Veterinary Research Communications (2026) 50:18
https://doi.org/10.1007/s11259-025-10974-8

RESEARCH

Pharmacokinetics and bioavailability of cefuroxime in Nile tilapia (*Oreochromis niloticus*)

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Received: 29 August 2025 / Accepted: 24 October 2025 / Published online: 1 November 2025

Abstract
Cefuroxime is a broad-spectrum antibiotic extensively utilized in humans and animals. Although it has been reported as beneficial against certain fish infections, pharmacokinetic studies are lacking. The purpose of this study was to evaluate the pharmacokinetics of cefuroxime following intravascular (IV, $n=72$), intraperitoneal (IP, $n=72$), intramuscular (IM, $n=72$), and oral ($n=72$) administration of 20 mg/kg in Nile tilapia (*Oreochromis niloticus*) maintained at 29 ± 1.5 °C. Two hundred and eighty-eight fish were equally distributed among four treatment groups: IV, IP, IM, and oral. Blood samples were obtained from 6 fish per group at 12 distinct time intervals over a duration of 96 h. Cefuroxime plasma concentrations were quantified with high-performance liquid chromatography and subsequently evaluated through non-compartmental analysis. Following IV injection, the $t_{1/2\lambda z}$ was 8.04 h, the V_{dss} was 1.03 L/kg, and the Cl_T was 0.14 L/h/kg. The C_{max} of cefuroxime was 53.38±4.28 µg/mL at 0.25 h for IP injection, 28.70±3.41 µg/mL at 0.5 h for IM injection, and 6.77±0.81 µg/mL at 1 h for oral administration. Bioavailability was 80.26% (IP), 69.05% (IM), and 24.35% (oral). This study found that a dosing interval of 24 h for IP and IM injection or 8 h for oral administration is efficient for treating bacteria with a MIC value of ≤1 µg/mL. The findings of this study indicate that IP and IM injections of cefuroxime are applicable in tilapia. However, since oral administration is important in aquaculture, studies are needed to develop new formulations with better absorption, to demonstrate therapeutic efficacy in infected fish, and to determine the tissues residue depletion.

Keywords Cefuroxime · Different routes · Nile tilapia · Pharmacokinetic

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Introduction

Although native to Africa, Nile tilapia (*Oreochromis niloticus*) has been introduced to numerous countries both within and outside the continent. Introduced in the latter half of the 20th century, particularly in Southeast Asia and the Americas, they are now primarily cultivated for aquaculture and to enhance fisheries (El-Sayed and Fitzsimmons 2023). In the 1970 s, this fish was dubbed the "Aquatic Chicken," later referred to as the "Fish of the 1990 s," and it is now recognized as the "Food Fish of the 21 st Century" (Pradeep et al. 2010). The production of farmed tilapia rose significantly from 28,260 tons in 1970 to 6,776,415 tons in 2023. Among the tilapia species, Nile tilapia is the most widely cultivated, accounting for 5,195,915 tons of the total production (FAO 2025). Tilapia is popular because of its high nutritional value, nice flavor, marketability, and simplicity of cultivation and breeding (Bardhan et al. 2024; Corum et al. 2022a). Tilapia is very resistant to bacterial infections when housed in surroundings with optimal water quality, temperature, and growth conditions (Plumb and Hanson 2010). However, negative factors such as stress, excessive stocking, low water temperature, and poor water quality in tilapia farming induce bacterial infections. It has been reported that the following bacteria cause infection in tilapia: *Aeromonas* spp., *Pseudomonas* spp., *Vibrio* spp., *Streptococcus* spp., *Staphylococcus* spp., *Yersinia* spp. and *Francisella* spp. (Plumb and Hanson 2010).

Cefuroxime is a second-generation cephalosporin antibiotic and is categorized as a β-lactam agent (Omole et al. 2025). The cepham nucleus's methoxy-imino side chain at position 7 enhances its resistance to β-lactamase hydrolysis (Padhi et al. 2015). Cefuroxime binds to penicillin-binding proteins through its β-lactam rings and impairs transpeptidation or cross-linking in the formation of the peptidoglycan cell wall of susceptible bacteria, resulting in bacterial death (Omole et al. 2025). Cefuroxime is available in injectable (cefuroxime sodium) and oral (cefuroxime axetil, pro-drug) preparations and is used in humans for upper and lower respiratory tract infections, urinary tract infections, and skin and soft tissue infections (Perry and Brogden 1996). It is used in the treatment of these infections and mastitis in animals (Albarellos et al. 2016; Serrano 2005).

