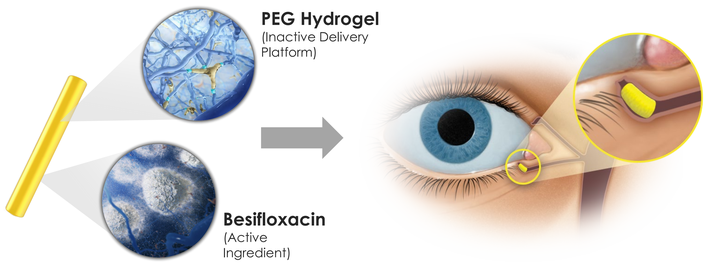
Pharmacokinetics of a Hydrogel-based Besifloxacin Intracanalicular Insert in Canines

Megan Priem; Ankita Desai; Chintan Patel, PhD; Charles Blizzard; Peter K. Jarrett, PhD; Michael H. Goldstein, MD

BACKGROUND

- Topical ocular antibiotics are often prescribed for postop antimicrobial prophylaxis or to treat bacterial conjunctivitis[1]
- Poor patient adherence to prescribed therapy regimens can result in subtherapeutic treatment and compromise patient outcomes[2]
- Sustained-release delivery of antibiotics may overcome some limitations of topical therapy such as reliance on patient self-dosing
- An intracanalicular insert was developed using polyethylene glycol (PEG) hydrogel as a vehicle to deliver besifloxacin to the ocular surface



STUDY OBJECTIVE

To evaluate the pharmacokinetics of besifloxacin delivered from a biodegradable hydrogel intracanalicular insert in a canine model

METHODS

- An insert was placed bilaterally into the inferior canaliculus of 20 beagle dogs on day 0
- Presence of the insert in the canaliculus was confirmed visually, then tear fluid was collected from n=10 eyes/timepoint with pre-cut 10 mm Schirmer tear strips at various timepoints through 42 days post-insertion
- Tear fluid samples were analyzed for besifloxacin content via liquid chromatography with tandem mass spectrometry

RESULTS

Figure 1. Tear Fluid Pharmacokinetic Profile of Besifloxacin Intracanalicular Inserts in Beagle Dogs

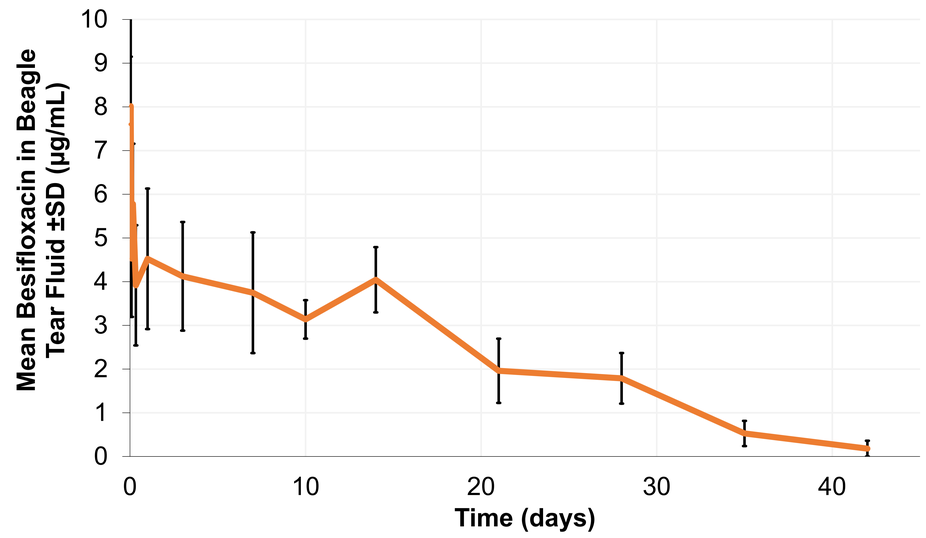


Table 1. Tear Film Besifloxacin AUC_{0-24}/MIC_{90} Ratios for Four Common Bacterial Conjunctivitis Pathogens

Time (Days)	S. aureus (MIC_{90} of 0.25 µg/mL)	S. pneumoniae (MIC_{90} of 0.125 µg/mL)	S. epidermis (MIC_{90} of 0.5 µg/mL)	H. Influenzae (MIC_{90} of 0.06 µg/mL)
1	437	874	219	1821
3	415	830	207	1729
7	378	755	189	1574
10	330	661	165	1377
14	345	689	172	1436
21	288	577	144	1201
28	180	360	90	750
35	111	222	56	463
42	34	68	17	141

RESULTS (CON'T)

- Mean besifloxacin levels in tear fluid samples demonstrated a sustained drug release profile with elevated levels through 2 weeks followed by tapering over time (presented in **Figure 1**)
- Besifloxacin gradually cleared from the tear fluid by 35-42 days
- All AUC_{0-24}/MIC_{90} values were >100 for 21 days for H. influenzae, S. aureus, S. epidermis, and S. pneumoniae suggesting the insert produced bactericidal levels of besifloxacin for common ocular isolates of conjunctivitis (presented in **Table 1**)

CONCLUSIONS

- **Pharmacokinetic profile of a hydrogel-based besifloxacin intracanalicular insert was characterized by controlled-release of besifloxacin to the tear film**
- **Insert produced clinically effective drug levels capable of killing most common isolates of bacterial conjunctivitis for 21 days**
- **Single dose besifloxacin intracanalicular insert may reduce the need for patients to self-administer antimicrobial therapy**

Disclosures: All authors are employees of Ocular Therapeutix, Inc.

Funding: This study was funded by Ocular Therapeutix, Inc.

Abbreviations: AUC, area under the concentration-time curve; MIC, minimum inhibitory concentration

References: 1. Matossian C, Nattis AS, Nijm LM, et al. Real-World Time Savings on Patient Education and Call-Backs Related to Post-Cataract Therapy Using an Intracanalicular Dexamethasone Insert. Presented at the American Society of Cataract and Refractive Surgeons Annual Meeting. July 23-27, 2021. Las Vegas, NV. **2.** Feng A, O'Neill J, Holt M, et al. *Clin Ophthalmol*. 2016;10:1505-1511.

Presented at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in Denver, CO | May 2, 2022