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Bioavailability Study of Cefepime After Intravenous and Intramuscular Administration in Normal Broiler Chickens

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ABSTRACT:

The bioavailability of cefepime in normal broiler chickens was investigated after single intramuscular and intravenous administrations at a dose of 100 mg/kg b.wt. Serum concentrations of cefepime were determined by using high performance liquid chromatography (HPLC). Following compartmental analysis, a two-compartment open model best described the concentration-time data of cefepime after intramuscular and intravenous administration. After intramuscular administration, the drug reached its maximum serum concentrations (C_{max}) of 193.06 ± 2.27 µg/ml at maximum time (T_{max}) of 1.138 ± 0.012 h, absorption half-life ($t_{1/2ab}$) was 0.491 ± 0.027 h and (AUC_{0-t}) was 1127.58 ± 14.48 µg/ml/h. Following a single intravenous injection, the drug was detected till 24 hours, distribution half-life ($t_{1/2\alpha}$) was 0.217 ± 0.036 h, elimination half-life ($t_{1/2\beta}$) was of 4.608 ± 0.145 h and clearance (CL) was 0.090 ± 0.002 (mg/kg)/(µg/ml)/h, volume of distribution at steady state (V_{dss}) was 0.586 ± 0.11 (mg/kg)/(µg/ml) and bioavailability was 104.30 ± 2.34 %. Limits of detection and quantification were 0.03 and 0.10 µg/ml, respectively.

Keywords: *Cefepime – Bioavailability –HPLC – broiler chickens*

INTRODUCTION

Cefepime is a parenteral fourth-generation cephalosporin antibiotic with an extended spectrum of antimicrobial activity. It is active against many Gram-positive and Gram-negative bacteria, including most members of the family *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* (Chong *et al.*, 1993; Thornsberry *et al.*, 1993) with reduced susceptibility to extended-spectrum β-lactamases (Jacoby and Cerreras ,1990). The chemical structure of cefepime allows it to bind to penicillin-binding proteins and to penetrate through the outer membrane of Gram-negative bacteria more rapidly than most cephalosporins. In humans, it is approved for treatment of lower respiratory tract, intra-abdominal, complicated and uncomplicated urinary tract infections, and uncomplicated skin and skin structure infections (Okamoto *et al.*, 1993). It has also been shown to be therapeutically equivalent to cefotaxime and ceftriaxone in the treatment of pediatric meningitis (Saez Llorens *et al.*, 1995).

Its mechanism of action is similar to the other cephalosporins by disrupting the synthesis of the peptidoglycan layer forming the bacterial cell wall. The peptidoglycan layer is important for cell wall structural integrity. The pharmacokinetics of cefepime has been extensively investigated in various animal species as rats and monkeys (Forgue *et al.*, 1987), rabbits (Goudah *et al.*, 2006; Abd El-Aty *et al.*, 2007; Rule *et al.*, 2010), horses (Guglick *et al.*, 1998), foals and dogs (Gardner and Papich, 2001), cow calves (Ismail, 2005b; Patel *et al.*, 2006; Pawar and Sharma, 2008; Patel *et al.*, 2012), ewe (Ismail, 2005a), goats (El-Rabbat *et al.*, 2010; Rule *et al.*, 2001; Bhavsar *et al.*, 2008; Prawez *et al.*, 2010; El-Hewaity, 2014), bull

camels (Goudah *et al.,* 2009), sheep (Patel *et al.,* 2010) and buffalo calves (Joshi and Sharma 2007; Joshi and Sharma 2009). Currently, there are no available data on the pharmacokinetics of cefepime in broiler chickens.

Therefore, this study was performed to investigate pharmacokinetics profile in broiler chickens.

MATERIAL AND METHODS

1- Materials

Drug

Cefepime hydrochloride powder (Maxipime® 1g, Bristol-Myers Squibb, NY, USA) was reconstituted with sterile pyrogen free water to yield a final concentration of 10% according to the manufacturer's guidelines.

