Topical Ophthalmic Delivery of Quercetin and Resveratrol using Elastin-like Recombinamer Nanoparticles

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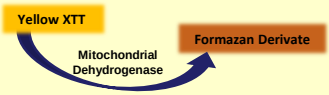
INTRODUCTION

Natural polyphenols, Quercetin (**QUE**) and Resveratrol (**RSV**), have been proven to be efficient in the treatment of ocular surface diseases related to oxidative stress, like Dry Eye Disease (**DED**) [1,2]. Unfortunately, their application as a topical ophthalmic treatment is limited by their poor physico-chemical characteristics. Therefore, our aim was to encapsulate QUE, RSV or the combination of both polyphenols into Elastin-like recombinamer nanoparticles (**ELR-NPs**) and test their biocompatibility and antioxidant activity *in vitro* on a Human Corneal Epithelial (**HCE**) cell line and assess their penetration of corneal tissues *ex vivo* on excised porcine eyes.

METHODS

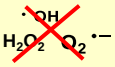
Cell Viability



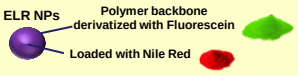
- The **biocompatibility** of **ELR NPs** containing QUE, RSV or both with **HCE** cells was assessed through the **XTT assay.**

Intracellular ROS Scavenging Activity

- The **ability** of the formulations to **scavenge** intracellular **ROS** was tested in UV-B exposed and unexposed (control) HCE cells, using **H_2DCFDA**, a fluorescent indicator of ROS.



Ex vivo Penetration of Corneal Tissues



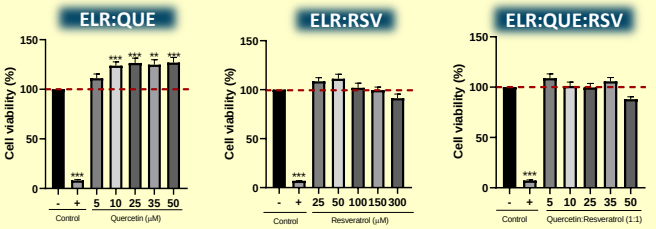
- To evaluate the penetration through *ex vivo* porcine corneal tissues, **NPs** were **loaded** with **Nile Red**, a fluorescent probe used as **model of hydrophobic drug**. Free Nile Red was used as a control.

RESULTS

- The **concentration** of **NPs** used for the experiments was as follows: **ELR:QUE 5-50µM**, **ELR:RSV 25-300 µM** and **ELR:QUE:RSV 5-50 µM**.

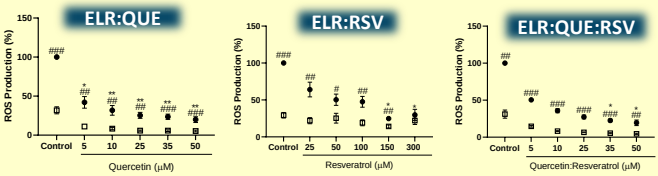
Cell Viability

- **None** of the **NPs** affected the **viability** of the **HCE** cells.
- As **negative** and **positive** controls **cell medium** and **BAK** (0.005%) were used

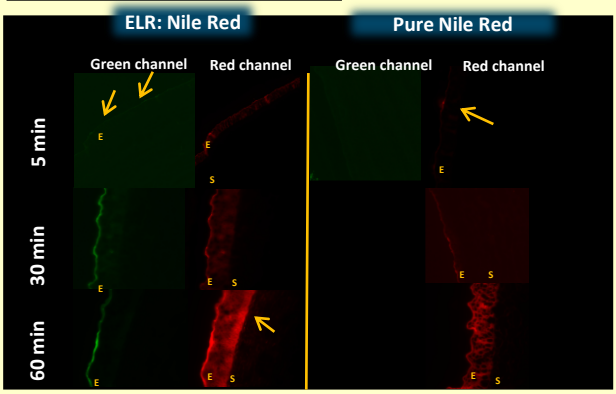


Intracellular ROS Scavenging

- UV-B induced intracellular **ROS** were **significantly decreased** by all types of **NPs.**
- This response was **dose dependent.**
- Cells exposed to UV-B are marked with a (●) in the graphs; while the unexposed ones with (□).



Ex vivo Penetration of Corneal Tissues



- **Encapsulated Nile Red** showed **improved penetration** of porcine corneal tissues **compared** to the **pure compound**.
- The penetration improvement was **time-dependent**.
- **ELR NPs** (green fluorescence) **remain** on the **epithelium surface**, releasing the payload Nile Red in the corneal tissues
- **E**- *Corneal Epithelium*; **S**- *Corneal Stroma*

All data are means ± SEM of three independent experiments. * p<0.05, ** p<0.01, *** p<0.001 in comparison to the control; # p<0.05, ## p<0.01, ### p<0.001 intergroup comparison.
The statistical analysis of data was performed via ANOVA followed by Games-Howell or Tukey's post-hoc tests.

CONCLUSIONS

- All NPs tested were **biocompatible** with **HCE cell** line.
- All formulations showed **good ability** to **scavenge** intracellular **ROS** species.
- **Nile Red loaded in NPs had better** *ex vivo* **penetration of porcine corneas** in respect to the free fluorophore.

References: **1-** Abengózar-Vela A *et al.* Quercetin and Resveratrol Decrease the Inflammatory and Oxidative Responses in Human Ocular Surface Epithelial Cells. *Invest. Ophthalmol. Vis. Sci.* 2015;56(4):2709-2719 **2-** Abengózar-Vela A *et al.* , Topical Quercetin and Resveratrol Protect the Ocular Surface in Experimental Dry Eye Disease *Ocul Immunol Inflamm*. 2019;27(6):1023-1032

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