

## Fluoroquinolones

### **Table 1 (supplement). Corneal and aqueous concentrations of topically applied fluoroquinolones**

The extrapolated first quartile concentration provides a concentration that can be used to decide if the MIC of the isolated bacteria is expected to be above or below the anticipated concentration in the cornea and aqueous. If the MIC is below this first quartile concentration, it would be reasonable to expect the bacteria to be inhibited by that antimicrobial. Standard deviation (SD). # Based on the normal distribution of the concentrations, hence the mean, SD and quartile need to be interpreted with caution. Median used where available. Penetrating keratoplasty (PK), cataract surgery (CS).

Although the reported corneal concentrations of FQs are high, the associated standard deviations are also high. The coefficients of variance are high for ciprofloxacin, moxifloxacin, ofloxacin, levofloxacin and gatifloxacin, particularly in comparison to besifloxacin. This means that the concentrations achieved are not consistent around the mean. Because the actual data is not available in the listed references, the first quartile concentration has been extrapolated from the reported mean and standard deviation based on a normal distribution unless the median was available. Data is not available in articles so we cannot check the normality. The pharmacokinetics of the fluoroquinolones in corneal ulceration is unknown, so caution is needed in extrapolating the data.

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Antimicrobial	Animal (A) /Human (H) model	Treatment Regimen	Epithelium intact or abraded	Mean Corneal Concentration (mg/kg) $\pm$ SD (median)	#First quartile concentration in Cornea (mg/kg)	Mean Aqueous Concentration (mg/L) $\pm$ SD (median)	#First quartile concentration in the aqueous (mg/l)	Ref
Ciprofloxacin 0.3%	H	One drop at 30 min intervals 4.5-5h (8 doses) prior to PK	Intact	14.87 (7.41) mg/L	3.71	0.51 (0.42)	0.21	(1)
	H	One drop 15 and 10 mins prior to PK	Intact	9.92 $\pm$ 10.99 (NA)	2.50	0.13 $\pm$ 0.23 (NA)	0	(2)
	H	Group 1: Home administration. One drop every 4h for 24h prior to PK	Intact	Group 1: 8.82 $\pm$ 8.24 (NA)	3.26	NA	NA	(3)
		Group 2: Two drops applied by trained professional every 15 mins for 4h prior to PK	Intact	Group 2: 116.2 $\pm$ 336.94 (NA)	0			
		Group 3: Same as group 2	Group 3: Abraded	Group 3: 938.3 $\pm$ 1081.5 $\mu$ g/g (NA)	208.29			
	H	One drop every 15 mins for first hour then every hour prior to PK	Intact	5.28 $\pm$ 3.4 Range: 1.43 - 10.58 $\mu$ g/g (NA)	2.99	NA	NA	(4)
	H	Group A: 1-2 drops four times a day for two days prior to CS.	Intact	NA	NA	Group A: 0.067 $\pm$ 0.048 (NA)	0.035	(5)
Group B: 1-2 drops every 10 minutes in the hour prior to CS. Total of five doses.		Intact			Group B: 0.186 $\pm$ 0.131 (NA)	0.098		
Group C: Combined regime of A and B.		Intact			Group C: 0.242 $\pm$ 0.207 (NA)	0.10		
H	One drop every 15 minutes for 4 doses prior to CS.	Intact	NA	NA	0.08 $\pm$ 0.113 (NA)	0.037	(6)	

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	H	One drop every 15 minutes for 5 doses and then every 30 minutes for 3 doses before CS.	Intact	NA	NA	1.13 ± 1.90 (NA)	0	(7)
	H	Group 1: One drop at three 2hr intervals one day prior and three drops at 1h intervals on the day of CS.  Group 2: One drop at 15 minute intervals, nine times, on the day of CS.	Intact  Intact	NA	NA	Group 1: 0.127 ± 0.081 (Range 0.031 - 0.339)  Group 2: 0.380 ± 0.328 (Range 0.33 - 1.388)	0.072  0.16	(8)
	H	Enucleated eyes immersed in Ciprofloxacin for 10 minutes	Intact	3.46 with standard error 0.512 (95% CI 2.60 - 4.61)	1.99	1.02 with standard error 0.142 (95% CI 0.78 - 1.34)	0.59	(9)
<b>Moxifloxacin 0.5%</b>	A	38 µL instilled  Group 1: After 10 minutes eyes removed.  Group 2: After 1 hour eyes removed.	Intact	Group 1: 18.60 ± 19.99 (NA) after 10 mins  Group 2: 11.7 ± 6.50 (NA) after 1 hour	Group 1: 5.11 After 10 mins  Group 2: 7.31 After 1 hour	Group 1: 1.62 ± 0.04 (NA) After 10 mins  Group 2: 1.68 ± 0.07 (NA) After 1 hour	Group 1: 1.59 After 10 mins  Group 2: 1.63 After 1 hour	(10)
	H	Two drops administered three times prior to PK	Intact	12.66 ± 8.93 (10.53)	5.27	1.40 ± 1.17 (1.08)	0.54	(11)
	H	One drop 60 mins prior to CS	Intact	NA	NA	0.67 ± 0.50 (0.49)	0.25	(12)
	H	Enucleated eyes immersed in Moxifloxacin for 10 minutes	Intact	14.38 with standard error 1.886  95% CI (11.12 - 18.55)	9.62	4.78 with standard error 0.621  95% CI (3.69 - 6/133)	3.21	(9)
<b>Levofloxacin 0.5%</b>	H	One drop 15 and 10 mins prior to PK	Intact	18.23 ± 20.51 (NA)	4.39	0.37 ± 0.55 (NA)	0	(2)

