

HP- β -Cyclodextrin: a simple but effective strategy to improve the physico-chemical characteristics of resveratrol and quercetin for ocular application

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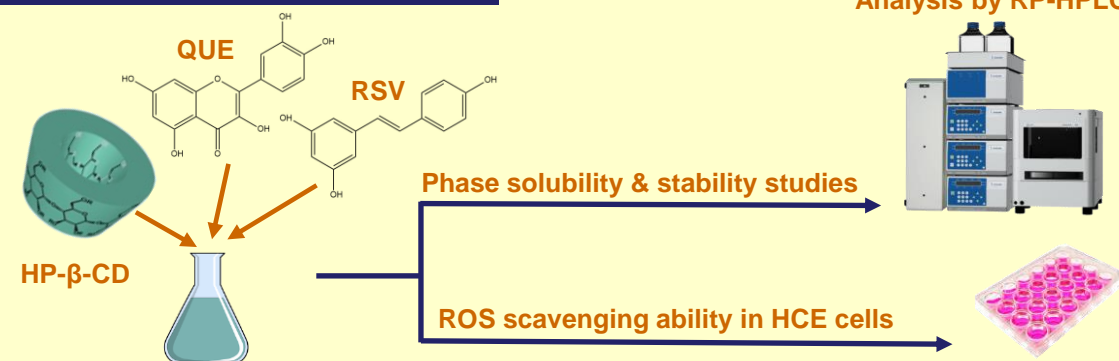
INTRODUCTION

Oxidative stress and inflammation play an important role in the etiology of Dry Eye Disease (DED), which affects more than 30% of the population worldwide.¹ Quercetin (QUE) and resveratrol (RSV), two naturally occurring compounds, have revealed to possess promising properties in the treatment of DED.

Because of their poor physico-chemical characteristics a formulation strategy is required.² Cyclodextrins have been widely used to improve the solubility but as well the stability of lipophilic drugs.³

Therefore, our aim was to study the influence of Hydroxypropyl- β -cyclodextrin (HP- β -CD) on the characteristics of QUE and RSV.

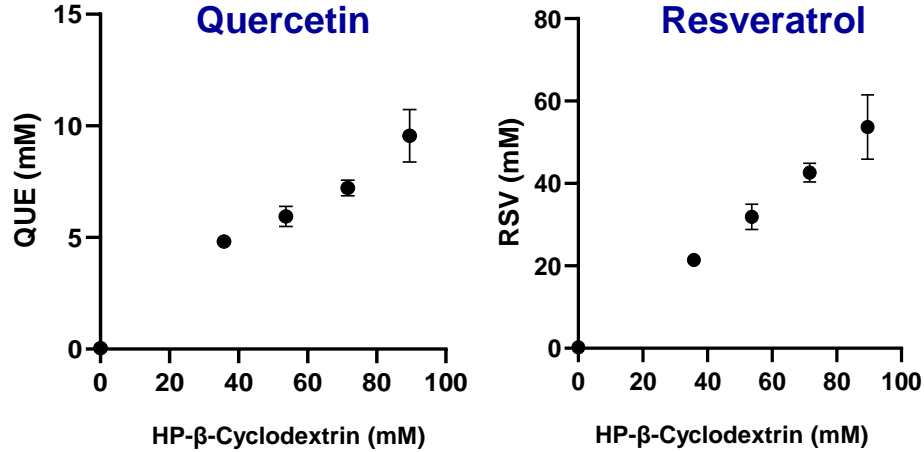
METHODS



- ✓ The **influence** of different concentrations of **HP- β -CD (5, 7.5, 10 and 12.5% w/v)** on the **solubility** of **QUE** and **RSV** was examined. HP- β -CD was added to an excess of QUE or RSV and left incubated on **25°C** for **24h** after which the samples were analysed for QUE and RSV content.
- ✓ The **stability profile** of free compounds and those in complex with CD was assayed at **25°C**. At scheduled time points the content of QUE or RSV was analysed by RP-HPLC.
- ✓ The **ability** of the most promising combinations **to scavenge intracellular ROS species** was assayed in exposed and unexposed (control) **Human Corneal Epithelial (HCE)**⁴ cells using **H₂DCFDA** (2',7'-Dichlorofluorescein diacetate), a fluorescent indicator of ROS.

