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PHARMACOKINETICS AND TISSUE RESIDUES OF CEFQUINOME IN NORMAL AND *SALMONELLA ENTRETIDIS* INFECTED CHICKENS

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ABSTRACT

The pharmacokinetics of cefquinome was studied following intravenous and intramuscular (single & repeated) injection. Cefquinome was assayed by High performance liquid chromatography method Following a single intravenous injection of 2 mg/kg body weight of cefquinome in normal chickens, plasma concentration-time curve was best described by a three compartments model with elimination half-life ($t_{0.5(\beta)}$ = 0.712 hour), volume of distribution (V_{dss}=389.23 ml/kg) and total clearance of the drug (Cl_{tot}= 0.048 ml/kg/min). Following a single intramuscular administration of 2 mg/kg body weight cefquinome in normal chickens, the peak plasma concentration (C_{max}) was 3.53 µg/ml was achieved at a maximum time (T_{max}) of 2.80 hour. The mean systemic bioavailability was 106.82%. The plasma concentrations of cefquinome following repeated intramuscular administration of 2 mg/kg body weight once daily for three consecutive days in normal and experimentally *Salmonella entretidis* infected chickens showed a lower significant values recorded in experimentally *Salmonella entretidis* infected chickens than in normal ones. Cefquinome showed accumulative behavior in plasma of chickens. Cefquinome was assayed in plasma, heart, liver, lung, kidney, breast muscle, thigh muscle and skin after 24, 48, 72, 96, 120 and144 hours post last dose following administration of 2 mg/kg body weight every 24 hours. Results of this study indicated that cefquinome was useful for treatment of *Salmonella entretidis* infections in chickens.

KEYWORDS: Pharmacokinetics, cefquinome, tissue residues, chickens.

INTRODUCTION

Cefquinome sulphate (Cobactan)® is used in veterinary practice solely not only for large and small animals but also for poultry against Gram-positive and Gram-negative bacteria. Cefquinome sulphate is a fourth – generation cephalosporin antibiotic effective against a broad spectrum of bacteria and is highly resistant to β-lactamases that are produced by most clinically important bacteria.[1] It is bactericidal by preventing the synthesis of the cell wall. The pharmacokinetics of cefquinome has been investigated in many animal species including dog, pig, piglet, calves, sheep, horse, rabbit and duck respectively.[2-7] However, this study was done to investigate several data about pharmacokinetics of cefquinome and tissue residues in chickens.

Therefore, the aim of present work was undertaken to study the pharmacokinetic parameters of cefquinome after intravenous and intramuscular injection in normal and experimentally *Salmonilla entritidis* infected chickens. Also, the bioavailability of cefquinome was calculated after intramuscular administration in normal chickens. Residues for cefquinome in chicken's tissues were studied in normal and *Salmonilla entritidis* infected chickens.

MATERIALS AND METHODS

Drug

Cefquinome was used in this study under the trade name (Cobactan®, sterile suspension for injection). Each ml of the suspension contains 29.64 mg Cefquinome sulphate which is equivalent to 25 mg cefquinome which was manufactured by Intervet, GmbH, Germany.

Experimental birds

Forty two clinically normal Harbard chickens of 6 - 8 weeks age were used in this investigation. The mean weights of chickens were 1.78 ± 0.0358kg. Chickens were obtained from poultry farms in El Giza government, Egypt. Chickens were feed balanced ration free from antibiotics for two weeks to ensure complete excretion of any drugs from their bodies. Water and feed free from antibacterial additives were *adlibitum*.

Experimental design

The chickens were divided into 3 groups:

Group 1

It included 6 normal chickens. Each bird was injected intravenously into the left wing vein with 2 mg cefquinome /kg b.wt. These chickens were left for 15 days after the intravenous injection to ensure complete excretion of cefquinome from their bodies. Then each chicken were injected intramuscularly into thigh muscle with 2 mg of cefquinome /kg b.wt to calculate bioavaibility of cefquinome in normal chickens.

Group 2

It included 18 chickens. Each bird was injected intramuscularly into thigh muscle with 2 mg cefquinome /kg. b.wt, once daily for three consecutive days. Plasma samples were taken, then tissue samples were taken for assaying drug residues after the last sampling.

