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PHARMACOKINETICS OF A SINGLE INTRAVENOUS INJECTION OF CEFQUINOME IN RABBITS

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ABSTRACT

The current study was carried out to investigate the pharmacokinetic profile of cefquinome following a single IV injection in ten New Zealand white rabbits (2-2.5 kg body weight). Cefquinome was injected intravenously (2mg/kg body weight) and blood samples were collected before drug administration and up to 24h after injection. Cefquinome plasma concentrations were measured using HPLC (high- performance liquid chromatography). The result showed that the plasma concentration of cefquinome was 9.13 ± 0.43 µg/mL at 5min post injection then declined gradually to 0.73 ± 0.18µg/mL after 2 hours. No cefquinome concentration could be detected at 4h post injection. The major pharmacokinetic parameters (Mean ± SEM) were T1/2 λz 0.52 ± 0.05h, AUC0-∞ 9.13 ± 0.63 h*µg/mL, Cl 239.25 ±14.61 mL/h/kg, Vz 170.89 ± 9.7 mL/kg and MRT0-∞ 0.75 ±0.06 h.

INTRODUCTION

Rabbits are considered a good source of animal proteins all over the world. Nutritionists recommend rabbit meat over other meats as it is easily digestible and has lower fat content. Furthermore, rabbits are fur producing animal **(Okerman, 1994).** For this economic importance, it is essential to protect the rabbit industry from many threatening diseases. This can be accomplished by using antibiotics.

Antibiotics have a crucial role in the treatment of infectious diseases. However, the use of these antibiotics may lead to the development of drug- resistant bacteria **(Ferguson, 2004);** therefore, there is a need for more effective antibiotics against these resistant strains.

Knowledge about the pharmacokinetic and pharmacodynamic characteristics of antibiotics are needed to determine the accurate dose required to destroy the invading bacteria and to prevent resistance development against these antibiotics **(Mouton, 2002).** Among the well-developed antibacterial agents being widely used in veterinary medicine are cephalosporins.

Cephalosporins are the largest family of antibiotics of the β-lactam group with bactericidal activity against a wide range of micro-organism **(Preston, 1992).** According to their spectrum of activity, they are grouped into 5 generations. Cefquinome is a 4th generation cephalosporins, which is used in most European countries. It differs from earlier cephalosporins by having a quaternary ammonium side chain, which enhances the outer membrane permeability and its effect against Gram- negative bacteria. It is highly stable to β- lactamases (**Bryskier, 1997; Murphy et al., 1994**).

The present work was performed to assess the pharmacokinetics of cefquinome following a single IV injection in rabbits. This may help for design of future studies to investigate the possibility for using cefquinome in rabbits.

MATERIALS AND METHODS

Drugs and chemicals:

Cefquinome sulphate (COBACTAN®, 4.5%) was provided from Intervet International Company, Cairo, Egypt.

HPLC analytical grade acetonitrile and methanol were obtained from Lab scan chemical industries, Poland. TFA (Tri flouroacetic acid) was purchased from Merck-Schuchardt, Germany.

Rabbits:

Ten healthy New Zealand white rabbits (2-2.5 kg) of both sexes procured from a private rabbitary were used in this experiment. The rabbits were housed individually in cages in ventilated room**.** All rabbits had free access to water and non-medicated pellet diet. After two weeks period of accommodation, all rabbits were received a single intravenous (IV) injection of cefquinome sulphate at 2 mg/kg into the marginal vein of one ear **(Hwang et al., 2011).**

Blood Sampling:

Blood samples of 2 ml each were collected from ear vein at time 0 (before cefquinome injection), and 5, 15, 30 min and 1, 2, 4, 6, 9, 12, 24 h post-cefquinome injection. The samples were collected in test tubes containing EDTA and centrifuged at 1,000 X g for 10 min. The plasma samples were collected and stored at-20 ^{o}Cuntil cefquinome analysis.

Preparation of samples

Cefquinome sulfate stock solution was prepared as 1mg/mL of cefquinome base. Cefquinome standards were made at 0, 0.09, 0.195, 0.391, 0.781, 1.56, 3.12, 6.25, 12.5, 25 µg/mL using blank rabbit plasma as a diluent. Cefquinome was extracted form plasma by precipitation of protein (**Uney et al., 2011).** A 200 µl aliquot of standard or plasma sample was placed in microcentrifuge tube and 400µL of methanol was added, after mixing for 10 seconds, it was centrifuged at 2000 X g for 10 min. After centrifugation, 300µL of clear supernatant was added to 150 µL of water and mixed, then it was analyzed by HPLC.

Analytical assay of cefquinome:

Plasma concentrations of cefquinome were estimated using a previously published HPLC method **(Uney et al., 2011).** The HPLC system (Thermo Scientific Company, USA) consists of pump, degasser and auto sampler. The separation was done on hypersil gold (C18 (5µm, 150 mm × 4.6 mm) column. The mobile phase was acetonitrile: TFA 0.1% at ratio of 50:50 with isocratic method and flow rate of 1mL/ min. The detection was performed with PDA detector set at 268 nm wave length. The injection volume was 50µl. Concentration of cefquinome in plasma samples was measured by the software (Chromo Quest 5.0). The retention time was 1.8 min.

