Rosmarinic Acid Contact Lenses as a Plant-Derived Therapeutic Strategy for the Diabetic Eye

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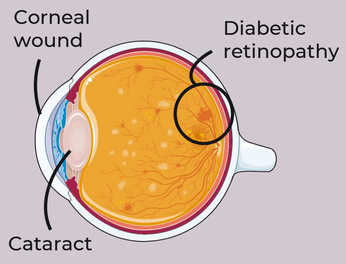
Introduction

Current treatments for diabetes-related eye conditions (e.g., intraocular injections, eye drops) are often invasive and poorly suited for long-term use. Drug-eluting contact lenses (CLs) offer a non-invasive and patient-friendly alternative with improved ocular drug retention and bioavailability[1].

As interest grows in natural therapeutic compounds, **rosmarinic acid (RA)**, a natural polyphenol, emerges as a promising candidate due to its antioxidant, anti-inflammatory, and neuroprotective properties[2].

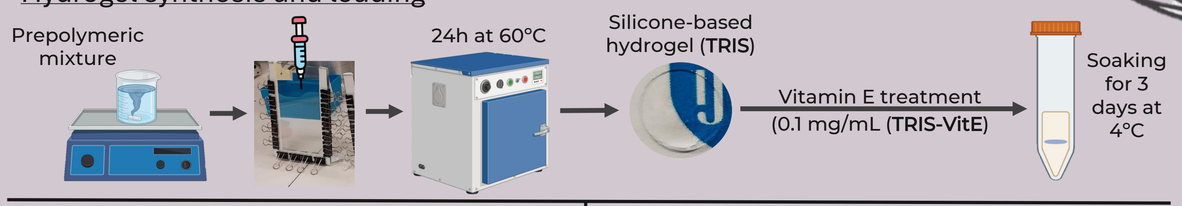


Objective

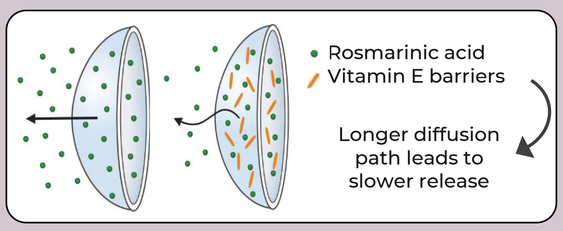
Development and optimisation of **daily silicone-based CLs** able to achieve **therapeutic** ocular concentrations of RA for the treatment of **diabetic ocular diseases**.

Methods

Hydrogel synthesis and loading



Vitamin E treatment



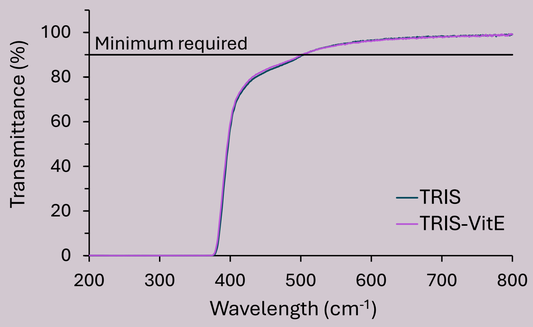
System's assessment

- Material characterization
- *In vitro* releases (static *vs* dynamic)
- Biocompatibility assessment
- *Ex vivo* drug permeability assay
- Antioxidant assay (DPPH assay)
- Anti-inflammatory and neuroprotective assay (immunostaining)

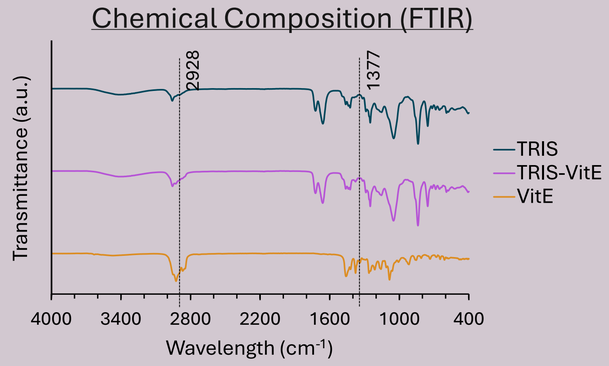
Results & Discussion

Hydrogel characterization

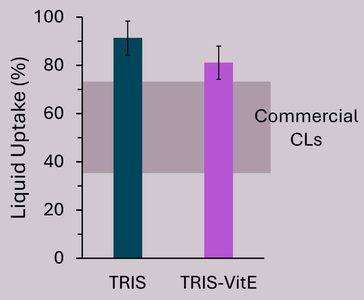
Light Transmittance



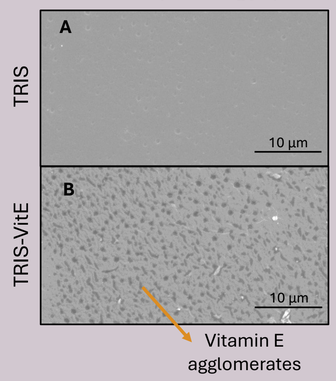
Chemical Composition (FTIR)