Group 3

It included 18 chickens. Each bird was orally challenged with 1 ml of *Salmonella entritidis* suspension (*S. entritidis* strain of poultry origin was obtained from poultry department, animal health research institute- Dokki, Giza, Egypt) from a concentration of 1.3X 10^8 C.F.U/1ml according to Ishola and holt.[8] After the appearance of symptoms of bacteraemia as diarrhea, lack of appetite and ruffled feathers, each chicken was injected intramuscularly with 2 mg cefquinome /kg b.wt. every 24 hours for three consecutive days. After that plasma and tissue samples were taken for assaying of residues till disappearance of the drug from tissue.

Collection of samples

Blood samples

Blood samples were collected from either right or left wing vein following intravenous or intramuscular administration in normal and experimentally infected chickens. Blood samples are collected after 0.083, 0.167, 0.25, 0.5, 1, 2, 4, 8, 12 and 24 hours of administration in single study and after 0.25, 0.50, 1, 2, 4, 8, 12 and 24 hours in the first day, second, third dose in the same study in repeated intramuscular administration in normal and experimentally *Salmonella entritidis* infected chickens. Plasma samples were separated by centrifugation and stored in plastic vials until assay of cefquinome.

Tissue samples

Three chickens were slaughtered at the end of the third day of repeated intramuscular administration of cefquinome in normal and experimentally *Salmonella entritidis* infected

chickens, Tissue samples from blood, liver, kidney, lung, heart, breast muscle, thigh muscle, skin and blood were taken for assaying of residues of cefquinome at 24, 48, 72, 96, 120 and144 hours after the last sampling.

Analytical procedures

Calibration curve

The calibration curves of plasma and tissues were prepared with nine different concentrations between 0.039 and 10 µg/ml using blank chicken plasma and deionized water respectively. A calibration curve was obtained by plotting the cefquinome peak areas versus known concentrations. The equation was calculated by the least-squares method using linear regression. The minimum quantitative limit (LOQ) of the assay was 0.156 µg/ml and 0.039 µg/ml for plasma and deionized water respectively. The standard curve of cefquinome in chicken plasma and deionized water was linear between 0.156 and 10µg/ml, and 0.039 and 10 µg/ml respectively, the value of the correlation coefficient (r) was > 0.99**.**

Assay of blood samples

Cefquinome was assayed in plasma by HPLC method according to Maes *et al*.[9] This method for the quantification of the total concentration of cefquinome involved a deproteinization of the plasma and a back –extraction of acetonitrile with dichloromethane. 400 µl of acetonitrile was added to 200 µl of plasma for deproteinization and vortex – mixed. After centrifugation of the samples for 10 minutes at 10000 g, the supernatant was brought into a new Eppendorf vial. Then 600 µl of dichloromethane was added. After vortex-mixing for 15 seconds, the samples were again centrifuged at 10000 g, for 10 minutes. The top layer was transferred into an auto sampler vial.

Condition of High Performance Liquid Chromatography (HPLC)

The mobile phase consistence and chromatographic conditions are carried out according to Li et al.[2] The mobile phase was filtered and degassed. The injection volume of samples was 20 µl, the flow rate was fixed at 1.0 ml/min, column temperature was 30 ^{o}C and the ultra violet detector wavelength was set at 268 nm.

Assay of tissue samples

The extraction of cefquinome from chicken tissues was carried out according to Junza et al.[10] which is a modified method from Granelli and branzell.[11] and Chico et al.[12] Accurately weighed 4 grams of finely minced chicken tissues (used after thawing) placed into

50 ml polypropylene test tube. Then 10 ml methanol: water (80:20, v/v) was added and the mixture was centrifuged 3000rpm for 5 minutes. The suspended solution was decanted into 50 ml glass tube and nitrogen drying, then reconstituted with 2 ml of water. The mixture was filtered through 0.45 µm nylon membrane filter. The filtrate was put into auto-sampler vial and analyzed under the same chromatographic condition as plasma samples.

Pharmacokinetic analysis

The pharmacokinetic parameters were calculated by winnonlin program, version 1.1 and other parameters according to Baggot a & b.[13,14]

Statistical analysis

Data were expressed as mean ± S.E. The obtained data were statistically analyzed using student t-test Snedecor and Cochran.[15] to express the differences between groups and pharmacokinetic parameters.