Method Validation

The method was validated in terms of linearity, LOD (limit of detection), LOQ (Limit of quantification), recovery, specificity, stability, precision and accuracy.

Data analysis:

Data of plasma cefquinome concentration were presented as (Mean ± SEM). The pharmacokinetic parameters were determined using the non- compartmental model as previously described **(Hwang et al., 2011)** with WinNonlin 4.1 software, Pharsight, CA**.** The $AUC_{0-\infty}$ was calculated using the log-linear trapezoid rule.

RESULTS

There were no adverse effects following IV administration of cefquinome in rabbits.

Cefquinome standard concentration 0, 0.09, 0.195, 0.391, 0.781, 1.56, 3.12, 6.25, 12.5, 25 µg/mL and their corresponding peak response (area under peak) were illustrated in table (1) and shown in figure (1). Linearity is noticed within range of 0.09 and 25 µg/ml with a correlation coefficient (r^2 =0.996). The LOD and LOQ (The limit of detection and quantification) of cefquinome was 0.09µg/mL.

The mean plasma concentration of cefquinome after a single IV injection at a dose of 2mg/kg in rabbits were recorded in table (2) and Fig(2).

The recorded results showed that the plasma concentration of cefquinome was 9.13 ± 0.43µg/mL at 5 min post injection then declined gradually till reached 0.73 ± 0.18 µg/mL at 2 h post injection. No cefquinome concentration could be detected thereafter.

The pharmacokinetic parameters of cefquinome after IV administration were displayed in table (3). The drug was eliminated with $T_{1/2\ \lambda z}$ (elimination half- life) of 0.52 ± 0.05 h. The drug was cleared from the body at a rate of 239.25 ± 14.61 mL/h/kg. The $AUC_{0-\infty}$ was 9.13 ± 0.63 h*µg/mL and the $MRT_{0-\infty}$ (mean residence time) was 0.75 ± 0.06 h.

Table (1): Concentration of cefquinome standard (µg/ml) and their corresponding peak response (area under curve).

Peak response (Y)	Concentration(µg/ml)(X)
49613	0.09
98456	0.195
182863	0.391
323028	0.781
617245	1.561
922406	3.12
1661316	6.25
2785059	12.5
5487081	25

Table (2): Plasma concentration of cefquinome (µg/mL) after a single IV injection of (2mg/kg) in healthy rabbits. Data are presented as mean ± SEM. (n=10).

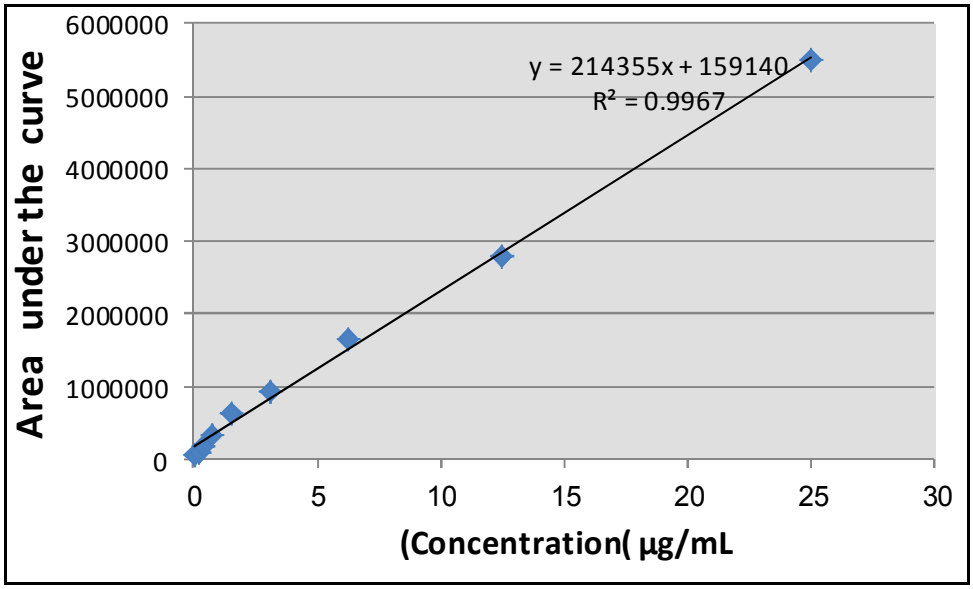
Time of sampling	Mean ± SEM
5 min	9.13 ± 0.43
15 min	7.06 ±0.30
30 min	5.33 ± 0.25
1h	3.48 ± 0.29
2h	0.73 ± 0.18
4h	ND*
6h	ND*