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	H	Two drops administered three times prior to PK	Intact	5.95 ± 4.02 (5.24)	2.62	0.89 ± 0.86 (0.59)	0.30	(11)
	H	Group A: 1-2 drops 4x/day for 2 days prior to CS.  Group B: 1-2 drops every 10 minutes in the hour prior to surgery. (Total 5 doses)  Group C: Combined regime A and B.	Intact  Intact  Intact	NA	NA	Group A: 284.8 ± 193.2 (NA)  Group B: 1135.6 ± 589.5 (NA)  Group C: 1618.6 ± 779.8 (NA)	154.39  737.68  1092.23	(5)
	H	One drop every 15 minutes for 4 doses prior to CS.	Intact	NA	NA	0.728 ± 0.656 (NA)	0.511 (as reported in the paper)	(6)
<b>Besifloxacin 0.6%</b>	A	32 µL was instilled  Group 1: after 10 minutes eyes removed.  Group 2: after 1 hour eyes removed	Intact	Group 1: 6.01 ± 1.43 (NA)  Group 2: 5.51 ± 1.01 (NA)	Group 1: 5.04  Group 2: 4.83	Group 1: 1.70 ± 0.04 (NA)  Group 2: 1.71 ± 0.08 (NA)	Group 1: 1.67  Group 2: 1.66	(10)
	H	One drop 60 mins prior to CS.	Intact	NA	NA	0.13 ± 0.58 (0.0086)	0.0043	(12)
<b>Ofloxacin 0.3% (if not otherwise noted)</b>	H	One drop of 15 and 10 mins prior to PK	Intact	10.77 ± 5.90 (NA)	6.79	0.13 ± 0.11 (NA)	0.06	(2)
	H	One drop every 15 minutes for 5 doses and then every 30 minutes for 3 doses before CS.	Intact	NA	NA	2.06 ± 1.06 (NA)	1.34	(7)

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	H	Group 1: Three 3 x 1 drop at 2hr intervals 1 day prior and 3 drops at 1h intervals on the day of CS.  Group 2: Nine times 1 drop at 15-minute intervals on the day of CS.	Intact  Intact	NA	NA	Group 1: 0.304 ± 0.204 (Range 0.031 - 0.984)  Group 2: 0.564 ± 0.372 (Range 0.064 - 1.455)	0.16  0.31	(8)
	H	Enucleated eyes immersed in 0.5% Ofloxacin for 10 minutes.	Intact	6.48 with standard error 0.613 (95% CI 5.37 - 7.78)	4.73	1.26 with standard error 0.127 (95% CI 1.02 - 1.53)	0.93	(9)
<b>Gatifloxacin 0.3%</b>	H	Two drops administered three times prior to PK	Intact	4.71 ± 3.39 (4.44)	2.22	0.65 ± 0.80 (0.41)	0.20	(11)
	A	45 µL was instilled  Group 1: after 10 minutes eyes removed  Group 2: after 1 hour eyes removed	Intact	Group 1: 4.35 ± 2.61 (NA)  Group 2: 2.36 ± 2.45 (NA)	Group 1: 2.59  Group 2: 0.71	Group 1: 0.06 ± 0.00 µg/g (NA)  Group 2: 0.10 ± 0.08 µg/g (NA)	0.06  0.05	(10)
		H		One drop every 15 mins for four doses prior to CS.	Intact	NA	NA	0.12 ± 0.076 (0.117)

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