Chickens

This study was conducted on twelve apparently healthy broiler chickens of 1.5±0.2 kg. All chickens were obtained from El-Arabia poultry breeding farm. They were housed separately in cages. Chickens were fed on balanced drug free ration for two weeks to ensure complete excretion of antibacterial from their bodies. Water was supplied *ad-libitum*. Chickens were reared in room maintained at 12 h lighting cycle. The room was maintained at constant temperature and relative humidity of 45% to 65%.

Experimental design

The chickens were divided into 2 groups:

Group (1)

It included 6 normal chickens. Chickens were individually weighted before drug administration, and doses were calculated precisely for each bird. Six chickens were given a single dose of cefepime as 100 mg/kg b.wt through IM. injection to the thigh muscle.

Group (2)

It included 6 normal chickens. Chickens were individually weighted before drug administration and doses were calculated precisely for each bird. Six chickens were given a single dose of cefepime as 100 mg/kg b.wt through i.v. in to the right wing vein.

Blood samples (0.5-1 ml) were collected after IM and IV injection from brachial and cutaneous ulnar veins at time 0, 5, 10, 15, 30 min and 1, 2, 4, 8, 10, 12, 24 hours after drug administration. The samples were left to clot at room temperature then centrifuged at 3500 rpm for 10 minutes and serum was harvested and stored frozen at -20 ºC until analyzed for cefepime.

2-Methods

Estimation of cefepime level in serum: Cefepime was extracted from serum according to the method described by (**Dogan *et al.*, 2013**). In an Eppendorf tube**,** 500 µL aliquot of chicken serum was added, then total volume was completed to 1 ml with addition of 10% TCA (Trichloroacetic acid), after centrifugation at 6,000 rpm for 5 min, supernatants were filtrated with 0.45 µm syringe filter and transferred into the auto-sampler vial for analysis.

The concentration of cefepime was determined by high performance liquid chromatography (HPLC) according to (Callejon Mochon *et al.*, 2005). The mobile phase consists of 10 mM phosphate buffer (PH7) Methanol; 75:25 which always freshly prepared, filtered and degassed. The injection volume of samples was 20 µl, the flow rate was fixed at 1.0 ml/min, column temperature was 25ºC and the ultraviolet detector wavelength was set at 256 nm.

Preparation of standard curves of cefepime in serum:

Standard concentrations of cefepime were prepared in antibiotic free chicken's serum and deionized water. Cefepime hydrochloride (purity ≥ 98.0%) was purchased from Sigma (3050 Spruce Street, Saint Louis, MO 63103, USA). The standard curves for serum, and deionized water were linear between 0.10 and 100 µg/ml. A calibration curve was obtained by plotting the cefepime peak areas versus known concentrations. The equation was calculated by the least-squares method using linear regression. The assay was sensitive, reproducible and linearity was observed from 0.1 to 100 µg/ml. The retention time of cefepime was 1.666 min. Limit of detection and quantification were 0.03 µg/ml and 0.10 µg/ml respectively.

Pharmacokinetic analysis:

The pharmacokinetic parameters were calculated by PK Solver: An add-in program for Microsoft Excel, version 2.

Statistical analysis:

The data were calculated as mean ± standard deviation. All statistical analysis was p according to (Berly and Lindgren 1990).

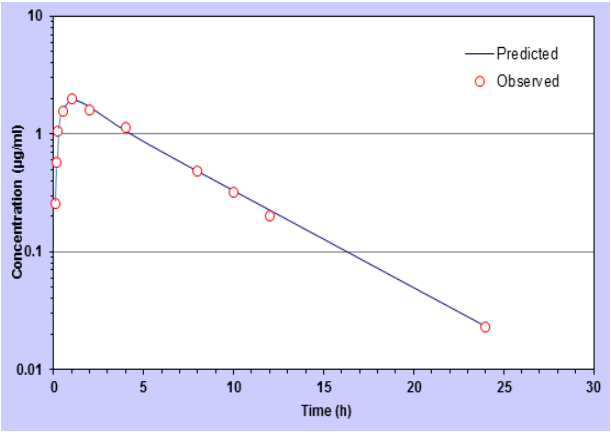
RESULTS:

Serum Cefepime disposition after intramuscular administration:

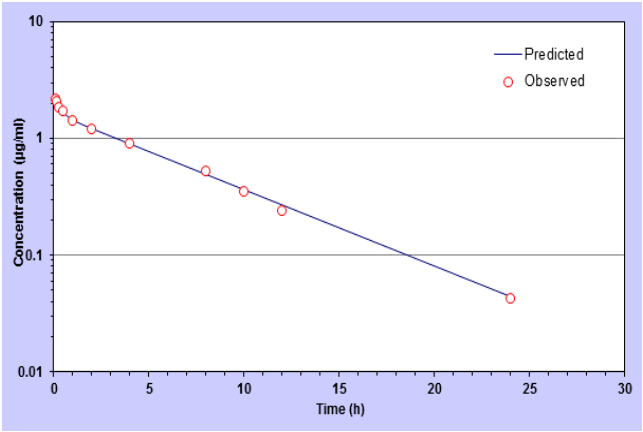
Following a single intramuscular administration of cefepime, the serum concentration-time data was best fitted to two compartments open model. Cefepime was detected in serum in a therapeutic level for 24 hours with mean value 2.28 ± 0.32 µg/ml (**Fig. 1**). The serum concentration-time data of cefepime (100 mg/kg b.wt) following intramuscular injection in normal chickens was best fitted to a two compartments open model. The pharmacokinetic parameters following a single intramuscular administration of cefepime were recorded in (**Table 1**). The obtained results revealed that the absorption rate constant (K_{ab}) was 1.42 ± 0.077 h^{-1}, while absorption half-life ($t_{1/2ab}$) was 0.491 ± 0.027 h. Cefepime reached its maximum concentrations (C_{max}) 193.06 ± 2.27 µg/ml after maximum time equal to (T_{max}) 1.138 ± 0.012 h. The elimination half-life ($t_{1/2\beta}$) was 3.670 ± 0.125 h. Cefepime was cleared by all clearance processes (Cl/F) in the body at rate of 0.088 ± 0.001 µg/ml/h. The area under serum concentration time curve of cefepime after a single intramuscular administration (AUC_{0-t}) was 1127.58 ± 14.48 µg/ml/h and the bioavailability were 104.30 ± 2.34 %.

Serum Cefepime disposition after intravenous administration:

Following a single intravenous injection of cefepime (100 mg/kg b.wt.) in normal chickens, the serum concentration-time data of cefepime was best fitted to two compartments open model. Cefepime was detected 24 hours after administration with mean values of 4.28 ± 0.37µg/ml (**Fig.2**). The pharmacokinetic parameters of cefepime after a single intravenous injection recorded in (**Table 1**). The distribution half-life ($t_{1/2\alpha}$) was 0.217 ± 0.036 h, and volume of distribution at steady state (V_{dss}) was 0.586 ± 0.11 (mg/kg)/(µg/ml). Cefepime was eliminated with half-life ($t_{1/2\beta}$) value of 4.608 ± 0.145 h and cleared by all clearance processes (CL) in the body at a rate 0.090 ± 0.002 µg/ml/h.



[Fig. (1).] Mean ± SD serum concentration (µg/ml) of cefepime in healthy chickens after single intramuscular injection of 100 mg/kg b.wt.



[Fig. (2).] Mean ± SD serum concentration (µg/ml) of cefepime in healthy chickens after single intravenous injection of 100 mg/kg b.wt.

Table (1). Mean±SD pharmacokinetics parameters of cefepime after single intramuscular and intravenous administration of 100 mg/kg b.wt