Bacterial fish infections are considered a significant risk factor in the aquaculture industry, leading to significant economic losses amounting to billions of dollars each year. Antibacterial agents serve as the principal defensive mechanism against bacterial infections (Terzi et al. 2020). Because approved antibiotics are limited in the aquaculture sector, their overuse leads to the development of resistance. Therefore, alternative antibiotic options are needed (Corum et al. 2019). Cefuroxime is utilized across several animal species (Albarellos et al. 2016; Serrano 2005); nevertheless, data about its use in fish remains insufficient. In vivo studies have shown that it is effective against bacterial infections in goldfish (Srinivasan and Venkateswaran 2016). In vitro studies have reported that *Aeromonas* spp. and *Streptococcus* spp. bacteria isolated from fish are sensitive to cefuroxime (Chonoko et al. 2014; Kaskhedikar and Chhabra 2010; Paniagua et al. 2006) and that it enhances the antibacterial effect of florfenicol against various pathogens isolated from fish (Lee et al. 2010). However, to our knowledge, the pharmacokinetics of cefuroxime have not been established in any fish species. Pharmacokinetics allows the quantitative assessment of drug absorption, distribution, metabolism, and excretion, and a comprehensive understanding of these factors is crucial for designing an optimal therapeutic dosing regimen for the target species (Dhillon and Gill 2006). Anatomical, physiological, and environmental (water temperature) variations among fish species may alter the pharmacokinetics of drugs (Corum et al. 2022b). Therefore, performing pharmacokinetic studies in the target fish species is critical for the success of the treatment. This study aimed to ascertain the pharmacokinetics of cefuroxime in Nile tilapia after intravascular (IV), intraperitoneal (IP), intramuscular (IM), and oral administration at a dosage of 20 mg/kg. The information obtained from this study will contribute to the determination of appropriate administration routes and efficacy of cefuroxime in tilapia.

Materials and methods

Animals

The Institutional Animal Care and Use Committee of Mindanao State University approved the ethics committee permission (2019/01), and the experimental research was conducted at the Naawan campus (Naawan, Misamis Oriental, Philippines). Fish exhibiting no indications of trauma or sickness and with normal body conditions and behaviors were assessed as clinically healthy. A total of 288 healthy Nile tilapia (*Oreochromis niloticus*), each weighing between 100 and 120 g, were utilized in this study. They were randomly distributed into eight plastic fiber tanks, each with a capacity of 400 L, containing 36 fish per tank. Before the experiment began, the fish were acclimatized for 10 days in their tanks to help them adjust to the environmental conditions. Throughout the experimental period, the water temperature was kept at 29 ± 1.5 °C, and a natural light/dark cycle was maintained using ambient daylight. The fish were fed the commercial pellet feed (Tilapia Breeder Pellet, Tateh Aquafeeds, Quezon City, Philippines) twice a day until they were satiated. To eliminate the effect of dietary components

on the absorption of cefuroxime, the fish were subjected to a 12-h fasting period both prior to and following medication administration.

Drug administration and sampling

Commercial formulations of cefuroxime were used for parenteral (cefuroxime sodium, Aksef, 750 mg, powder for injection, Istanbul/Türkiye) and oral (cefuroxime axetil, Aksef, 500 mg, tablets, Istanbul/Türkiye) administration. To administer drugs to fish, the formulations were diluted to a concentration of 10 mg/mL with sterile water. A total of 288 fish were separated into four different administration groups, each consisting of 72 fish. Each group ($n=72$) was divided into 12 subgroups ($n=6$) to reflect the sampling times, and six fish were used at each sampling time. Cefuroxime was administered at a dosage of 20 mg/kg by IV ($n=72$, caudal vessel), IP ($n=72$, peritoneal cavity), IM ($n=72$, epaxial muscle), and oral ($n=72$, via the gastric gavage) route. Drug application and sample collection procedures on fish were carried out under anesthesia (tricaine methane sulfonate, MS-222, 200 mg/L). Blood samples (1 mL) were obtained from the caudal vessel of each fish at 0, 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72, and 96 h. Blood samples were obtained with a 26-G needle connected to a 1 mL syringe and transferred into tubes containing heparin. Plasma samples were subsequently obtained using centrifugation at 4,000 ×g for 10 min, then frozen and preserved at −20 °C until further analysis.