RESULTS

Following a single intravenous injection of 2 mg/kg b.wt. in normal chickens, cefquinome could be detected therapeutically for 24 hours post intravenous injection. The plasma concentration-time curve of cefquinome following intravenous injection showed that the drug obeyed a three compartments open model. The disposition kinetics of cefquinome following a single intravenous and intramuscular administration were recorded in table (1) and showed in figure (1).

Intramuscular administration of 2 mg/kg.b.wt every 24 hours for three consecutive days in normal and *Salmonella entretidis* infected chickens revealed a lower significant plasma cefquinome concentration at all-time sampling in salmonella entretidis infected chickens than in normal chickens. The pharmacokinetic parameters of cefquinome after repeated intramuscular administration in normal chickens were compared to those in *Salmonella entretidis* infected chickens (Table 2).

Tissue samples from liver, kidney, lung, heart, breast muscle, thigh muscle, skin and blood were taken for assaying of residues of cefquinome at 24, 48, 72, 96, 120 and144 hours after the last Intramuscular administration of 2 mg/kg.b.wt from normal chickens were compared to those in *Salmonella entretidis* infected chickens (Table 3).

Table1: Pharmacokinetic parameters of cefquinome following a single intravenous and intramuscular injection of 2 mg/kg b.wt. in normal chickens (n=6).

Parameter	Unit	Intravenous $\bar{x}$ + SE	Intramuscular $\bar{x}$ + SE
Body weight	kg	1.64 ± 0.034	1.78 ± 0.036
C°	µg/ml	8.72 ± 0.458	9.21 ± 0.027
A	µg/ml	1.78 ± 0.079	4.40 ± 0.016
α	h^{-1}	0.917± 0.031	1.44 ± 0.011
$t_{0.5\,\alpha}$	h	0.768 ± 0.023	0.482 ± 0.004
B	µg/ml	5.24 ± 0.473	4.81 ± 0.016
β	h^{-1}	0.997± 0.067	0.936 ± 0.002
$t_{0.5\,\beta}$	h	0.712 ± 0.050	0.741 ± 0.001
C	µg/ml	1.70 ± 0.039	---
γ	h^{-1}	0.051± 0.003	---
$t_{0.5\gamma}$	h	13.88 ± 0.925	---
K_{12}	h^{-1}	0.713 ± 0.032	0.120 ± 0.002
K_{21}	h^{-1}	1.06 ± 0.011	0.142 ± 0.002
K_{13}	h^{-1}	0.631± 0.031	---
K_{31}	h^{-1}	0.272 ± 0.014	----
V_1	ml/kg	232.70 ± 12.48	----
V_2	ml/kg	156.49 ±10.11	----
V_3	ml/kg	578.21± 31.22	----
Vdss	ml/kg	389.23 ± 20.65	------
K_{10}	h^{-1}	0.212 ± 0.006	0.237 ± 0.002
Cl_{tot}	ml/kg/min	0.048 ± 0.002	0.832 ± 0.003
AUMC	$\mu g.h^2/ml$	675.03 ± 65.66	----
MRT	h	17.33 ±1.04	-----
$K_{(01)}$	h^{-1}	-------	0.423 ± 0.018
$t\ 0.5_{(k01)}$	h	-------	1.65 ± 0.062
$T\ max_{(calc.)}$	h	-------	2.80 ± 0.019
$C\ max_{(calc.)}$	µg/ml	-------	3.53 ± 0.015
$t_{0.5(k10)}$	h	------	2.93 ± 0.029
AUC	µg /ml/h	41.24 ± 1.40	38.79 ± 1.24

A, B and C Zero time plasma drug concentration intercepts of biphasic intravenous disposition curve. The coefficient B is based on the terminal exponential phase (µg/ml); α & β, Hybrid rate constant of biphasic intravenous disposition curve values of α and β are related to the slopes of distribution and elimination phase respectively, of biexponential drug disposition curve (h^{-1}); AUC, Total area under the plasma drug concentration versus time curve from t = 0 to t = α after administration of a single dose; C°, Drug concentration in the plasma at zero time immediately after a single intravenous injection (µg/ml); C max, Maximum plasma concentration of drug in blood after extra vascular administration (µg/ml); Cl tot, The total clearance of a drug, which represents the sum of all clearance processes in

Table 2: Pharmacokinetic parameters of cefquinome in normal (N) and experimentally *Salmonella entretidis* infected chickens (I) during repeated intramuscular injections of 2 mg/kg. b.wt. once daily for three consecutive days (n=6).