	Mean ± SD	Pharmacokinetic Parameters of Cefepime	
Parameters	Units	Intramuscular	Intravenous
A	µg/ml	2707.10 ± 871.36	76.50 ± 3.65
α	h^{-1}	1.31 ± 0.08	3.26 ± 0.50
B	µg/ml	219.54 ± 11.09	163.59 ± 4.39
β	h^{-1}	0.189 ± 0.006	0.151± 0.005
K_{ab}	h^{-1}	1.42 ± 0.077	—
K_{10}	h^{-1}	0.321 ± 0.016	0.216 ± 0.007
k_{12}	h^{-1}	0.403 ± 0.022	0.922 ± 0.123
k_{21}	h^{-1}	0.780 ± 0.099	2.278 ± 0.378
$t_{1/2\alpha}$	H	0.529 ± 0.030	0.217 ± 0.036
$t_{1/2\beta}$	H	3.670 ± 0.125	4.608 ± 0.145
$t_{1/2ab}$	H	0.491 ± 0.027	—
V_1/F	(mg/kg)/(µg/ml)	0.274 ± 0.014	0.417 ± 0.006
CL/F	(mg/kg)/(µg/ml)/h	0.088 ± 0.001	0.090 ± 0.002
V_2/F	(mg/kg)/(µg/ml)	0.143 ± 0.015	0.169 ± 0.009
CL_2/F	(mg/kg)/(µg/ml)/h	0.110 ± 0.004	0.384 ± 0.048
Vdss	(mg/kg)/(µg/ml)	—	0.586 ± 0.11
T_{max}	H	1.138 ± 0.012	—
C_{max}	µg/ml	193.06 ± 2.27	—
AUC $_{0-t}$	µg/ml.h	1127.58 ± 14.48	1081.41 ± 20.50
AUC $_{0-inf}$	µg/ml.h	1140.10 ± 15.78	1110.90 ± 23.30
AUMC	µg/ml.h^2	6232.71 ± 198.27	7234.99 ± 340.05
MRT	H	5.466 ± 0.106	6.51 ± 0.189
F	%	104.30 ± 2.34	—

A, zero-time intercept of the distribution slope; α, distribution rate constant; B, Zero-time intercept of decline in serum concentration of drug; β, elimination rate constant; k_{10}, first-order elimination rate constant from central compartment; k_{12}, rate constant for passage from central to peripheral compartment; k_{21}, rate constant for passage from peripheral to central compartment; $t_{1/2\alpha}$, the distribution half-life; $t_{1/2\beta}$, elimination half-life; T_{max}, The time at which the maximum concentration of drug was reached after extra vascular administration (h); C^0, serum drug concentration at t=0 (Immediately) following drug administration; C_{max}, Maximum serum concentration of drug in blood after extravascular administration (µg/ml); Cl,, total body clearance; CL_2, Inter-compartmental clearances; V_1, apparent volume of central compartment; V_2, apparent volume of peripheral compartment; V_{dss}, volume of distribution at steady state; AUC $_{0-t}$, area under the [serum drug concentration versus time] curve; AUC $_{0-inf}$, total area under the concentration–time curve from zero to infinity; AUMC, area under the first moment curve; MRT, mean residence time; F %, bioavailability.

DISCUSSION

In the present investigation, the drug disposition after IM. and IV. administration of (100 mg/kg) in chickens was best fitted by a two-compartment open model.

Following a single intramuscular administration, cefepime was rapidly and efficiently absorbed in chickens. The reported half-life of absorption ($t_{1/2ab}$) was (0.49±0.03h) which is similar to cefepime recorded in ewes (0.49±0.05h) (Ismail, 2005a). However, it disagree with cefepime reported in goats (0.77±0.34; 0.25±0.02; 0.16±0.01 h, (Bhavsar *et al.*, 2008; Prawez *et al.*, 2010; El-Hewaity, 2014), respectively, bull camels (2.5 ± 0.27 h, Goudah *et al.*, 2009) and calves (0.29 ± 0.02; 0.17 ± 0.01 h, (Ismail, 2005b; Patel *et al.*, 2012) respectively.

In comparison to other cephalosporin, the absorption half-life of cefepime in chicken agreed with those reported in Cefquinome in piglets (0.41 ± 0.36h, (Li, *et al.*, 2008) but disagreed with that reported in Ceftiofur in chickens (0.759 ± 0.03 h) (Dalia *et al.*, 2015), Ceftiofur in rabbits (0.09 ± 0.03 h, Kamil, *et al.*, 2015), Cefquinome in black swans 0.12 h (Zhao *et al.*, 2017), Ceftiofur sodium in adult cockatiels and Amazon parrots 0.28 ; 0.93 h (Tell *et al.*,1998), Cefquinome in chickens 0.07 ± 0.02 h (Xie, *et al.*, 2013) and Cefquinome in ducks 0.12± 0.02h (Liguo Yuan *et al.*, 2011)

The difference is probably due to the difference in the dosage level since we used a dose of 100 mg/kg b.wt.