*ND = Non detected

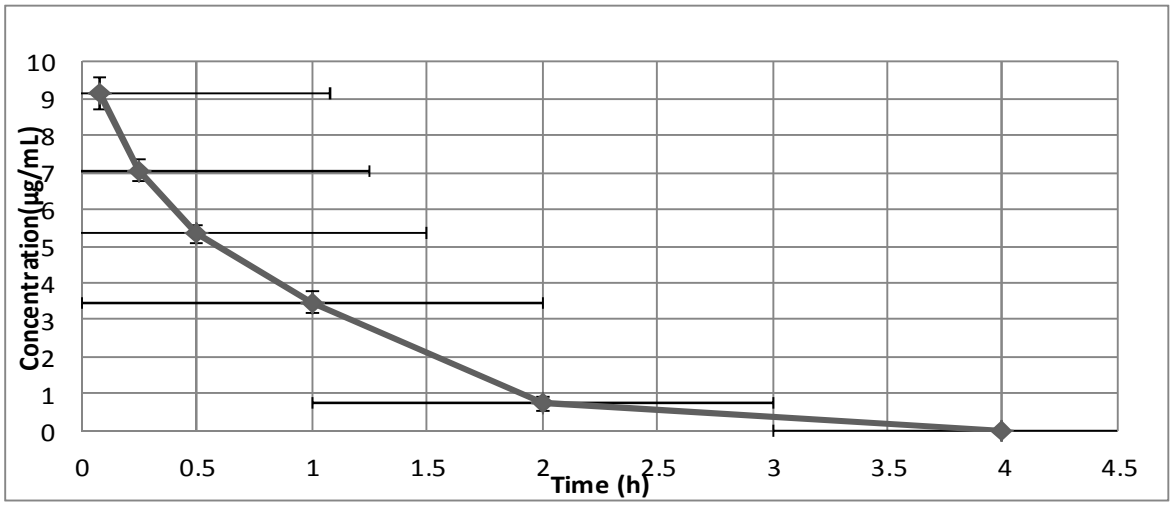
Table(3): Pharmacokinetics parameters of cefquinome after a single IV injection of 2mg/kg in healthy rabbits (n=10).

Parameter	Unit	Mean ± SEM
Λz	1/h	1.47 ± 0.16
$T_{1/2\ \lambda z}$	h	0.52 ± 0.05
$AUC_{0-\infty}$	h*µg/mL	9.13 ± 0.63
V z	mL/kg	170.89 ±9.7
Cl	mL/h/kg	239.25 ± 14.61
$MRT_{0-\infty}$	H	0.75 ±0.06

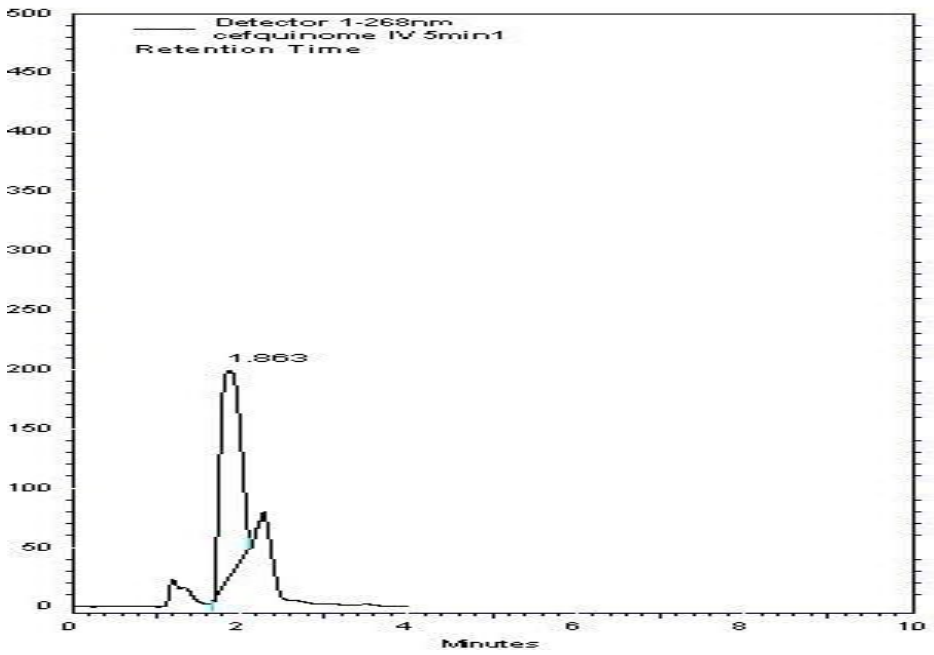
$T_{1/2}$ λz: Half-life of elimination phase; Λz: Rate constant associated with terminal phase;AUC0-∞: Area under the plasma concentration -time curve extrapolated to infinity; Vz: Volume of distribution of the drug observed; Cl: Clearance of drug observed; $MRT_{0-\infty}$: Mean residence time