Parameter	unit	First day x̄ ±SE		Second day x̄ ±SE		Third day x̄ ±SE	
		N	I	N	I	N	I
Body weight	Kg	1.73 ± 0.025	1.90 ± 0.026***	1.75 ± 0.026	1.75 ± 0.028	1.79 ± 0.025	1.79 ± 0.024
C°	µg/ml	9.22 ± 0.020	5.69 ± 0.148***	12.26 ± 0.006	8.17 ± 0.212***	15.04 ± 0.024	10.35 ± 0.290***
A	µg/ml	4.40 ± 0.014	3.34 ± 0.084***	6.42 ± 0.009	4.23 ± 0.113***	7.73 ± 0.022	5.22 ± 0.125***
α	h^{-1}	1.44 ± 0.017	1.06 ± 0.025***	3.63 ± 0.013	0.493 ± 0.013***	0.610 ± 0.001	0.44 ± 0.011***
$t_{0.5(\alpha)}$	h	0.483 ± 0.006	0.654 ± 0.016***	0.191± 0.001	1.41± 0.035***	1.14 ± 0.003	1.58 ± 0.041***
$K_{(01)}$	h^{-1}	0.416 ± 0.020	0.317 ± 0.008***	0.384 ± 0.015	0.316 ± 0.008**	0.324 ± 0.001	0.314 ± 0.007
$t_{0.5(k01)}$	h	1.68 ± 0.074	2.19 ± 0.057***	1.82 ± 0.074	2.19 ± 0.059**	2.14 ± 0.008	2.21 ± 0.057
K_{12}	h^{-1}	0.119 ± 0.003	0.094 ± 0.003***	0.124 ± 0.001	0.152 ± 0.426	0.125 ± 0.001	0.196 ± 0.005***
K_{21}	h^{-1}	0.143 ± 0.003	0.043 ± 0.001***	0.126 ± 0.001	0.32 ± 0.008***	0.101± 0.003	0.022± 0.006***
T max (calc.)	h	2.78 ± 0.043	2.31 ± 0.065***	2.80 ± 0.009	2.28 ± 0.059***	3.03 ± 0.021	2.39 ± 0.060***
C max (calc.)	µg / ml	3.38 ± 0.186	1.55 ± 0.040***	3.90 ± 0.012	2.26 ± 0.054***	5.20 ± 0.012	2.43 ± 0.063***
B	µg/ml	4.82 ± 0.023	2.35 ± 0.061***	5.84 ± 0.015	3.94 ± 0.098***	7.31± 0.013	5.13± 0.113***
β	h^{-1}	0.935 ± 0.002	0.122 ± 0.003***	0.132 ± 0.001	0.132 ± 0.003	0.114 ± 0.001	0.151 ± 0.004***
$t_{0.5\beta}$	h	0.742 ± 0.002	5.67 ± 0.147***	5.24 ± 0.048	5.26 ± 0.126	6.11± 0.063	4.59± 0.119***
Cl_{tot}	L/kg/h	0.847± 0.014	0.714± 0.019***	0.623 ± 0.003	0.269 ± 0.007***	0.456 ± 0.004	0.486 ± 0.011*
AUC	µg/ml/h	38.35 ± 1.18	29.79 ± 0.834***	42.09 ± 0.424	39.71 ± 1.11	62.15 ± 0.476	43.57 ± 1.05***

the body (ml/kg /min); K_{12}, First – order transfer rate constant for drug distribution from central to peripheral compartment (h^{-1}); K_{21}, First order transfer rate constant for drug distribution from peripheral to central compartment (h^{-1}); K_{13}, First - order elimination rate constant for disappearance of drug from central compartment (h^{-1}); $t_{0.5(\alpha)}$, Distribution half - life (h); $t_{0.5(\beta)}$, Elimination half - life ; $t_{(0.5\gamma)}$ the terminal phases(h); t max, The time at which the maximum concentration of drug was reached after extravascular administration (h); V_{1c},