HPLC conditions

The plasma concentrations of cefuroxime were quantified by high-performance liquid chromatography (HPLC) with ultraviolet detection using a modification of a previously reported method (Albarellos et al. 2016). The HPLC system (Shimadzu, Tokyo, Japan) was equipped with a model DGU-20 A degasser, a model CTO-10 A column oven, a model LC-20AT pump, a model SIL 20 A auto-sampler, and a model SPD-20 A UV detector. The chromatographic separation utilized a Gemini™ C18 column (4.6 × 250 mm; 5 µm) at 40 °C. The mobile phase consisted of acetonitrile (25%) and potassium dihydrogen phosphate buffer (0.05 M, pH:4, 75%) with a flow rate of 1 mL/min. The quantification wavelength was established to be 274 nm. Data analysis was conducted using Shimadzu Corp.'s LC Solution program.

Validation of the analytical method

The chromatographic process was verified in accordance with EMA (2011) criteria. Cefuroxime (98.0%, Sigma-Aldrich, Taufkirchen, Germany) stock solutions were prepared in ultrapure water at a concentration of 1 mg/mL. Calibration standards were created using a pool of blank tilapia plasma supplemented with eleven quantities of cefuroxime ranging from 0.04 to 100 µg/mL. Standard curves were obtained by linear regression of cefuroxime peak areas against known concentrations. The evaluation of quality control samples (0.1, 4 and 40 µg/mL) was performed five times on five separate days to ascertain recovery, precision, and accuracy. The recovery was determined by comparing the peak areas of quality control concentrations with the peak areas of working standards at the same concentration. The precision was assessed using the percentage coefficient of variation, whereas accuracy was evaluated as bias.

Sample extraction

Plasma samples from whole fish were analyzed for cefuroxime in accordance with the previously reported method (Albarellos et al. 2016). Two hundred µL of plasma sample was transferred to a microcentrifuge tube, and 50 µL of trichloroacetic acid was added. Plasma was precipitated by vortexing (30 s) and centrifugation (10 min at 10,000 x g). The supernatant was transferred to HPLC autosampler vials, and 20 µL of it was injected into the system.

Pharmacokinetic analysis

The chromatogram data acquired from HPLC analysis were recorded in an Excel file. Then, plasma concentrations were calculated, and plasma concentration-time curves were plotted. Plasma concentrations were reported as mean ± standard deviation (SD) values. Since six different fish were used at each sampling time, pharmacokinetic parameters were calculated from mean plasma concentrations as reported in previous studies (Corum et al. 2024). Pharmacokinetic parameters of cefuroxime were determined by the non-compartmental analysis using WinNonlin software (6.1.0.173, Pharsight Corp., Mountain View, CA, USA). The definitions and abbreviations of pharmacokinetic parameters are provided in the footnote of Table 1. The C_{max} and Tmax were ascertained from the individual plasma concentration–time curves. The λ_z was determined utilizing the absolute values from over three data points using log-linear regression analysis. The $t_{1/2\lambda z}$ was calculated using the formula $t_{1/2\lambda z} = 0.693/\lambda_z$. The log trapezoidal method was employed for the AUC for IV administration, while the linear-up log-down method was employed for other administration routes. The absolute bioavailability (F) was calculated using $(AUC_{IP,IM,\ oral}/AUC_{IV}) \times 100$. In addition, MRT, Cl_T, V_{dss}, and AUC_{extrap} % values were calculated.

Table 1 Plasma pharmacokinetic parameters following intravascular (IV), intraperitoneal (IP), intramuscular (IM) and oral administrations of cefuroxime at a single dose of 20 mg/kg in Nile tilapia (*Oreochromis niloticus*) at 29 ± 1.5 °C ($n = 6$)

Parameter	IV	IP	IM	Oral
$t_{1/2\lambda z}$ (h)	8.04	9.12	10.07	14.86
AUC_{0-48} (h*µg/mL)	136.73	109.15	93.63	31.16
$AUC_{0-\infty}$ (h*µg/mL)	138.61	111.25	95.71	33.75
AUC_{extrap} (%)	1.36	1.89	2.18	7.69
$MRT_{0-\infty}$ (h)	7.11	8.10	8.44	14.54
MAT (h)	-	1.00	1.33	7.43
Cl_T (L/h/kg)	0.14	-	-	-
V_{dss} (L/kg)	1.03	-	-	-
C_{max} (µg/mL)	-	53.38±4.28	28.70±3.41	6.77±0.81
T_{max} (h)	-	0.25	0.5	1
F (%)	-	80.26	69.05	24.35

