Introduction

Nowadays, over 90% of ophthalmic drugs are administered topically in the form of eye drops [1]. However, the residence time of the drug in the eye is short and only 1% to 7% of the administered drug is absorbed through the eye, leading to poor drug bioavailability and, in some instances, undesirable side effects [2].

Typically, drug release experiments are conducted under static conditions but, under normal physiological conditions, the human eye presents a reduced tear volume and a tear turnover rate that varies between 1 and 4 µL/min. Thus, to study drug release kinetics in the eye, static conditions do not seem the most appropriate.

Aims

The present work involves the development of a novel microfluidic cell designed to simulate physiological conditions of the eye (temperature, tear volume and flow rate) and therefore more appropriate to test the release of drugs from contact lenses.

Contact lenses were prepared with two types of materials: a hydroxyethylmethacrylate (HEMA) based hydrogel and a silicone based hydrogel. The former hydrogel was loaded with an antibiotic (levofloxacin, LVF) and the latter, with an antiseptic (chlorhexidine, CHX).

Experimental

Two different types of hydrogels were prepared by thermal polymerization:

- HEMA/PVP (98/2, w/w)
- TRIS/NVP/HEMA (40/40/20, w/w)

The hydrogels were loaded by soaking for 14 hours, at 4°C. HEMA/PVP was loaded with LVF (5 and 10 mg/mL solutions) and TRIS/NVP/HEMA with CHX (5 mg/mL solutions).

The experiments were carried out at 35°C using a microfluidic cell (image below) and in static conditions (2,6mL/lens).

In vitro controlled drug release from contact lenses materials under physiological ocular tear flow

Results and Discussion

Differences in drug release profiles were observed between the two materials. The results obtained under physiological tear flow conditions using the microfluidic cell demonstrate in both cases (HEMA/PVP LVF and TRIS/NVP/HEMA CHX) extended drug release for a minimum of 3 days, while the experiments performed in static conditions, showed a maximum release time of 24 hours.

The comparison of the concentration profiles with the MICs shows that in the case of HEMA/PVP/LVF the concentration of the LVF loading solution had to be increased from 5mg/mL to 10mg/mL, in order to exceed the MIC of Pseudomonas aeruginosa, while for TRIS/NVP/HEMA [CHX] 5 mg/mL, therapeutic levels for Staphylococcus aureus were maintained along 7-10 hours.

Conclusions

Results demonstrate that the hydrodynamic conditions significantly affect the drug release kinetics of drugs from therapeutic contact lenses and that extrapolation of results obtained in static conditions to in vivo behaviour should be done with care.

Both systems seem to be promising for the production of drug loaded daily disposable soft contact lenses.

References


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