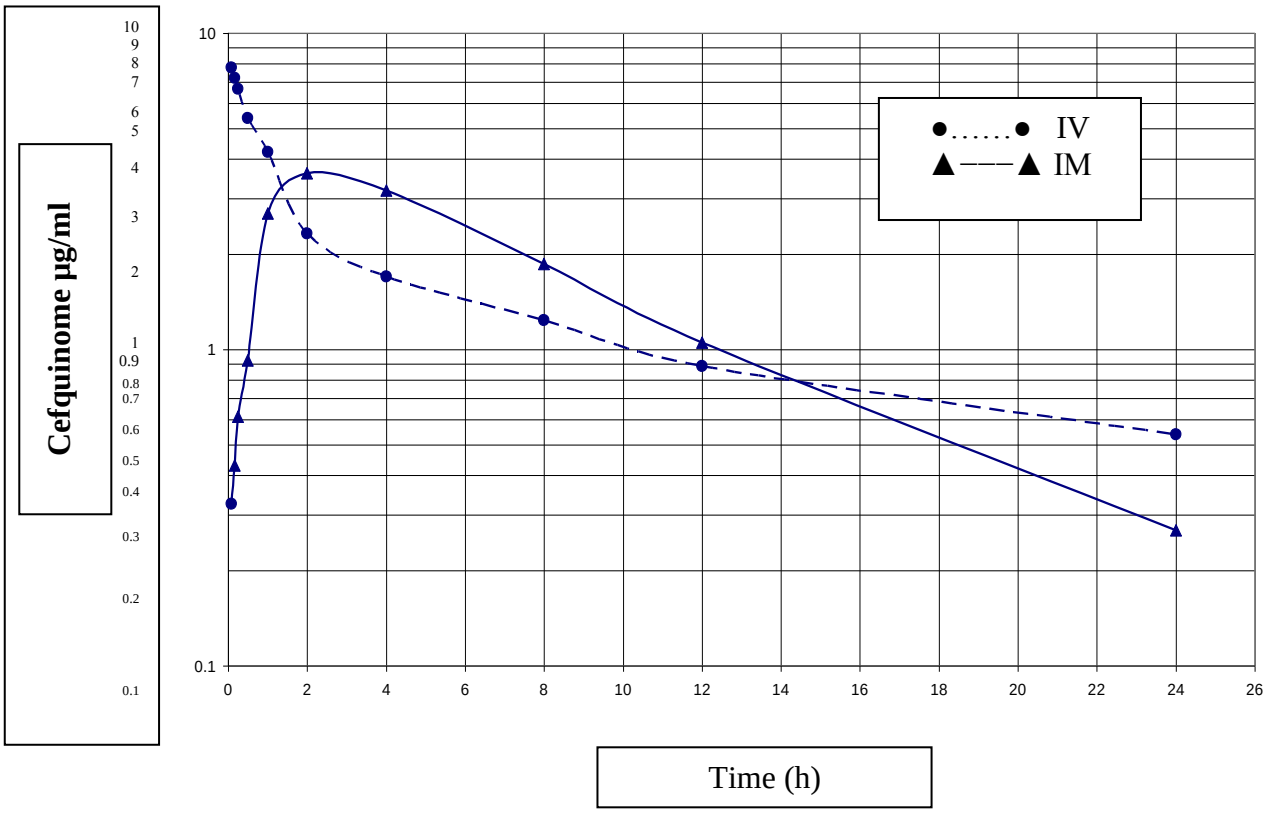
The apparent volume of central compartment (ml/kg); $V_{d(B)}$, The apparent volume of distribution Which calculated by extrapolation method (ml/kg); $V_{d(area)}$, The apparent volume of distribution which was calculated by the area method (ml/kg); V_{dss}, The apparent volume of distribution which was calculated by Steady - state method (ml/kg).

* P<0.05, ** P<0.01, *** P<0.001.

Table 3: Plasma (µg/ml) and tissue (µg/g) concentrations of cefquinome in normal (N) and experimentally *salmonella entretidis* infected chickens (I) during repeated intramuscular injections of 2 mg /kg.b.wt. once daily for three consecutive days (n=3).