Cefepime reached to a maximum serum concentration (T_{max}) after (1.14±0.01 h) which nearly similar to cefepime that previously reported in bull camels 1.0±0.02 h (Goudah *et al.*, 2009), calves 1.1±0.08 h (Ismail, 2005b), goats 0.91±0.08h (El-Hewaity, 2014) and ewes 1.1±0.2 h (Ismail, 2005a) but disagreed with those reported in calves 0.75 h; 0.75 h (Joshi and Sharma, 2007; Patel, *et al.*, 2012) respectively, goats 0.80±0.11h; 0.5h (Bhavsar et al., 2008; Prawez *et al.*, 2010), rabbits 0.5 h (Goudah *et al.*, 2006) and sheep 0.75 h (Patel *et al.*, 2010).

In comparison to other cephalosporin, the time to reach a maximum serum concentration (T_{max}) was disagreed with those reported in Ceftiofur in chickens 2.51± 0.088 h, (Dalia, *et al.*, 2015),Cefquinome in broiler chickens 2.8±0.19h, (El-Mahdy, *et al.*, 2015), Ceftiofur in rabbits 0.25 h (Kamil, *et al.*, 2015), Cefquinome in black swans 0.39 h (Zhao *et al.*, 2017), Ceftiofur crystalline-free acid in American black ducks 24 h, (Hope *et al.*, 2012), Ceftiofur sodium in adult cockatiels and Amazon parrots 0.5 h, (Tell, *et al.*, 1998),Ceftiofur crystalline free acid in American flamingos 7.49 ±1.9 h (Kilburn, *et al.*, 2015), Ceftiofur crystalline-free acid in healthy adult helmeted guinea fowl 19.3 ±9.71 h (Kimberlee, *et al.*, 2011), Cefquinome in chickens 0.25 ± 0.06 h (Xie, *et al.*, 2013) and Cefquinome in ducks 0.38 ± 0.06 h (Yuan *et al.*, 2011).

The mean peak serum concentration of cefepime (C_{max}) was (193.06±2.27 µg/ml) after i.m administration of 100 mg/kg.bw. These values were much higher than those recorded in goats 49.32±10.33; 15.75±2.39; 16.49±0.53 µg/ml, (Bhavsar *et al.*, 2008; Prawez, *et al.*, 2010; El-Hewaity, 2014) respectively, calves 30.2±0.09; 21.7±1.1 µg/ml, (Ismail, 2005b; Joshi and Sharma 2007) respectively, bull camels 51.6 ± 6.14 µg/ml, (Goudah, *et al.*, 2009), sheep 26.34 ± 1.44 µg/ml, (Patel, *et al.*, 2010), rabbits 114.93±9.51 µg/ml, (Goudah, *et al.*, 2006).

Variation in species as well as doses could be considered the causes of these variations.

The bioavailability (F%) of cefepime in normal chickens was (104.3±2.34%) which was agrees with those reported in cefquinome in cattle 104±7.13 %, (Shan, *et al.*, 2013) and sheep 103±8% (Patel, *et al.*, 2010) but higher than that reported in cefepime in goats 86.45 ±17.39; 69±6; 92.66% (Bhavsar *et al.*, 2008; Prawez, *et al.*, 2010; El-Hewaity, 2014) respectiveely, calves 95.3±10.5; 95.7±7.44%, (Ismail, 2005b; Joshi and Sharma 2007) respectively, bull camels 91.7± 12.35% (Goudah, *et al.*, 2009), and ewes 86.8±7.5 % (Ismail, 2005a).