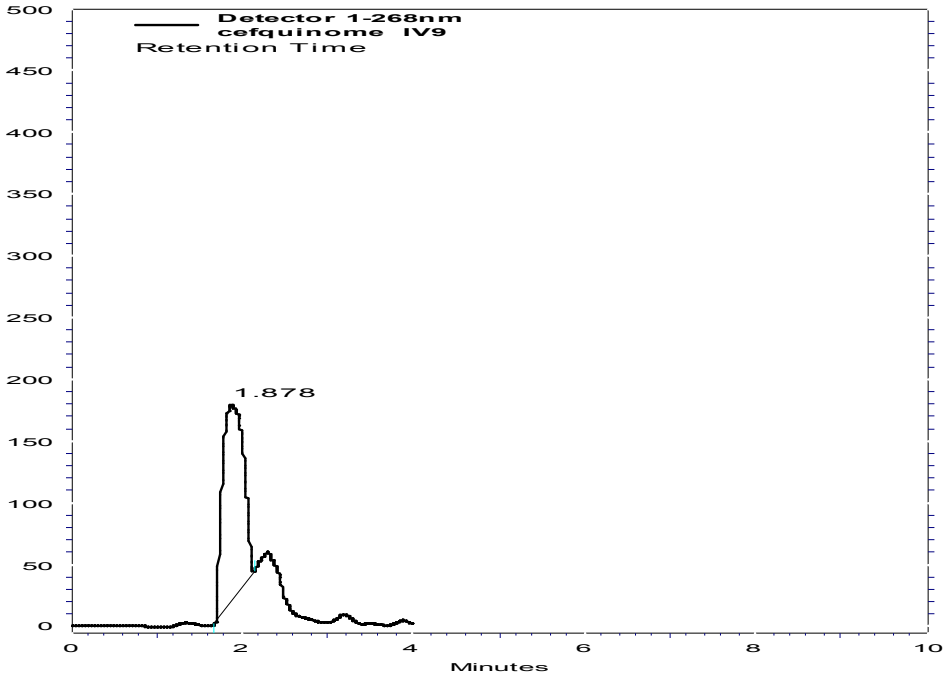
Fig(1): Standard curve of cefquinome in rabbit plasma



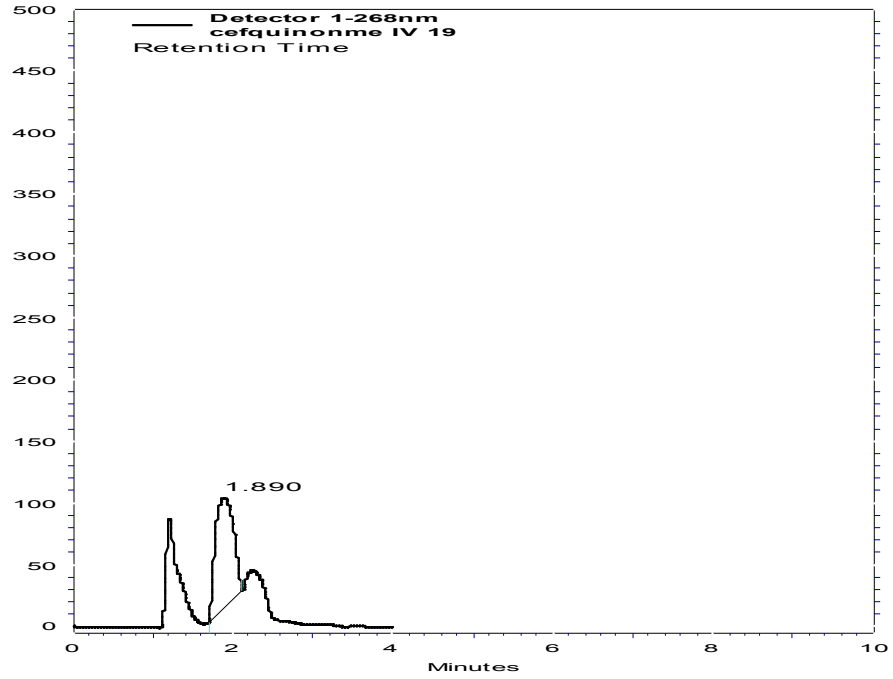
Fig(2): Plasma concentration-time profile of cefquinome following a single IV injection of 2 mg/kg in healthy rabbits



Fig(3): Chromatogram of cefquinome concentration in rabbit plasma sample at 5 min after a single IV injection of 2 mg/kg.



Fig(4): Chromatogram of cefquinome concentration in rabbit plasma sample at 15 min after a single IV injection of 2 mg/kg.



Fig(5): Chromatogram of cefquinome concentration in rabbit plasma sample at 30 min after a single IV injection of 2 mg/kg.