Time / Tissue	After 24 hours		After 48 hours		After 72 hours		After 96 hours		After 120 hours	
	N	I	N	I	N	I	N	I	N	I
Blood (µg/ml)	0.69 ± 0.019	0.52 ± 0.008**	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Liver (µg/gm)	5.54 ± 0.047	3.96± 0.093***	4.5 ± 0.092	3.05± 0.117**	3.02 ± 0.084	2.19± 0.056*	1.96 ± 0.057	1.03 ± 0.05**	1.23 ±0.039	N.D
Kidney (µg/gm)	6.4 ± 0.176	4.6 ± 0.32*	5.31 ± 0.145	3.5 ± 0.286*	3.81 ± 0.088	2.50 ± 0.12*	2.88 ± 0.023	1.23 ± 0.056***	0.759 ± 0.026	N.D
Heart (µg/gm)	4.00 ± 0.088	2.31 ± 0.05***	3.20 ± 0.12	1.44 ± 0.051***	1.48 ± 0.103	0.86 ± 0.07**	0.26 ± 0.009	N.D	N.D	N.D
Lung (µg/gm)	4.66 ± 0.087	2.88 ± 0.042***	3.30 ± 0.115	1.70 ± 0.046***	2.05 ± 0.073	0.98 ± 0.084***	0.37 ± 0.039	N.D	N.D	N.D
Breast M. (µg/gm)	2.52 ± 0.70	0.49 ± 0.033*	1.32 ± 0.47	0.23 ± 0.012*	0.37 ± 0.10	N.D	N.D	N.D	N.D	N.D
Skin (µg/gm)	2.08 ± 0.145	0.41 ± 0.017***	0.72 ± 0.115	0.22 ± 0.02***	0.25 ± 0.101	N.D	N.D	N.D	N.D	N.D
Thigh M. (µg/gm)	2.28 ± 0.101	0.28 ± 0.003***	1.22 ± 0.24	0.15± 0.002*	0.324 ± 0.102	N.D	N.D	N.D	N.D	N.D

* P<0.05, ** P<0.01, *** P<0.001.



"Fig. 1" Semi logarithmic plots of plasma of cefquinome concentrations in normal chicken following a single intramuscular injection of 2 mg/kg bwt. (▲−−− ▲) in chicken previously given the same dose by a single intravenous injection (●……●) (n=6).

DISCUSSION

In the present investigation intravenous injection of 2 mg of cefquinome /kg B. wt. in normal chickens showed that the disposition best fitted a three compartments open model. The obtained result was disagreed with those reported previously for cefquinome in normal chickens given cefquinome intravenously at a dose of 1 mg /kg B. wt.[16] and normal chickens given cefquinome intravenously at a dose of 2 mg /kg B. wt.[17] and also disagreed with those reported for cefquinome in normal duck given cefquinome intravenously at a dose of 5 mg /kg B.wt.[6]

The V_{dss} is a clearance – independent volume of distribution that is used to calculate the drug amount in the body under equilibrium conditions. In this study, the V_{dss} for cefquinome was 0.389 l/kg, this obtained result was similar to those reported for cefquinome in normal chickens given cefquinome intravenously at a dose of 2 mg /kg B.wt (0.49 l/kg).[17] and also similar to those reported for cefquinome in normal chickens given cefquinome intravenously at a dose of 1 mg /kg B.wt (0.21 l/kg).[16] The limited cefquinome distribution to the tissue

could be explained by the less hydrophobic nature and low PKα values of 2.51 or 2.91 of the compound. Similar findings of cefquinome were also observed in young pigs, sows, calves and dog.[2, 7, 18]

Cefquinome was transferred from central to peripheral compartment at a slower rate k_{12}=0.713 h^{-1} than its passage from peripheral compartment to central compartment k_{21}=1.06 $h^{-1,}$ these values were similar to that reported for other cephalosporines as ceftiofur in chickens (k_{12}=0.274 h^{-1} and k_{21}=0.997 h^{-1}).[19]

The elimination half-life ($t_{0.5(\beta)}$) of cefquinome following a single intravenous injection was equal to 0.720 h which considered a relatively shorter $t_{0.5(\beta)}$ than in piglet, pigs, horses and even ducks.[2,20,5,6] The reported result agreed with $t_{0.5(\beta)}$ in normal chickens given cefquinome intravenously at a dose of 2 mg /kg B.wt.[17] also shorter than that of ceftiofur in healthy chickens (4.23 h).[21] but similar to that of ceftriaxone in young broilers (0.6-1.4 h).[22]

The rate of total body clearance Cl_{tot} of cefquinome following intravenous injection in the present study was 0.048 ml/kg/min this obtained result was agreed with those reported for cefquinome in normal chickens (0.037 l/kg/h).[16]