Following intravenous administration, the distribution half-life ($t_{1/2\alpha}$) is closely similar to cefepime that previously reported in goats 0.20 ± 0.004; 0.20 ± 0.002 h, (Bhavsar, *et al.*, 2008; El-Hewaity, 2014), buffalo calves 0.18 ± 0.05 h (Joshi and Sharma 2007), sheep 0.2 ± 0.02 h (Patel, *et al.*, 2010), calves 0.2 ± 0.02 h; 0.25 ± 0.07 h, (Ismail, 2005b; Pawar and Sharma 2008) and ewes 0.18 ± 0.008 h (Ismail, 2005a). Longer half-life of distribution was recorded for

cefepime in bull camels 0.30 ± 0.05h, (Goudah, *et al.,* 2009), horses 0.39 ± 0.18 h (Guglick, *et al.,* 1998) and neonatal foals and adult dogs 0.30 ± 0.16 h; 0.39 ± 0.21 h, (Gardner and Papich 2001) respectively.

In comparison to other cephalosporins, the half-life of distribution is nearly similar to that previously reported in Cefquinome in yellow cattle 0.29 ± 0.05h (Shan, *et al.,* 2013), Cefquinome in piglets 0.27 ± 0.21h (Li, *et al.,*2008), Cefquinome in broiler chickens 0.155 h (Maha, *et al.,* 2005) and Cefquinome in ducks 0.19 ± 0.05h (Yuan, *et al.,* 2011) but not agreed with that reported for Ceftiofur in rabbits 0.34 ± 0.07 h (Kamil *et al.,* 2015), Cefquinome in black swans 0.31 ± 0.03 h, (Zhao, *et al.,* 2017) Cefquinome in chickens 0.43 ± 0.19 h, (Xie, *et al.,* 2013), Ceftiofur in chickens 0.70 ± 0.38 h, (Shen, *et al.,* 2009).

The volume of distribution (V_{dss}) was closely related to cefepime that reported in goats 0.44 ± 0.01; 0.35 ± 0.03 mg/kg, (Bhavsar, *et al.,*2008; El-Hewaity, 2014) respectively, calves (0.42 ± 0.08; 0.43 ± 0.03; 0.52 ± 0.03 mg/kg (Patel, *et al.,* 2006; Joshi and Sharma, 2007; Patel, *et al.,* 2012) respectively and sheep 0.42 ± 0.02 mg/kg, (Patel *et al.,* 2006) but higher than that reported in bull camels 0.10 ± 0.04 mg/kg, (Goudah, *et al.,* 2009), calves 0.21 ± 0.01 mg/kg (Ismail, 2005b), ewes 0.32 ± 0.01 mg/kg, (Ismail, 2005a) and neonatal foals and adult dogs 0.18 ± 0.05; 0.14 ± 0.04 mg/kg (Gardner and Papich 2001) respectively.

In comparison to other cephalosporin, The volume of distribution was closely related to that reported in Cefquinome in piglets 0.46 ± 0.1h, (Li *et al.,* 2008) and Cefquinome in chickens 0.49 ± 0.05 mg/kg, (Xie, *et al.,* 2013) but disagreed with that recorded in Ceftiofur in rabbits (260 ± 71 mg/kg, (Kamil *et al.,* 2015), Cefquinome in black swans 0.32 ± 0.17 mg/kg (Zhao, *et al.,* 2017),Cefquinome in chickens 0.43 ± 0.19 mg/kg, (Xie, *et al.,* 2013), Cefquinome in chickens 0.21 mg/kg (Maha, *et al.,* 2005), Cefquinome Sulfate in rabbits 0.75 ± 0.029 mg/kg (Qiang, *et al.,* 2013), Cefquinome in ducks 0.41 ± 0.04 mg/kg, (Yuan *et al.,*2011) and Ceftiofur in chickens 0.18 ± 0.05 mg/kg, (Shen, *et al.,* 2009).

