Ocular Distribution of Moxifloxacin (MX) from Sustained-Releasing (SR) Hydrogel Films in New Zealand White (NZW) Rabbits

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Purpose
Moxifloxacin (MX) is a marketed fluoroquinolone ophthalmic solution used to treat bacterial conjunctivitis and corneal ulcers. For ulcers, treatment includes hourly eye drop applications for several days. To improve patient compliance, alternate dosing regimens and drug delivery options are being evaluated. Jade developed a sustained release (SR) system, a HyStem® Hyaluronic acid (HA) film loaded with MX, applied to the lower fornix of the eye, reducing multiple applications. Absorption Systems developed an LC-MS/MS method to evaluate MX distribution in ocular tissue. The in-life position of this rabbit study is presented on poster board for symposium.

Methods
Films were applied to the eyes of NZW rabbits 3 weeks after third eyelid removal. OD eyes were treated with MX-film (Figure 1). OS received SR (HyStem®) film only or untreated control. Tears, aqueous humor (AH), and conjunctival samples were collected at Day 1, 2, 3, 5, and 7. Of the treated eyes (OD), 3 rabbits received a low dose (30 µg/eye) and 3 rabbits received a high dose (100 µg/eye). AH was collected via paracentesis; tears were collected via capillary tube placed at medial canthus; conjunctival tissue was collected from enucleated eyes. LC MS/MS method for MX was developed and qualified in simulated tear fluid and NZW AH and conjunctival tissues to assess the method accuracy and precision over a range of 0.5 to 1000 ng/mL. The intra-assay coefficient of variation (CV) for quality control samples ranged from 1.5 to 10%, 4.7 to 11%, and 4.7 to 7.7% in simulated tears, aqueous humor, and conjunctiva, respectively. Conjunctival samples were homogenized with a polygon in 20% methanol:water. Samples were extracted via acetonitrile and 4.7 to 7.8% in simulated tears, aqueous humor, and conjunctiva homogenate, respectively. Conjunctival tears were collected via capillary tube placed at medial canthus; conjunctival tissue was collected from enucleated eyes.

Results
The method was qualified in each of the matrices to assess accuracy and precision over a range of 0.5 to 1000 ng/mL. Presently, all AH samples were below the limit of quantification, 0.5 ng/mL. Conjunctival tissue showed MX levels in the high dose group on Day 1; the low dose and high dose groups of the remaining days were BLOQ (Table 2). Low dose MX in the tear fluid ranged from 2.22 ng/mL on Day 1 to 8.75 ng/mL Day 2, and BLOQ on Day 3-7 (Table 3). The high dose tear levels were from 11.1 ng/mL Day 1 to 1.72 Day 2, Day 3 0.70 ng/mL, and BLOQ from Day 5 (Table 3, Figure 3). No levels of MX were detected in the OS (control) eyes. MX film retention was best when placed in the lower fornix. High dose MX film yielded higher MX levels over time in tears and conjunctiva vs. the low dose MX film. Studies are in development to improve ocular surface retention time in order to extend drug release on the ocular surface and into the tissue. These data are consistent with Jade’s efficacy and in vitro release data.

Conclusions
MX film retention was best when placed in the lower fornix. High dose MX film yielded higher MX levels over time in tears and conjunctiva vs. the low dose MX film. Studies are in development to improve ocular surface retention time in order to extend drug release on the ocular surface and into the tissue. These data are consistent with Jade’s efficacy and in vitro release data.

Reference