Evaluation of the efficacy of a novel formulation of moxifloxacin, specifically designed for sustained intraocular release, in experimental endophthalmitis

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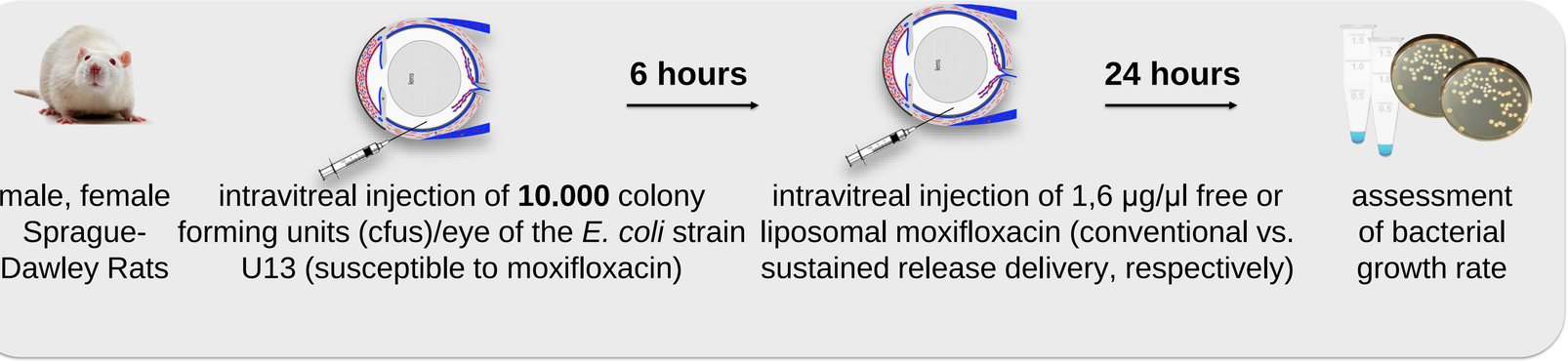
Introduction

Bacterial endophthalmitis can lead to significant vision loss even after prompt and proper treatment, partially due to the limited time of antibiotics' residence in the vitreous cavity.

The purpose of this study was to evaluate the efficacy of a novel drug formulation, which is specifically designed for sustained intraocular release of moxifloxacin, in an experimental model of *Escherichia coli* (*E. coli*) – induced endophthalmitis.

Methods

- All animal experiments followed the guidelines of the Association for Research in Vision and Ophthalmology (ARVO) Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by the Animal Committee of University of Crete Medical School.
- A **recently developed novel liposomal** formulation of moxifloxacin was used [active loaded moxifloxacin PC:CHOL (2:1)].
- Clinical scores were evaluated *in vivo* with slit lamp biomicroscopy and direct ophthalmoscopy.
- Animals were euthanised at **30** hours post treatment, eyes were enucleated and proceeded for the assessment of the bacterial growth rate.