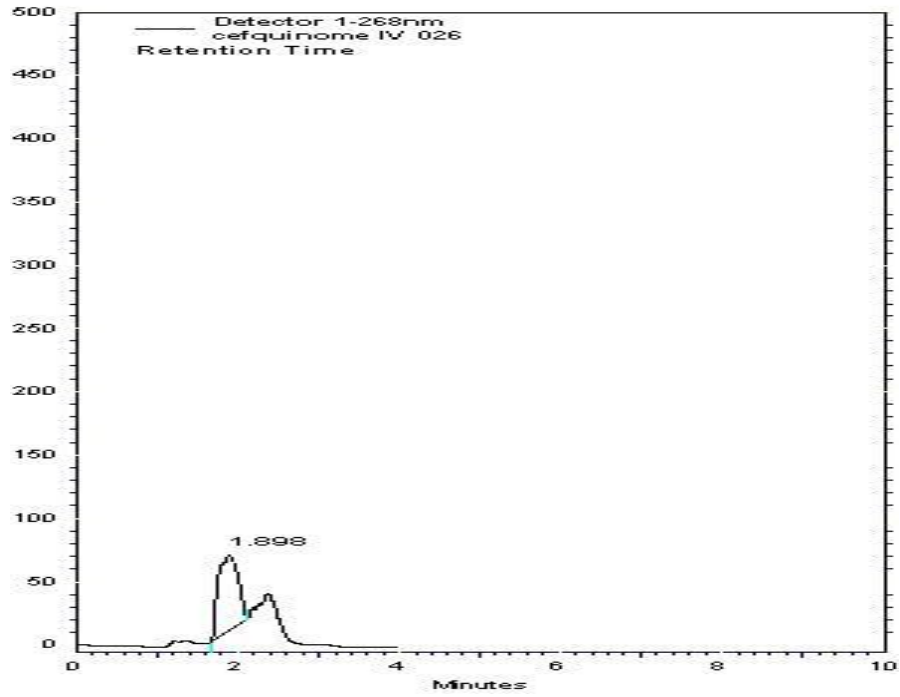


Fig (6): Chromatogram of cefquinome concentration in rabbit plasma sample at 1 h after a single IV injection of 2 mg/kg.

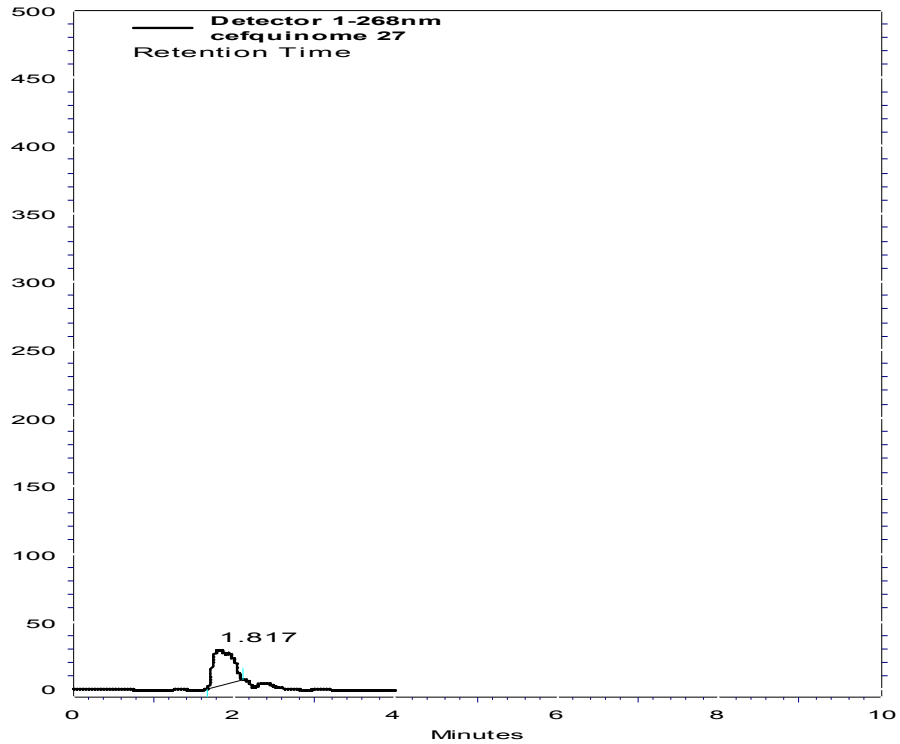


Fig (7): Chromatogram of cefquinome concentration in rabbit plasma sample at 2 h after a single IV injection of 2 mg/kg.

DISCUSION

Treating many animal species like mammals, birds, reptiles and fish is a unique challenge that encounter veterinarians. Veterinarians are responsible not only for selecting drugs but also for determining the precise dosage regimen for selected drugs. Determining the dosage regimen of remedies is a very hard task due to the variation in the expression of receptors, enzymes and signal transduction molecules between species **(Giorgi, 2012).** The differences between species in drug response can be attributed to either variations in drug pharmacokinetics or drug pharmacodynamics **(Riviere et al., 1997).** Therefore, using a drug in a new animal species required knowledge about its pharmacokinetic and pharmacodynamic features**.**

Fourth- generation cephalosporins are widely used for treatment of infections in animals all over the world. Cefquinome, an aminothiazolyl cephalosporin, is a 4th generation cephalosporin, being used solely in veterinary field **(Murphy et al., 1994).** It is active against a wide range of bacteria (as *Staphylococcus spp., Streptococcusspp., Pasteurella spp., Pseudomonas spp*., and members of the family *Enterobacteriacea)* **(Limbert et al., 1991; Shipgel et al., 1997 and Guerin-Faublee et al., 2003).**

The use of cefquinome for treatment of common infections in rabbits requires information on its pharmacokinetic characteristics to calculate the potential dosage regimen against susceptible microorganisms. Hence, the present study was carried out to determine pharmacokinetic profile of

cefquinome in rabbits following its IV injection in a single dose of 2 mg/kg body weight.

