

PK/PD Analysis by Nonlinear Mixed-Effects Modeling of a Marbofloxacin Dose Regimen for Treatment of Goat Mastitis Produced by Coagulase-Negative Staphylococci

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Table S1. Final I_{max} model parameters of marbofloxacin in CAMHB and goat milk against coagulase-negative staphylococci isolated from goat mastitis.

	Estimates (RSE;%)	IIV (RSE;%)	Shrinkage (%)
Parameter estimates			
E _{0pop}	1.46 (3.27)	0.16 (5.02)	-0.105
gamma _{pop}	4.59 (5.35)	0.756 (5.01)	0.383
I _{maxpop}	5.59 (0.701)	0.0988 (5.03)	-0.692
IC _{50pop}	19.4 (1.98)	0.087 (5.06)	-0.37
Covariate estimates			
beta_E ₀ _MIC	0.391 (13)	-	-
beta_IC ₅₀ _MILK	0.451 (2.62)	-	-
beta_IC ₅₀ _MIC	0.386 (7.7)	-	-
Correlations estimates			
corr_IC ₅₀ _E ₀	0.163 (42.6)	-	-
corr_I _{max} _E ₀	0.401 (14.9)	-	-
corr_gamma_E ₀	0.0905 (77.7)	-	-
corr_I _{max} _IC ₅₀	0.0807 (87.9)	-	-
corr_gamma_IC ₅₀	0.255 (26.2)	-	-
corr_gamma_I _{max}	-0.186 (36.8)	-	-
Error model parameters			
b	0.0147 (2.12)	-	-

RSE: Relative standard error; IIV: Inter-individual variability.

Table S2. Results of PK/PD analysis in serum and milk of the proposed dose regimen of marbofloxacin (10 mg/kg/24h) administered by intramuscular route in goats with mastitis produced by coagulase-negative staphylococci.

AUC value	AUC/MIC	Median	P05	P95
Serum (MIC = 0.4 µg/mL)				
AUC _{first}	P05 = 57.08	-3.55436	-4.56796	-2.60947
	Median = 88.88	-3.70868	-4.68305	-2.85198
	P95 = 131.24	-3.75305	-4.66661	-2.94904
AUC _{mean}	P05 = 47.45	-3.46896	-4.50259	-2.39889
	Median = 75.734	-3.68008	-4.66156	-2.81225
	P95 = 113.448	-3.74024	-4.65319	-2.96586
Serum (MIC = 0.8 µg/mL)				
AUC _{first}	P05 = 28.64	-1.27798	-2.70029	-0.0700124
	Median = 44.48	-2.95776	-4.09258	-1.72183
	P95 = 65.61	-3.32412	-4.31541	-2.22557
AUC _{mean}	P05 = 29.66	-1.45019	-2.87012	-0.305033
	Median = 47.336	-2.96934	-3.99165	-1.75763
	P95 = 70.9	-3.2893	-4.23362	-2.37383
Milk of infected mammary gland (MIC = 0.4 µg/mL)				
AUC _{first}	P05 = 54.1	-3.7477	-4.61082	-2.77467
	Median = 85.78	-3.74086	-4.61906	-2.78744
	P95 = 127.99	-3.739	-4.59428	-2.73958
AUC _{mean}	P05 = 56.42	-3.16079	-4.27621	-1.9656
	Median = 94.64	-3.61244	-4.57233	-2.64988
	P95 = 145.55	-3.70789	-4.6152	-2.89966
Milk of infected mammary gland (MIC = 0.8 µg/mL)				
AUC _{first}	P05 = 27.05	1.22958	-0.344938	2.27413
	Median = 42.89	-1.00153	-2.38362	0.632599
	P95 = 64	-2.85098	-3.93108	-1.55831
AUC _{mean}	P05 = 28.21	1.23185	-0.488319	2.34401
	Median = 47.29	-1.53703	-2.9647	-0.45877
	P95 = 72.755	-2.98746	-4.01723	-1.79676

P05: 5% percentile; P95: 95% percentile. Results are expressed in reduction of log₁₀ CFU/mL.