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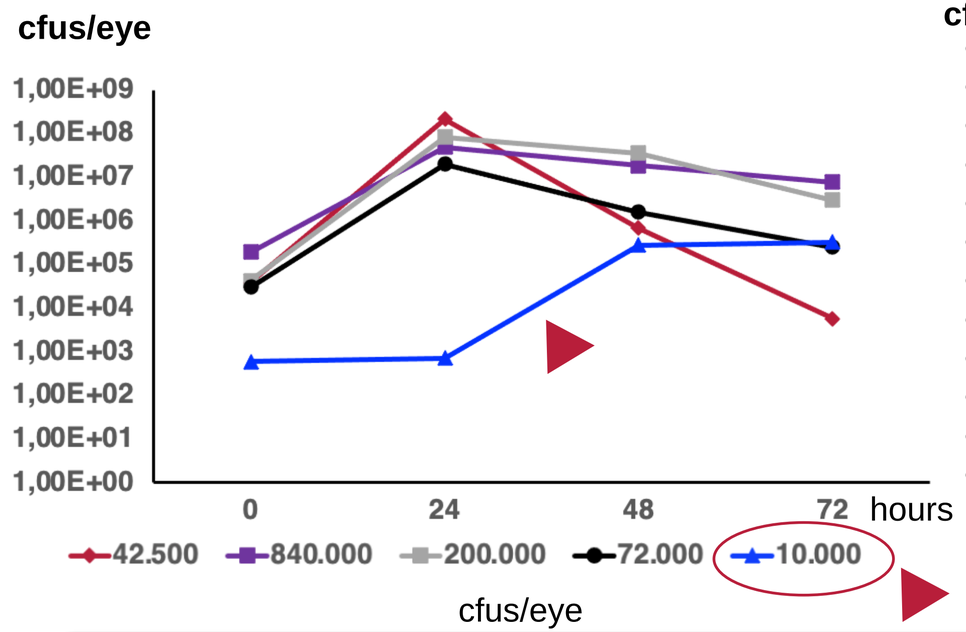
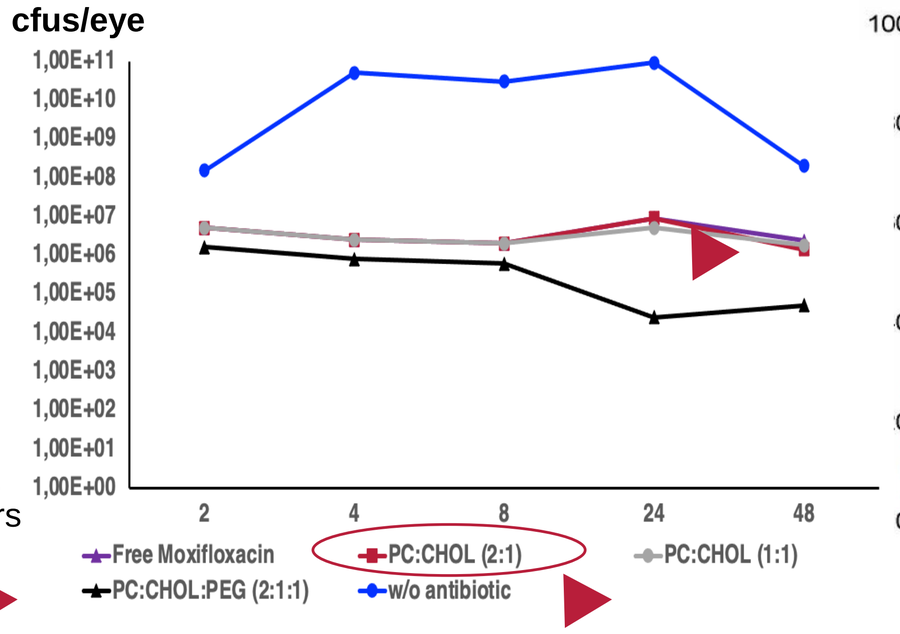
Results

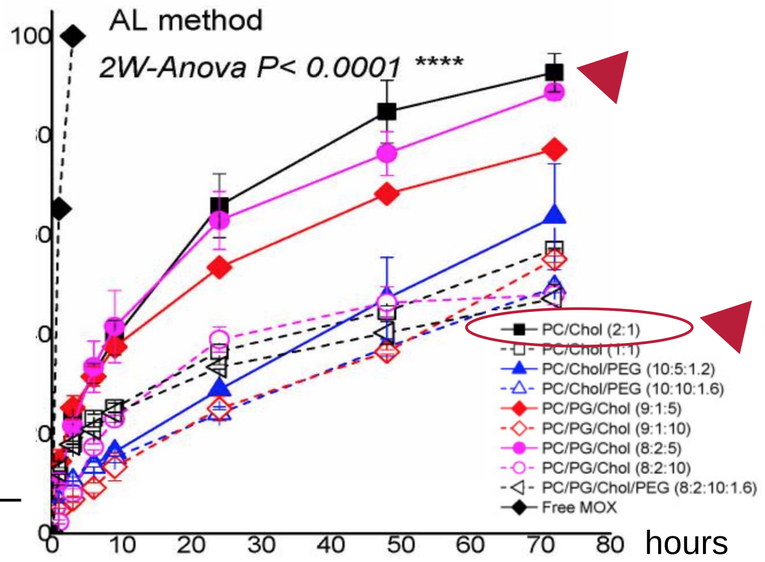
Bacterial growth rate following intravitreal inoculation of *E.coli*



Efficacy of different liposomal formulations *ex vivo*



Release kinetics of moxifloxacin of different active loaded (AL) liposomes



- Among all the bacterial inoculum sizes that were tested of the *E.coli* strain that is **susceptible to moxifloxacin** (U13), only the **lowest** inoculum considered **suitable for potential pharmaceutical intervention.**
- An inoculum of 10.000 CFUs/eye of the *E.coli* strain U13, resulted in **conjunctival hyperaemia, purulent exudations, iritis, miosis, and posterior synechiae** at 24 hours.
- Two-thirds of the animals in each of three independent experiment (*n* = 12 for each experiment) had mild to moderate inflammatory scores at 24 hours and the signs of clinical inflammation were not progressed at 48 or 72 hours, while the bacterial load remained stable with an average of 10^5 CFUs/eye.
- However, one-third of the animals in each independent experiment, demonstrated significantly lower clinical scores while in many cases, inflammation was resolved at 72 hours.