High performance liquid chromatography (HPLC) was used to estimate the concentration of cefquinome in plasma and tissue samples. One of the major advantages of HPLC over microbiological method is that the lower detection limit make it a highly sensitive instrument.

In the present study, we used an external standard bioanalytical method. While, the use of an external standard is a scientifically accurate method **(Dolan, 2012),** an internal standard is frequently used nowadays to correct for variability introduced during sample preparation. In this study, the QC (quality control) samples were made in rabbit plasma and had good recovery, precision and accuracy explaining that the method is perfectly worked, this indicate the precise analysis of cefquinome without using internal standard.

The area under the plasma concentration-time curve (AUC) explains the extent of drug absorption. In the present study, IV administration of cefquinome sulfate (2 mg/kg) to healthy rabbits produced an AUC of 9.13 h*µg/mL; similar value (9.20 h*µg/mL) was recorded after IV administration at 1 mg/kg in yellow cattle **(Shan et al., 2015),** while **Hwang et al. (2011)** reported a higher value (11.08 h *µg/mL) in rabbits after IV injection of 2 mg/kg.

In the current study, the volume of distribution of cefquinome in rabbits following IV administration was 0.171±0.009 L/kg. This result was in consistent with that of **Hwang et al., (2011)** who reported that the volume of distribution in rabbits given cefquinome intravenously at a dose of 2 mg/kg B.wt. was 0.21±0.03 L/kg. Also, it was similar to that reported in other animal species such as dogs (0.20-0.24 l/kg) and calves **(**0.23 L/kg) **(Limbert et al., 1991)**, goats (0.202 L/kg) **(Batzias, 2009)** and horses (0.21 L/kg) **(Winther et al., 2010)**. The limited cefquinome distribution to tissue in the various species could be attributed to the hydrophilic nature and low PK_{α} values of 2.51 of cefquinome **(CVMP, 1995 and Li et al., 2008).**

The elimination half-life ($T_{1/2\lambda z}$) of cefquinome in the present study (0.52 h) was lower than its corresponding value in rabbits administered the same dose IV (0.93 h) by **Hwang et al. (2011).** The total body clearance of cefquinome in rabbits (239.25 mL/h/kg) was higher than (180 mL/h/kg) that reported by **Hwang et al. (2011)**. These variations could be attributed to the use of a different rabbit breed and/or a different assay method. **Toutain et al., (2004)** reported that the pharmacokinetic feature of drugs may be different between breeds of the same species.

A shorter elimination half-life of cefquinome was observed in rabbits ($T_{1/2\lambda z}$0.52 h) than that in goats (5.86 h) **(Dumka et al., 2013),** pigs (2.32 h) (**Lu et al., 2007),** piglets (1.85 h) (**Li et al., 2008),** and sheep (0.78 h) **(Uney et al., 2011).** There could be several possibilities for the shorter $T_{1/2\lambda z}$ of cefquinome in rabbits, including the rate of plasma protein binding and the pH of the urine; however, the answer is still unknown. **Barot et al. (2013)** found that rabbits have the lowest plasma protein binding of cefpirome of 4% as compared to buffalo calves, goats, monkeys, rats, mice and dogs. The effect of plasma protein binding on pharmacokinetics can be noticeable for drugs with high protein binding **(Taverne et al., 2016)**. However, cefquinome has a low plasma protein binding (5-15%)

(CVMP, 1995) which makes it unlikely to be the cause. Another unlikely reason for shorter $T_{1/2\lambda z}$ in rabbits may be due to the pH of urine affecting the elimination pharmacokinetics **(Riviere et al., 1997).** Rabbits are herbivores and thus the urine is alkaline (pH 8-9) and cefquinome is acidic drug. This may lead to rapid elimination of cefquinome and consequently, shorter $T_{1/2\ \lambda z}$. However, goats also have alkaline urine and have longer $T_{1/2\lambda z}$ of cefquinome, which makes this reason less viable. One potential reason that may not easily be disproved is that rabbits have less body fat. This, in turn, may influence the volume of distribution of cefquinome lead to rapid elimination and shorter $T_{1/2\ \lambda z}$. To the best of our knowledge, the shorter elimination half-life of cefquinome in rabbits has not been discussed previously.

Cefquinome is a time-dependent antimicrobial **(Thomas et al., 2006).** The main parameter used to assess its activity is the amount of time that its concentration stays above the target bacterial MIC (minimum inhibitory concentration) (T > MIC). The published cefquinome MIC_{90} (0.06-0.39) for most pathogenic bacteria **(Limbert et al., 1991; Chin et al., 1992; Murphy et al., 1994; Orden et al., 1999; Deshpande et al., 2000; Sheldon et al., 2004; Thomas et al., 2006; Wallmann et al., 2006).** In this study, the concentration of cefquinome was not detected in the plasma at 4 h post administration of 2 mg/kg cefquinome sulfate. Therefore, 2 h dosing interval is required to treat sensitive bacteria in rabbits. This dose- regimen would be inconvenient. Therefore, further study is needed to determine whether a higher dose of cefquinome would yield a more convenient and practical dose- regimen in rabbits.

