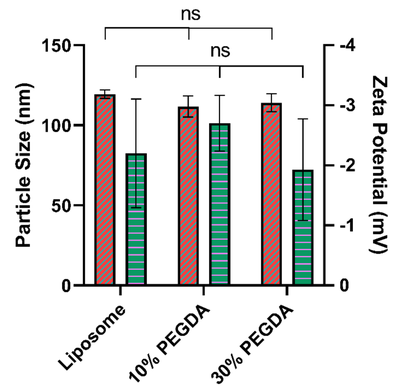
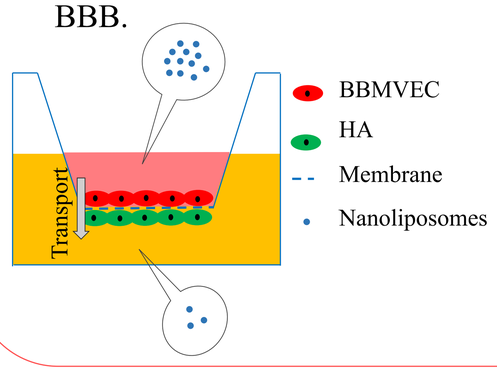
Results and Discussion

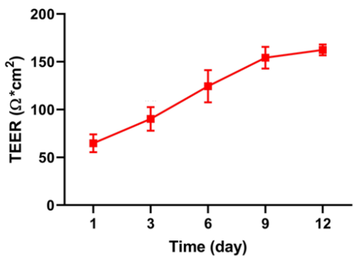
- Increasing the PEGDA gel volume ratio from 10 to 30% led to an increase in its Young's modulus of the bulk PEGDA hydrogel from 0.1 to 4 MPa.
- Notably, all three liposome groups showed similar size distribution with an average particle size of ~117 nm. Zeta potential measurements also revealed similar values of ~2.3 mV in all liposome groups, indicating similar surface properties.

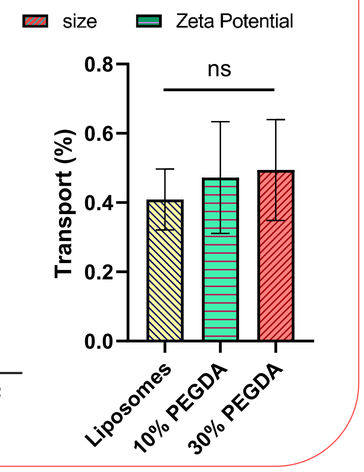


- The measured value of TEER for the BBB model was ~162 Ω.cm^2, indicating proper formation of tight junctions within the endothelial cell layer.
- When introduced to top side of the BBB model, all three groups of soft, intermediate, and hard liposomes were able to cross the BBB.
- While higher level of liposomal rigidity led to an increase in their transport percentage across the BBB model, the difference was not substantial.
- This finding suggests that the rigidity changes within the range examined here had no significant impact on the ability of liposomes to cross the BBB.









Conclusions

- ✓ Utilizing nanoliposomes filled with PEGDA hydrogel, this study examines the role of nanocarrier rigidity in their transport across a simple BBB model.
- ✓ The results showed that liposomes with all three rigidity levels were able to cross this BBB model. However, the rigidity differences among liposome groups did not have a significant effect on their BBB transport.
- ✓ Future studies will focus on widening the range of elasticity of liposomes to further explore the role of particle mechanical properties in transport across BBB.

References

[1] F. Mirab, et al., *2019 41st Annual International Conference of the IEEE (EMBC)*, 2019, pp. 3935-3938