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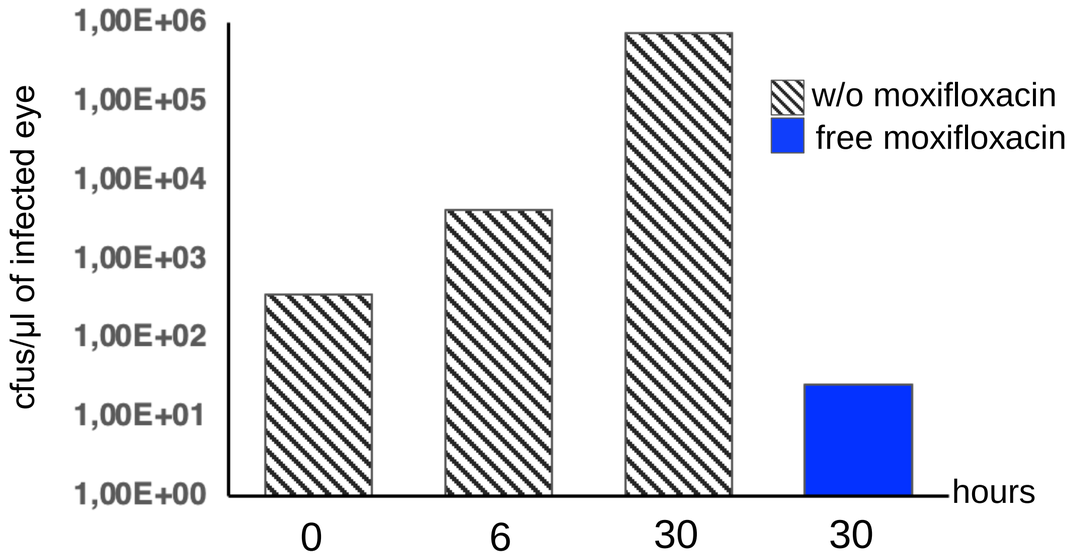
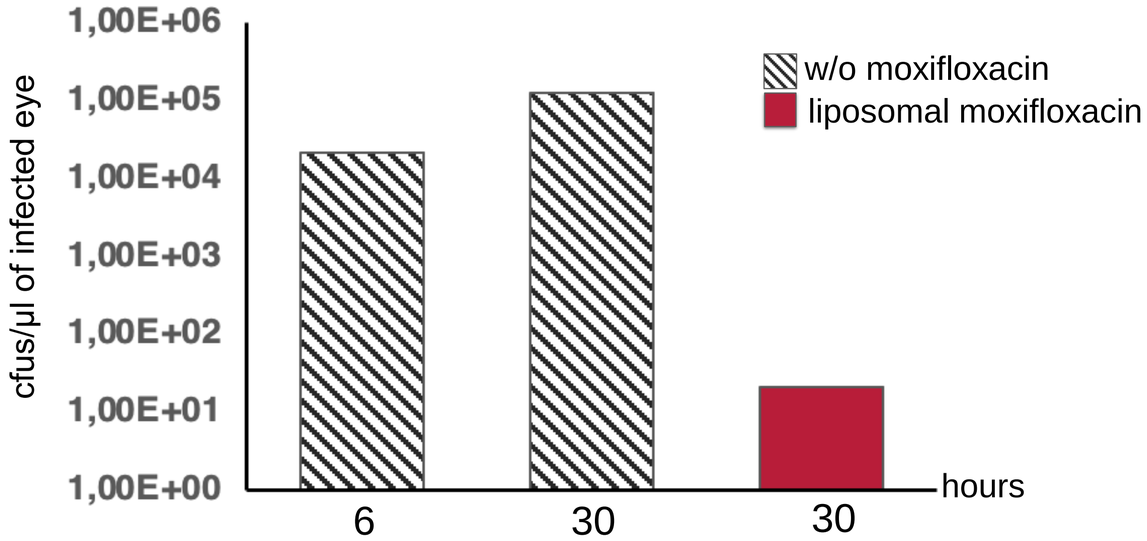
Efficacy of free moxifloxacin in experimental bacterial endophthalmitis



Efficacy of liposomal moxifloxacin in experimental bacterial endophthalmitis



Conclusions

- *E. coli* – induced endophthalmitis can be achieved in rats and is a highly reproducible model of experimental gram-negative bacterial endophthalmitis.
- Low inocula of *E. coli* strain U13 result in mild to moderate progress of the inflammatory signs, thus allowing pharmaceutical intervention.
- Liposomal moxifloxacin seems as effective as the free antibiotic at early time points.
- Further experimentation is currently ongoing in order to evaluate the efficacy of the novel moxifloxacin over a longer time frame.

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