REFERENCES

Barot, D.K., Bhavsar, S.K., Sadariya, K.A., Soni, H.H., Patel, R.J., Patel, J.H. and Thaker, A.M. (2013): Pharmacokinetics of cefpirome following intravenous and intramuscular administration in goats. *Israel Journal of Veterinary Medicine*,**68**, 106-110

Batzias, G. C. (2009): Cefquinome and amoxicillin in goats: PK/PD integration. *Journal of Veterinary Pharmacology and Therapeutics* (Suppl.1), (Vol. 32, pp. 68-68).

Bryskier, A. (1997): New concepts in the field of cephalosporins: C-3′ quaternary ammonium cephems (Group IV). *Clinical Microbiology and Infection*, *3*(s1).1-6.

Chin, N. X., Gu, J. W., Fang, W., and Neu, H. C. (1992): In vitro activity of cefquinome, a new cephalosporin, compared with other cephalosporin antibiotics. *Diagnostic Microbiology and Infectious Disease*, *15*, 331–337.

CVMP (Committee for veterinary medicinal products) **(1995):** Cefquinome. Summary Report. EMEA/MRL/005/95.European Agency for the Evaluation of Medicinal Products, London, UK.

Deshpande, L., Pfaller, M. A., and Jones, R. N. (2000): In vitro activity of ceftiofur

tested against clinical isolates of *Escherichia coli* and *Klebsiella pneumonia* including extended spectrum β-lactamase producing strains. *International Journal of Antimicrobial Agents*, *15*, 271–275.

Dolan, J.W.(2012): When should internal standard be used. LCGC North America, 30,474-480.

Dumka, V. K., Dinakaran, V., Ranjan, B., and Rampal, S. (2013): Comparative pharmacokinetics of cefquinome following intravenous and intramuscular administration in goats. *Small Ruminant Research*, *113*(1), 273-277.

Ferguson, J. (2004): Antibiotic prescribing: how can emergence of antibiotic

resistance be delayed? Australian Prescriber, 27, 39–42.

Giorgi, M. (2012): Veterinary Pharmacology: Is it still pharmacology's cinderella. *Clin. Exp. Pharmacol*, *2*, 103.

Guérin-Faublée, V., Carret, G., and Houffschmitt, P. (2003): In vitro activity of 10 antimicrobial agents against bacteria isolated from cows with clinical mastitis. *The Veterinary Record*, *152*(15), 466-471.

Hwang, Y. H., Song, I. B., Lee, H. K., Kim, T. W., Kim, M. S., Lim, J. H., ... and Yun, H. I. (2011): Pharmacokinetics and bioavailability of cefquinome in rabbits following intravenous and intramuscular administration. *Journal of Veterinary Pharmacology and Therapeutics*, *34*(6), 618-620.

Li, X. B., Wu, W. X., Su, D.,Wang, Z. J., Jiang, H. Y., and Shen, J. Z. (2008): Pharmacokinetics and bioavailability of cefquinome in healthy piglets. *Journal of Veterinary Pharmacology and Therapeutics*, *31*(6), 523-527.

Limbert, M., Isert, D., Klesel, N., Markus, A., Seeger, K., Seibert, G. and Schrinner, E. (1991): Antibacterial activities in vitro and in vivo and pharmacokinetics of cefquinome (HR 111V), a new broad-spectrum cephalosporin. *Antimicrobial Agents and Chemotherapy*, *35*(1), 14-19.

Lu, G. F., Yang, H. F., Li, Y. J., and JIANG, C. M. (2007): Pharmacokinetics of cefquinome sulfate suspension in pigs. *Journal-Yangzhou University Agricultural and Life sciences Edition, 28*(4), 18.

Mouton, J. W. (2002): Standardization of pharmacokinetic/pharmacodynamic (PK/PD) terminology for anti-infective drugs. International Journal of Antimicrobial Agents, 19(4), 355–358.

Murphy, S. P., Erwin, M. E., & Jones, R. N. (1994): Cefquinome (HR 111V) in vitro evaluation of a broad-spectrum cephalosporin indicated for infections in animals. *Diagnostic microbiology and infectious disease*, *20*(1), 49-55.

Okerman, L. (1994): Disease of domestic Rabbit" library of Vet. Med.2nd Ed. Black well science Ltd, U.K.

Orden, J. A., Ruiz, S. Q., Garcia, J. A., Cid, S. D., and Fuente, R. (1999): In

vitro activities of cephalosporins and quinolones against *Escherichia coli* strains isolated from diarrheic dairy calves. *Antimicrobial Agents and Chemotherapy*, *43*, 510–513.

Preston, D.A. (1992): Overview of the development of a new class of the β-lactam antibiotics: the carbacephems. The Antimicrobic Newsletter, 8, 58-63.