Cefuroxime sodium was used for IV, IP and IM administration, and cefuroxime axetil (prodrug) was used for oral administration

$t_{1/2\lambda z}$ Terminal elimination half-life; *AUC* Area under the concentration-versus time curve; AUC_{extrap}% Area under the plasma concentration–time curve extrapolated from tlast to ∞ in % of the total AUC; $MRT_{0-\infty}$ Mean residence time; *MAT* Mean absorption time; Cl_T Total body clearance; V_{dss} Volume of distribution at steady state; C_{max} Peak plasma concentration; T_{max} Time to reach peak plasma concentration; *F* Bioavailability

Results

Animals

Fish were healthy (swimming and behavior) throughout the acclimatization and experiment. Cefuroxime administered at a dose of 20 mg/kg IV, IP, IM or oral was well tolerated in fish.

Method validation

The working and calibration curves exhibited linearity with a R^2 value of > 0.994. The mean recovery of cefuroxime in tilapia plasma was greater than 97%. For cefuroxime in tilapia plasma, the limit of detection and lower limit of quantitation, based on a signal-to-noise ratio > 3 and > 6, were 0.02 and 0.04 µg/mL, respectively. The results showed that all intra- and inter-day coefficients of variation were below 6.12% for cefuroxime. The intra- and inter-day bias of cefuroxime was below 3.68%.

Pharmacokinetics

Figure 1 illustrates the plasma concentration-time profiles of cefuroxime in tilapia after the different routes of administration. Cefuroxime was detected in tilapia plasma up to 48 h by all administration routes. Table 1 presents the pharmacokinetic parameter estimates of cefuroxime in tilapia after IV, IP, IM, and oral administration. The C_{max} and T_{max} of cefuroxime were 53.38±4.28 µg/mL and 0.25 h for IP injection, 28.70±3.41 µg/mL and 0.5 h for IM injection, and 6.77±0.81 µg/mL and 1 h for oral administration. The absolute bioavailability of cefuroxime after IP, IM, and oral administration was 80.26%, 69.05%, and 24.35%, respectively. The C_{max}, T_{max}, and bioavailability values were different in IP, IM, and oral groups. Cefuroxime exhibited a