RESULTS-1

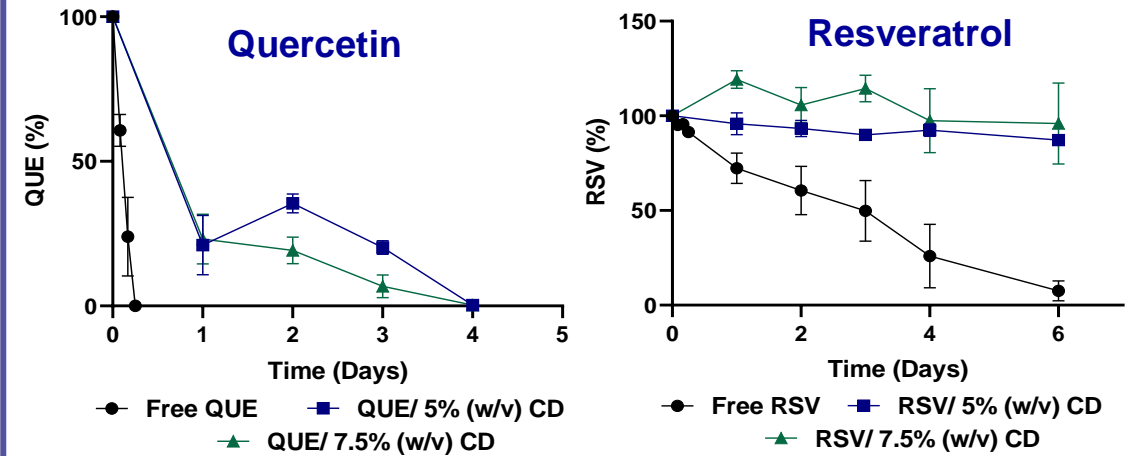
Phase Solubility studies



- ✓ Free QUE and RSV exhibited an aqueous solubility of 0.04 mM and 0.23 mM respectively, while in the complexed form with 5% (w/v) CD the solubility increased to 4.82 mM for QUE and 21.43 mM for RSV. This behaviour was also conserved with higher concentrations of CD, where a linear increase in the solubility of the two polyphenols was observed.

RESULTS-2

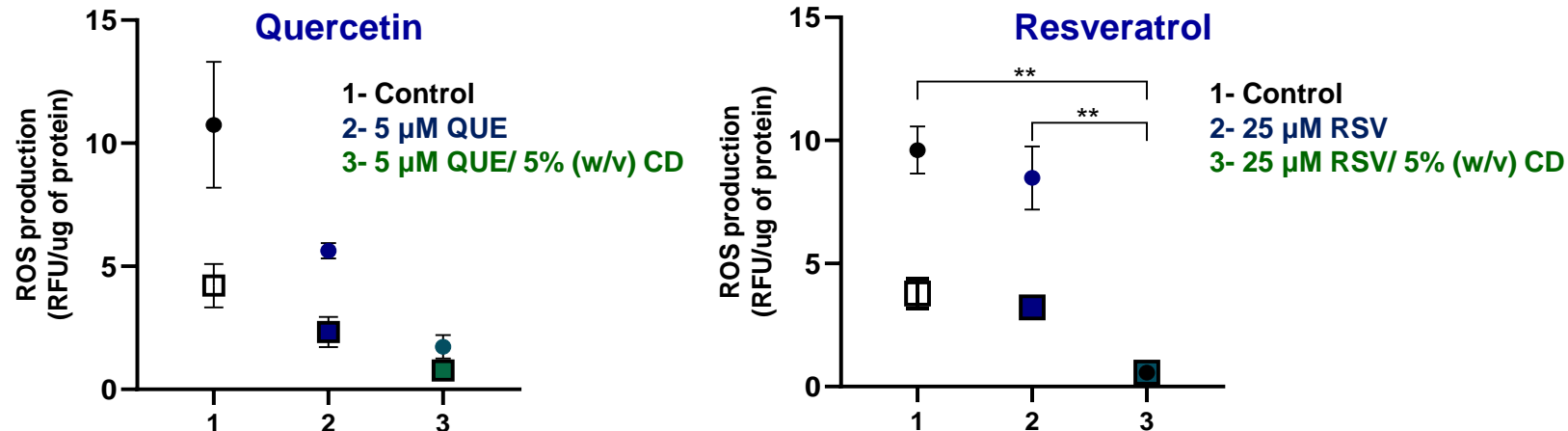
Stability studies



- ✓ In solution, free QUE was not detectable after 6h, while in a complexed form with 5% CD after 2 days we were able to detect 35% of the initial QUE. Complexed QUE completely degraded in 4 days. Free RSV degraded in a period of 6 days, while complexed with 5% CD maintained more than 90% of the initial concentration in the same period. The stability profile of QUE and RSV did not depend on the concentration of CD used.

RESULTS-3

Intracellular ROS scavenging ability



- ✓ 5 μM QUE complexed with 5% (w/v) CD was able to decrease the production of intracellular ROS in comparison to 5 μM free QUE and control cells.
- ✓ UV-B induced intracellular ROS was significantly decreased by 25 μM RSV complexed with 5% (w/v) compared to control cells treated with medium ($p < 0.01$) and compared to free 25 μM RSV ($p < 0.01$).
- ✓ Cell exposed to UV-B are marked with a (●) in the graphs; while the non exposed ones with (□).

Data are means \pm SEM of three independent experiments. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

CONCLUSIONS

- **Stability** and **solubility** of **QUE** and **RSV** were **improved** when they were in association with **HP- β -CD**
- The formulations between **QUE/CD** and **RSV/CD** were able to **protect HCE cells from oxidative stress**
- This formulation strategy of the two natural compounds is promising for the topical treatment of DED

References:

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