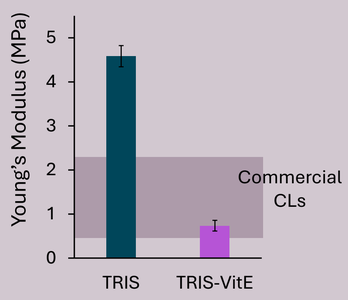
Liquid Uptake



Surface Morphology (SEM)



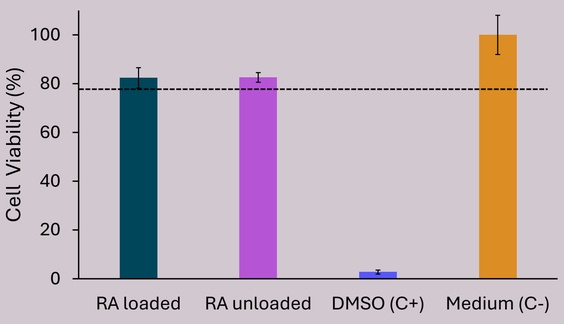
Stiffness



Biocompatibility

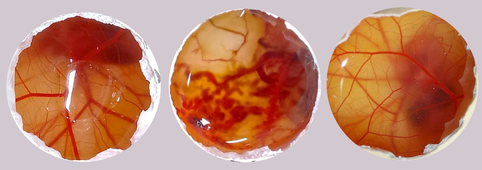
Cytotoxicity

In vitro (NIH/3T3 Mouse Fibroblasts)



Irritability

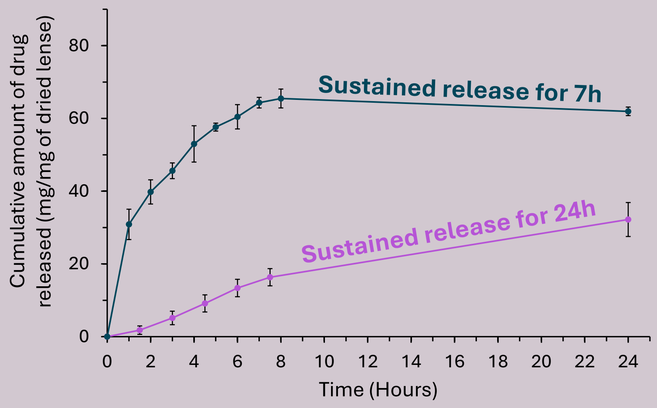
In ovo (HET-CAM assay)



- No signs of hemorrhage, coagulation or lysis.

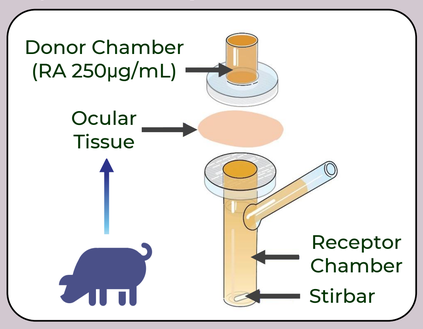
RA's Release in TRIS-VitE

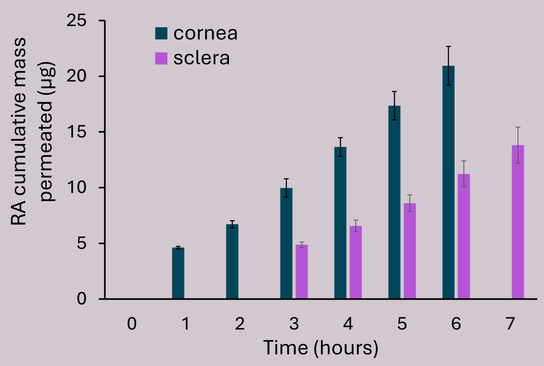
- Static release:
  - In sink conditions (in 3 mL)
- Hydrodynamic release:
  - Simulating ocular conditions (in 45µL of PBS, 3µL/min)