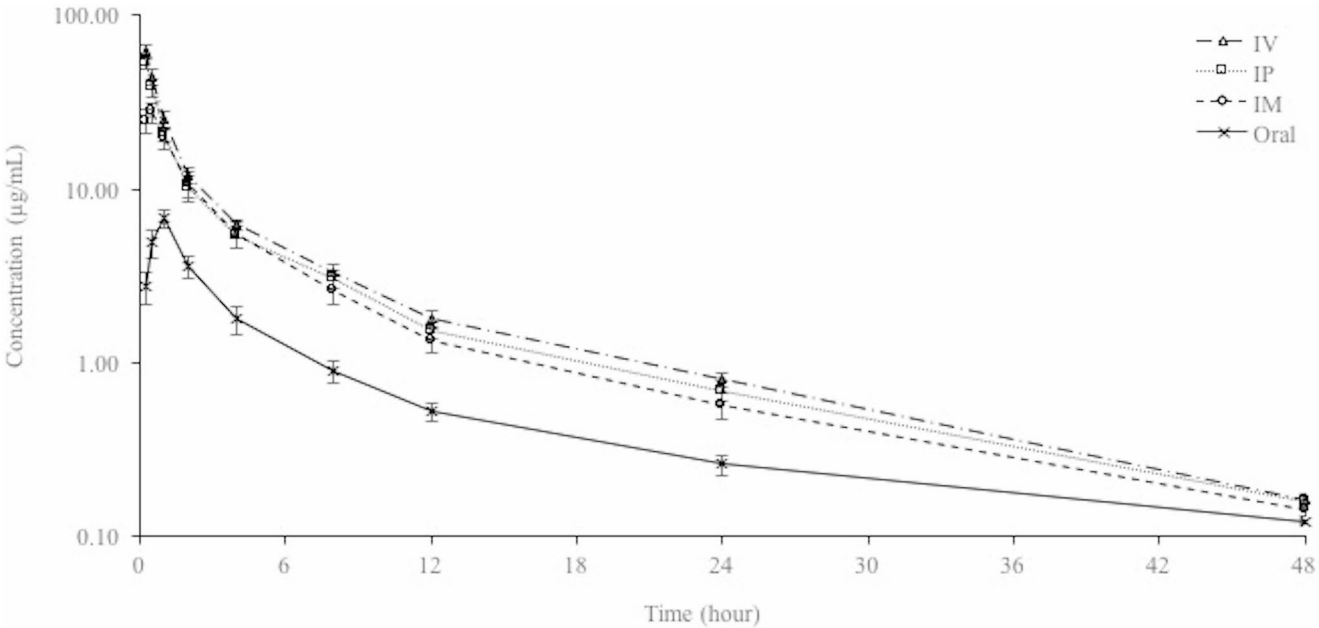

Fig. 1 Semi-logarithmic plasma concentration-time curves following intravascular (IV), intraperitoneal (IP), intramuscular (IM), and oral administrations of cefuroxime at a single dose of 20 mg/kg in Nile tilapia (*Oreochromis niloticus*) at 29 ± 1.5 °C (mean ± SD, $n = 6$)

$t_{1/2\lambda z}$ of 8.04 h, V_{dss} of 1.03 L/kg, and Cl_T of 0.14 L/h/kg following IV injection. The $t_{1/2\lambda z}$ values were longer in the IP, IM, and oral administration groups than in the IV group. The MAT value was 1 h, 1.33 h, and 7.43 h in the IP, IM, and oral groups, respectively. AUC_{extrap} was below 8% in all groups.

Discussion

Antibiotics are used in excess to treat bacterial disease in fish. Alternative treatments are necessary due to the emergence of antibiotic resistance resulting from extensive use (Corum et al. 2019). Pharmacokinetic and pharmacodynamic studies are crucial in using appropriate dosage regimens of drugs in any fish species (Serrano 2005). Cefuroxime is a broad-spectrum antibiotic widely used in humans and animals. This antimicrobial is effective against some fish infections and sensitive to bacteria in its spectrum of activity isolated from fish, but no pharmacokinetics studies exist. The information obtained for the first time in this study regarding the pharmacokinetics of cefuroxime in fish may contribute to its use in bacterial diseases in fish.

Cefuroxime did not cause any local or systemic side effects in tilapia after IV, IP, IM, and oral administration at a dose of 20 mg/kg. There is insufficient information regarding cefuroxime dosage in fish. It was applied to goldfish as a bath at a concentration of 10 mg/L for 5 days and was found to be safe in zebrafish at a concentration of 100 mg/L (Srinivasan and Venkateswaran 2016). Cefuroxime has been used in goats, calves, and dogs at doses ranging from 10 to 40 mg/kg (Albarellos et al. 2016; El-Sooud et al. 2000; Soback et al. 1989). Therefore, a 20 mg/kg dose of cefuroxime was administered to tilapia via different routes.

The V_{dss} is used to calculate the quantity of drug in the body under equilibrium conditions and is unaffected by clearance (Toutain and Bousquet-Mélou 2004a). Cefuroxime has an overall small volume of distribution due to its hydrophilic nature (Mrestani et al. 2004; Omole et al. 2025). The V_{dss} of cefuroxime in mammals has been reported to be 0.27–0.67 L/kg (Albarellos et al. 2016; El-Sooud et al. 2000; Soback et al. 1989). V_{dss} is an indicator of drug distribution into body tissues, and it is relatively small in mammals, indicating that the medication is minimally distributed into extravascular tissues. The V_{dss} after IV injection of cefuroxime to tilapia was 1.03 L/kg, which was larger than previously reported in mammals. This indicates that cefuroxime penetrates the tissue better in tilapia. The volume of distribution depends on the ratio of binding to body components and plasma proteins (Corum et al. 2024). The body components and physiological conditions exhibit considerable differences between mammals and fish (Corum et al. 2019). While the plasma protein binding ratio of cefuroxime is unknown in fish, it is 17–33% bound in mammals, and the binding ratio varies according to species (El-Sooud et al. 2000). The plasma protein concentration in trout is 50% of that in mammals, resulting in a lower drug binding ratio in fish (Kleinow et al. 1992). In addition, the binding ratio of acidic drugs in trout was lower than in mammals (Henneberger et al. 2020). The variations in body composition, physiological condition, and binding affinity among animal species may have resulted in increased V_{dss} of cefuroxime in tilapia.