Riviere, J.E., Martin-Jimenez, T., Sundlof, S.F. and Craigmill, A. L. (1997): Interspecies allometric analysis of the comparative pharmacokinetics of 44 drugs across veterinary and laboratory animal species. *Journal of Veterinary*

Pharmacology and Therapeutics, **20**, 453-463.

Shan, Q., Zhu, X., Liu, S., Bai, Y., Ma, L., Yin, Y., and Zheng, G. (2015): Pharmacokinetics of cefquinome in tilapia (Oreochromisniloticus) after a single intramuscular or intraperitoneal administration. *Journal of Veterinary Pharmacology and Therapeutics*, *38*(6), 601-605.

Sheldon, I. M., Bushnell, M., Montgomery, J., and Rycroft, A. N. (2004): Minimum inhibitory concentrations of some antimicrobial drugs against bacteria causing uterine infections in cattle. *Veterinary Record*,*155*, 383–387.

Shpigel, N. Y., Levin, D., Winkler, M., Saran, A., Ziv, G., and Böttner, A. (1997): Efficacy of cefquinome for treatment of cows with mastitis experimentally induced using Escherichia coli. *Journal of Dairy Science*, *80*(2), 318-323.

Taverne, F. J., van Geijlswijk, I. M., Heederik, D. J., Wagenaar, J. A., and Mouton, J. W. (2016): Modelling concentrations of antimicrobial drugs: comparative pharmacokinetics of cephalosporin antimicrobials and accuracy of allometric scaling in food-producing and companion animals. *BMC Veterinary Research*, *12*(1), 185.

Thomas, E., Thomas, V., and Wilhelm, C. (2006): Antibacterial activity of cefquinome against equine bacterial pathogens. *Veterinary Microbiology*,*115*, 140–147.

Toutain P.L. and Bousquet-Melou A. (2004): Volumes of distribution. J. Vet. Pharmacol. Ther., 27:441-453.

Uney, K., Altan, F., and Elmas, M. (2011): Development and validation of a high-performance liquid chromatography method for determination of cefquinome concentrations in sheep plasma and its application to pharmacokinetic studies. *Antimicrobial Agents and Chemotherapy*, *55*(2), 854-859.

Wallmann, J., Bottner, A., Goossens, L., Hafez, H. M., Hartmann, K., Kaspar, H., … Werckenthin, C. (2006): Results of an inter-laboratory test on antimicrobial susceptibility testing of bacteria from animals by broth microdilution. *International Journal of Antimicrobial Agents*, *27*,482–490.

Winther, L., Baptiste, K.E. and Friis, C. (2010): Antimicrobial disposition in pulmonary epithelial lining fluid of horses, Part III. Cefquinome. Journal of Veterinary Pharmacology and Therapeutics, 1365-2885.

الملخص العربي

دراسة المسار الحركى للسيفوكينوم فى الارانب بعد الحقن بجرعه واحده فى الوريد

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اجريت هذه التجربة على عدد ١٠ ارانب لدراسة المسار الحركى للمضاد الحيوى السيفوكينوم- أحد مركبات الجيل الرابع من مجموعة السيفالوسبورن- بعد اعطاؤه عن طريق الحقن الوريدى بجرعه واحده(٢ مجم/ كجم من وزن الجسم) فى الارانب.

تم جمع عينات من الدم فى انابيب تحتوى على مضاد للتخثر من كل الارانب عن طريق الوريد الاذنى بعد ٥،١٥،٣٠ دقيقه ، ساعه، ساعتين، ٤ ساعات، ٦ ساعات، ٩ ساعات، ١٢ ساعه، ٢٤ ساعه بعد اعطاء الدواء، تم فصل البلازما وحفظها لحين فحصها باستخدام جهاز الفصل الكروماتوجرافى العالى الاداء.

وقد كانت أهم النتائج التى توصلت اليها الدراسة ما يلى:

١- سجل أعلى تركيز لعقار السيفوكينوم فى مصل الارانب بعد اعطاؤه جرعه واحده بعد ٥ دقائق وكان ٩,١٣±٠,٤٣ ميكرجرام/ ميلليتر وقد قل التركيز تدريجيا حتى وصل الى٠,٧٣ ± ٠,١٨ ميكروجرام/ ميلليتر بعد ساعتين ثم اختفى من الدم بعد ٤ ساعات.

٢- فترة نصف عمر اخراج الدواء هى ٠,٥٢± ٠,٠٥ ساعه. وكانت قيم المساحة تحت منحنى التركيز ($AUC_{0-\infty}$) هى ٩,١٣±٠,٦٣. كما كان متوسط زمن بقاء (MRT0-∞) دواء السيفوكينوم هو٠,٧٥±٠,٠٦ساعه.

٣- يجب اعطاء السيفوكينوم للأرانب بجرعة ٢ مجم/كجم كل ساعتين لكى يحقق كفاءة ضد البكتريا وهذه الجرعة تعتبر غير مناسبه ولهذا نحن بحاجه الى اجراء دراسات اخرى باستخدام جرعات اكبر للوصول الى الجرعة العلاجية المناسبة.