Following a single intramuscular administration of 2 mg cefquinome /kg.b.wt, the drug reached its maximum plasma concentrations after 2 hours of administration (3.60 µg/ml). Cefquinome could be detected in plasma in a therapeutic level (0.268 µg/ml) at 24 hours. The mean peak plasma concentrations of cefquinome (C_{max}) was (3.53 µg/ml).These values were similar to those recorded for cefquinome in normal chickens (3.76 µg/ml) and (3.04 µg/ml).[16,17] pigs (3.36 µg/ml).[20] piglets (4.01 µg/ml).[2] On contrast, the obtained results were lower than those reported in rabbits (8.87 µg/ml).[3] and higher than the values recorded in sheep (2.60 µg/ml).[4] The T_{max} was (2.80 h) which was longer than those recorded for cefquinome in normal chickens (0.64 h) and (0.25 h).[16,17] ducks (0.38 h).[6] rabbits (0.25 h).[3] piglets (0.28 h).[2] pigs (0.83 h).[20] Although the recorded results were similar to those recorded in sheep and goat (2.61 h) and (2.62 h).[23] respectively. Also the recorded result for T_{max} was similar to those obtained for other cephalosporines as ceftiofur in normal chickens (2.51 h).[19] These variations might be attributed to anatomical differences between species, healthy status and the dose administered in each case.

The bioavailability of cefquinome in normal chickens was 106.82%. This value referred to an excellent absorption of cefquinome from its site of intramuscular administration. This value was higher than those recorded for ducks (93.28%).[6] rabbits (95.23%).[3] piglets (95.13%).[2] pigs (93.87%).[20] and sheep (98.31%).[4]

The obtained blood levels of cefquinome in *Salmonella entritidis* infected chickens were significantly lower than those in normal chickens following repeated intramuscular administrations. These lower blood concentrations in infected chickens might be attributed to the higher penetrating power of cefquinome to the diseased tissues. The relative higher plasma concentrations of cefquinome after the last dose compared to the first doses indicated the accumulation of cefquinome in blood during multiple dosing at 24 hours intervals for three consecutive days These observations agreed with data reported by Dalia *et al.*[19] who found that progressive daily increase in the mean serum concentrations following the intramuscular injection of ceftiofur in chickens given a daily dose of 10 mg/kg b.wt. for five consecutive days. But the obtained result was inconsistent with that reported by El-Hewaity *et al.*[23] who found no significant differences between the pharmacokinetic parameters of cefquinome in sheep and goats after repeated intramuscular doses.

Although the medical use of cefquinome has not been extended to poultry, a few publications have reported the *in vitro* antibacterial activities of cefquinome against bacteria of high incidence in poultry farms and the determined MIC value was 0.195 µg/ml.[24] against salmonella spp. The antibacterial effect of cefquinome was time dependent.[25] which is a common feature of β-lactams, suggesting that the time for plasma concentrations to reach and exceed the MICs was a critical factor for determining its efficacy.[26] The obtained results revealed that the cefquinome plasma concentrations after intravenous and intramuscular injection were 0.538 µg/ml and 0.268 µg/ml respectively which were higher than MIC for 24h.

Repeated intramuscular administration of 2 mg cefquinome /kg b.wt every 24 hours for three consecutive days in normal and experimentally *Salmonella entretidis* infected chickens revealed that the drug could be detected only in blood till 24hours post last dose and muscles (breast & thigh muscles) with skin till 96 hours post last dose and till 120 hours post last administration in heart and lung, and till 144 hours post last administration in liver and kidney. Results showed that kidney and liver contained the highest drug concentrations (6.4, 5.54 µg/g respectively), while the lowest drug concentrations was found in thigh muscle and

skin (2.28, 2.08 µg/g respectively), 24 hours after the stoppage of drug medication. This result slightly agreed with that recorded for cefquinome in chickens that reported by Maha Gaber.[16] who found that the highest concentration was in kidneys, liver and lung suggesting that cefquinome is excreted mainly by the kidneys.[24,27]

CONCLUSION

The intramuscular bioavailability of cefquinome is excellent, so it is recommended to be used against *Salmonella entretidis* infection. Repeated intramuscular administrations of cefquinome (2 mg/kg b.wt.) once daily for three consecutive days would provide an effective concentration against *Salmonella entretidis* in broiler chickens. Treated chickens must not be slaughtered before 6 days from last dose of repeated administration of cefquinome to withdraw the drug residues from all tissues of treated chickens.

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