The Cl_T of cefuroxime following IV injection in tilapia was 0.14 L/h/kg, which is lower than the previously documented rate (0.21–0.41 L/h/kg) in mammals (Padhi et al. 2015; Soback et al. 1989). No information is available on the metabolism and excretion of cefuroxime in tilapia. Biotransformation of cefuroxime was shown to be minimal in dogs, humans, and rats but considerable in cows (Roberts and Cerniglia 2025). It is excreted unaltered in the urine, primarily by glomerular filtration and tubular secretion (Ruiz-Carretero et al. 2000). Fish have a slower metabolic rate and lesser biotransformation enzyme capability than mammals (Kleinow et al. 1992). Kidney, bile, and gill play a role in the excretion of drugs from the body in fish (Christiansen et al. 1996; Evans et al. 2005). The lower Cl_T of cefuroxime in tilapia compared to mammals may be attributed to variations in metabolic and excretion pathways. The $t_{1/2\lambda z}$ of cefuroxime following IV injection in tilapia was 8.04 h, which is longer than the previously documented ratio (0.67–1.48 h) in mammals (El-Sooud et al. 2000; Padhi et al. 2015). The $t_{1/2\lambda z}$ is a hybrid parameter that is directly proportional to V_d and inversely proportional to Cl_T (Toutain and Bousquet-Melou 2004b). The longer $t_{1/2\lambda z}$ of cefuroxime in fish compared to mammals is due to its larger V_{dss} and lower Cl_T.

The $t_{1/2\lambda z}$ was longer after oral administration than after IV administration. Similarly, $t_{1/2\lambda z}$ was prolonged after oral administration in rats (Ruiz-Carretero et al. 2000). It has been reported that the $t_{1/2\lambda z}$ of some drugs may be longer after extravascular administration than after IV administration due to the flip-flop phenomenon (Yáñez et al. 2011). The flip-flop phenomenon occurs when the rate of absorption of a drug after extravascular administration is slower than the rate of excretion. In this case, the MAT value should be longer than the MRT value obtained for IV administration (Yáñez et al. 2011). However, in this study, the MAT value for oral administration was longer than MRT_{IV}. The longer $t_{1/2\lambda z}$ of the oral route may be due to the use of different drug formulations for parenteral (cefuroxime sodium) and oral (cefuroxime axetil) routes.

The bioavailability of cefuroxime was high after IP (80.26%) and IM (69.05%) injection but low after oral (24.35%) administration. The results demonstrated that

cefuroxime was well absorbed via IP and IM injection, and these findings are similar to those reported in calves (IM: 110.93%, Soback et al. 1989), goats (IM: 88–103%, El-Sooud et al. 2000), dogs (IM: 79.70%, Albarellos et al. 2016), and rats (IP: 80.64%, Ruiz-Carretero et al. 2000). Cefuroxime is not orally absorbed; hence, its prodrug, cefuroxime axetil, is utilized (Ruiz-Carretero et al. 2000). After oral administration, cefuroxime axetil is rapidly hydrolyzed to cefuroxime by nonspecific esterases present in the intestinal mucosa and blood (Padhi et al. 2015). The absorption of cefuroxime from the intestinal lumen is mediated by carriers and obeys the Michaelis-Menten equation (Mosher et al. 1992). Cefuroxime axetil exhibited low bioavailability (25.75%) in rats after oral administration, while it was not detectable in the blood of goats (Padhi et al. 2015; Ruiz-Carretero et al. 2000). Oral bioavailability may vary due to changes in esterase enzymatic activity and carrier protein levels among animal species (Padhi et al. 2015; Ruiz-Carretero et al. 2000). The oral administration of cefuroxime in tilapia is inappropriate, as the bioavailability must exceed 30% for antibiotic use in fish (Bowser and Babish 1991).

The C_{max} of cefuroxime at a 20 mg/kg dose in tilapia was 53.38±4.28 µg/mL at 0.25 h for IP injection, 28.70±3.41 µg/mL at 0.5 h for IM injection, and 6.77±0.81 µg/mL at 1 h for oral administration. These data indicate that cefuroxime has a short T_{max} and a high C_{max} in the order IP > IM > oral. The difference in C_{max} between the application groups may be due to differences in bioavailability (Duan 2010; Lea-Henry et al. 2018). After IM injection, short T_{max} has been reported in dogs (0.43 h) and goats (0.51 h, Albarellos et al. 2016; El-Sooud et al. 2000). The C_{max} obtained after IM injection at a dose of 20 mg/kg in tilapia was higher than that previously obtained in dogs (22.99 µg/mL, Albarellos et al. 2016) and goats (12.97 µg/mL, El-Sooud et al. 2000). This difference between animal species may be due to variations in the drug formulation and bioavailability, as well as anatomical and physiological differences.

