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# Pharmacokinetic Prediction of Levofloxacin Accumulation in Tissue and Its Association to Tendinopathy

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## ABSTRACT

Objectives: We investigated pharmacokinetic tissue distributions of Levofloxacin to explain adverse tendon incidents. Methods: The pharmacokinetic profiles of single and multiple dosing of 500 mg Levofloxacin following oral and IV infusion administration were simulated. Monte Carlo simulation was used to simulate the drug concentration profiles in plasma and tissue after seven dosing regimens while varying the drug ' s elimination and distribution rates to analyze the effects of changing those rates on Levofloxacin accumulation in tissue. Results: Simulated data following oral and IV administration reflect well the reported data (mean simulated plasma Cmax = 6.59 μg/mL and 5.19 μg/mL for IV and oral versus 6.4 μg/mL and 5.2 μg/mL for observed clinical IV and oral route, respectively). Simulations of seven repetitive doses are also in agreement with reported values. Low elimination rates affect the drug concentration in plasma and tissue significantly with the concentration in plasma rising to 35 μg/mL at day 7. Normal elimination rates together with escalation of distribution rates from plasma to tissue increase tissue concentration after 7 doses to 9.5 μg/mL, a value is more than twice that of normal. Conclusions: Simulation can be used to evaluate drug concentration in different tissues. The unexpectedly high concentrations in some cases may explain the reason for tendinopathy in clinical settings.

## KEYWORDS

Monte Carlo Simulation; Tendon Incidents; Levofloxacin; Pharmacokinetic

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