The total body clearance (CL) of cefepime following a single i.v administration in the present study was (0.090 ± 0.002 (mg/kg)/(μg/ml)/h). This obtained result agrees with cefepime that reported in goats 0.098 ± 0.0004 mg/kg/h (El-Hewaity, 2014), neonatal foals and adult dogs 0.08±0.02; 0.13±0.04 mg/kg/h, (Gardner and Papich 2001) respectively, but disagreed with those reported for Cefepime in calves (86.1 ± 3.65; 1.81 ± 0.16; 1.1 ± 0.08 mg/kg/h (Ismail, 2005b; Patel et al.,2006; Joshi and Sharma 2007), goats 1.1 ± 0.54; 2.19 ± 0.15 mg/kg/h, (Bhavsar *et al.,* 2008; Prawez *et al.,* 2010) respectively, bull camels 0.04 ± 0.01 mg/kg/h, (Goudah *et al.,*2009) and sheep 2.48 ± 0.09 (Patel *et al.,*2010).

In comparison to other cephalosporin, The total body clearance (CL) of cefepime was agreed with that recorded in Ceftiofur in chickens (0.08 ± 0.03 mg/kg/h) (Shen *et al.,* 2009) and Cefquinome in swine (0.09 ± 0.03 mg/kg/h) (Xiao *et al.,* 2015) but disagrees with that recorded in cefquinome in broiler chickens 0.037; 0.048 ± 0.002; 0.35 ± 0.04 mg/kg/h, (Maha *et al.,* 2005; Xie *et al.,* 2013; El-Mahdy *et al.,* 2015) respectively, Ceftiofur in chickens 0.345 ± 0.009 mg/kg/h, (Dalia *et al.,*2015), Ceftiofur in rabbits 108 ± 10 mg/kg/h (Kamil, *et al.,* 2015), Cefquinome in black swans 0.13 ± 0.04 mg/kg/h, (Zhao *et al.,*2017), Cefquinome Sulfate in rabbits 0.357 ± 0.015 mg/kg/h, (Qiang *et al.,*2013) and Cefquinome in ducks 0.22 ± 0.02 mg/kg/h (Yuan *et al.,* 2011).

The elimination half-life ($t_{½\beta}$) of cefepime following a single IV. administration (4.6 ± 0.15h) agrees with that reported in goats 3.34 ± 0.12 h, (El-Hewaity,2014), calves 3.7 ± 0.16 h, (Patel *et al.,*2006) but disagrees with those reported in calves 2.67 ± 0.29 ; 2.38 ± 0.16 h, (Ismail, 2005b; Joshi and Sharma 2007) respectively, bull camels 2.0 ± 0.23 h, (Goudah *et al.,*2009), goats 1.86 ± 0.54 ; 2.71 ± 0.08 h (Bhavsar *et al.,*2008; (Prawez *et al.,*2010) respectively, sheep 2.54 ± 0.12 h (Patel *et al.,* 2010), ewes 1.76 ± 0.07 h, (Ismail, 2005a), rabbits 2.94 ± 0.16 h, (Abd El-Aty *et al.,* 2007) and neonatal foals and adult dogs 1.65 ± 0.10 h ; 1.09 ± 0.27 h, (Gardner and Papich 2001) respectively.

In comparison to other cephalosporin, the elimination half-life of cefepime in chicken agrees with those reported in Ceftiofur in chickens (4.23 ± 0.05 h, Amer *et al.,* 1998) and Cefquinome in chickens (4.92 h) (Maha *et al.,*

2005) but disagrees with those reported in Cefquinome in chickens (1.29 ± 0.10 h, Xie *et al.*, 2013) and also Ceftiofur in chickens (0.61 ± 0.56 h, Shen *et al.*, 2009), Ceftiofur in rabbits (2.75 ± 0.59 h, Kamil Uney *et al.*,2015),Cefquinome in black swans (1.69 ± 0.85 h, Zhao *et al.*,2017), Cefquinome Sulfate in rabbits 8.75 ± 0.85 h, (Qiang *et al.*,2013) and Cefquinome in ducks 1.57 ± 0.06 h, (Yuan *et al.*, 2011).

CONCLUSION:

The bioavailability of cefepime is excellent and its maintenance in a therapeutic concentration for a long time following intramuscular injection indicate that cefepime is suitable for intravenous and intramuscular administration (100 mg/kg every 24 h interval) for the treatment for various infections in chicken.

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