The antibacterial effect of cephalosporin group antibiotics such as cefuroxime is time dependent and T > minimum inhibitor concentration (MIC)% data is used to evaluate their effectiveness (Durna Corum et al. 2022). For beta-lactams, T > MIC 50% of the dosing interval has been defined as optimal for bactericidal effect (Albarellos et al. 2016). In this study, the MIC value of cefuroxime was not determined for bacteria isolated from fish. The MIC value of cefuroxime for *Streptococcus* spp., *Staphylococcus epidermidis*, *Vibrio harveyi*, *Lactococcus garvieae*, and *Pseudomonas piscicida* bacteria isolated from fish was ≤1 µg/mL, while it was ≤4 µg/mL for *Edwardsiella tarda* bacteria (Lee et al. 2010). This study found that a dosing interval of 24 h for parenteral injection (IV, IP and IM) or 8 h for oral administration is efficient for treating bacteria with a MIC value of ≤1 µg/mL. For bacteria with MIC values ≤4 µg/mL, an 8-h parenteral injection (IV, IP, IM) or 2-h oral administration dosing interval was found to be effective. These data indicate that parenteral injection of cefuroxime is more advantageous than oral administration in tilapia.

The most common method for administering systemically effective antimicrobial drugs to cultured fish is the oral route (Noga 2010). However, oral administration has the significant disadvantage of causing insufficient medication absorption in ill fish due to loss of appetite. Despite some significant disadvantages such as high labor costs, tissue damage at the injection site, and the risk of infection, parenteral drug use may be preferred due to advantages such as smaller drug amounts, rapid onset of action, precise dosing, and stronger efficacy (Soo Seo et al. 2021; Terzi et al. 2020). Injectable formulations of a small number of antibiotics have been reported to be used in Korean aquaculture (Soo Seo et al. 2021). The pharmacokinetic results obtained in our study reveal that cefuroxime can be used in tilapia fish via IP or IM injection.

Some limitations apply to this research that was carried out on tilapia. The lack of investigation of cefuroxime's plasma protein binding ratio, metabolism, and excretion pathways were limiting factors. While oral administration to fish is mostly achieved via medicated feed, the oral gavage approach is preferred to ensure the exact dosage of cefuroxime, which constitutes a limitation. The study was conducted on healthy animals, and one of the limitations was that the pharmacokinetics and efficacy of cefuroxime were not determined in infected fish. Drug administration and blood collection were performed under anesthesia to minimize stress on the fish. However, physiological changes induced by anesthesia may affect the distribution of cefuroxime in the body, which was a limitation of the study.

Conclusion

This study shows that cefuroxime has a promising pharmacokinetic profile in tilapia, especially via IP and IM routes, which offer high bioavailability and effective plasma levels. These methods are ideal for severe or acute infections requiring rapid drug absorption and precise dosing. They are also preferred when oral absorption is compromised due to illness. Although oral administration had lower bioavailability, plasma levels may still be effective for 8 h against bacteria with MIC ≤ 1 µg/mL, and formulation improvements could boost its practicality. Future research should explore optimal oral dosing and tissue residue depletion to ensure safety, while investigating protein binding, metabolism, and excretion will enhance dosing accuracy. Furthermore, pharmacokinetic and pharmacodynamic studies of

cefuroxime in infected fish populations are needed. Overall, cefuroxime may be a promising antibiotic for tilapia, with IP and IM routes particularly suitable for aquaculture applications.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11259-025-10974-8.

Author contributions OC, KU, DDC, PM, OY, RCG: Investigation, Formal analysis, Methodology, Writing – original draft, Writing –review and editing. ET, DMA, VRN, SB, AYS: Investigation, Writing–review and editing.

Funding This study was supported by The Coordination of Scientific Research Projects, University of Kastamonu (Project No: KU-BAP01/2018–99).

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval The study was conducted in accordance The Institutional Animal Care and Use Committee of Mindanao State University, and approved (2019/01) by the Ethics Committee.

Competing interests The authors declare no competing interests.

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