Objective: Oxytetracycline is widely used to treat bacterial infections in aquaculture. Bath immersion is used as an alternative to parenteral and oral administration in aquaculture. The objective of the present study was to determine the population pharmacokinetics of oxytetracycline in Giant Danio (Devario aequipinnatus) fish after exposure by bath immersion (400 mg/L) for 12 hours. Bath immersion experiments were performed in water at three different hardness levels (containing 5 mg/L, 19 mg/L and 49 mg/L of calcium).

Methods: Pilot bath immersion treatments (25-400 mg/L oxytetracycline) helped determine the concentration required to achieve target concentration above MIC (1 µg/mL) for Edwardsiella ictaluri. Consequently, the main study was performed at 400 mg/L oxytetracycline with a 12hr-exposure. The blood samples were collected from 0 to 36 hrs post bath exposure and analyzed using LC-MS/MS. The intravenous pharmacokinetics of oxytetracycline was simulated using PK parameters derived via allometric scaling approach. The absolute dose for bath therapy was estimated using nonlinear mixed effect modeling approach after fixing the PK parameters.

Results: Target blood concentration was achieved after bath immersion (400 mg/L) performed for 12 hours. The observed Cmax (1.3 µg/mL) was well above MIC with the 5 mg/L calcium level but with increased calcium levels, Cmax decreased significantly (1.3 µg/mL to 0.5 µg/mL). The overall exposure of oxytetracycline decreased with the increase in the calcium level (7026.33 hr*ng/mL to 1915.90 hr*ng/mL). The two-compartment model with the oral extravascular infusion best fitted with the observed data.

Conclusions: The result suggested that high concentration of oxytetracycline (400 mg/L) in bath therapy is required in order achieve systemic concentrations in excess of MIC. Absorption of oxytetracycline is low after bath immersion therapy. Moreover absorption decreases with increase in the calcium so lowered water hardness during exposure will enhance uptake.