In vivo behaviour of RA

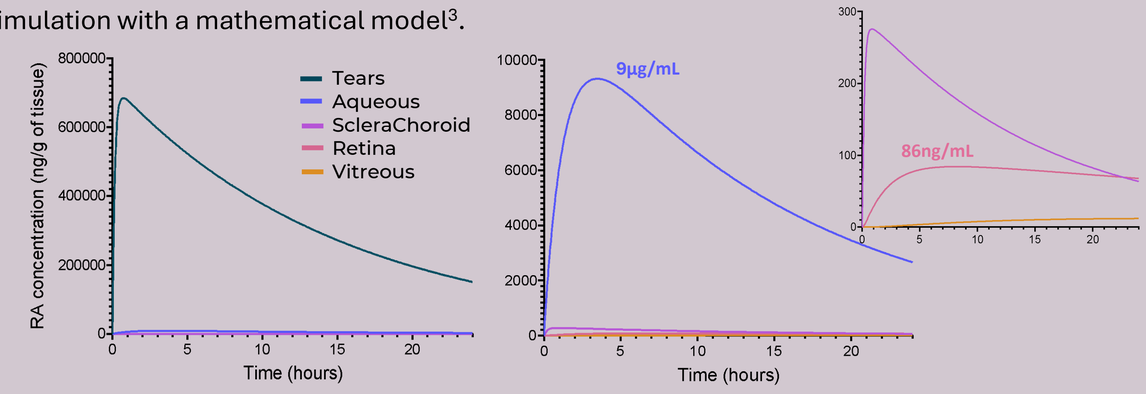
Tissue permeability





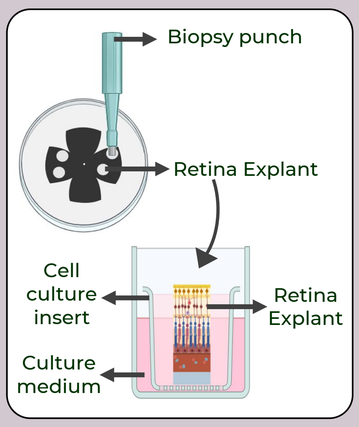
RA's ocular distribution

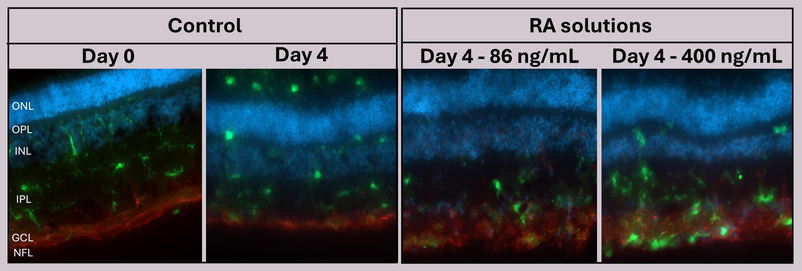
Simulation with a mathematical model[3].



Therapeutic potential

Anti-inflammatory activity[4]

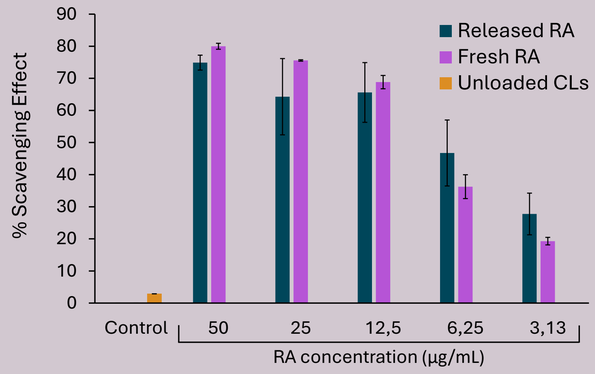




Reduced inflammatory response:
- Decreased microglial migration toward outer retinal layers.
- More microglia retained a ramified (resting) morphology.

- Potential to work as an anti-inflammatory agent in the retina

Antioxidant activity



- Potential to reduce oxidative stress in the aqueous humour, suggesting relevance for cataract prevention.

Conclusion

RA-eluting contact lenses **sustained drug release** for over 24 hours, met commercial **CLs standards**, enabled ocular **tissue permeation**, and preserved RA's **antioxidant** and **anti-inflammatory** activity, supporting their potential as a non-invasive, long-acting therapy for diabetic eye complications.

References

[1] I. Rykowska, et al., Molecules 2021, 16, 5577.
[2] L. C. Vieira, et al., Planta Med. 2020, 86, 1286–1297
[3] N. Toffoletto, et al., Pharm. Res. 2023, 40, 1939-1951
[4] Z. Lumack do Monte, et al., Manuscript in preparation. 2025

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