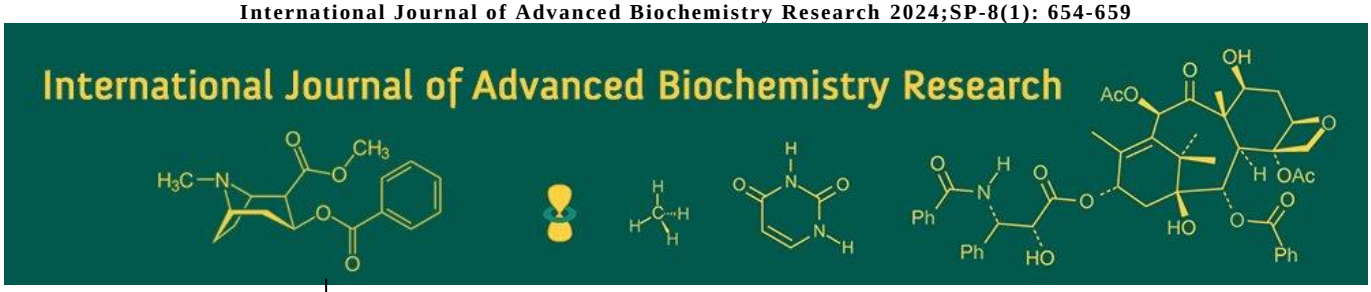

ISSN Print: 2617-4693
ISSN Online: 2617-4707
IJABR 2024; SP-8(1): 654-659
www.biochemjournal.com
Received: 02-11-2023
Accepted: 06-12-2023

M Champawat
Department of Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India

LN Sankhala
Department of Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India

P Sharma
Department of Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India

A Gaur
Department of Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India

Hemvati
Department of Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India

Corresponding Author:
M Champawat
Department of Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan, India

Effect of flunixin co-administration on pharmacokinetics of cefquinome following intramuscular administration in goats

M Champawat, LN Sankhala, P Sharma, A Gaur and Hemvati

DOI: https://doi.org/10.33545/26174693.2024.v8.i1Si.389

Abstract
Cefquinome, a fourth generation cephalosporin, having broad spectrum of activity against Gram-positive and Gram-negative bacteria and developed exclusively for veterinary use. Non-steroidal antiinflammatory drugs (NSAIDs) are commonly used with antimicrobial therapy in veterinary practice for the treatment of infectious diseases. The present study was taken to investigate the disposition kinetics of cefquinome at the dose rate of 2 mg kg^{-1} body weight and the effect of flunixin when co-administered intravenously at the dose rate of 2.2 mg kg^{-1} body weight on disposition kinetics of cefquinome in goats. Plasma concentrations were determined by microbiological assay method using MTCC equivalent (MTCC 1541) of Micrococcus luteus (ATCC 9341) as the test organism. Following intramuscular administration of cefquinome, the plasma concentration time profile was best described by one compartment open model. In the present study, following intramuscular administration of cefquinome in flunixin pretreated goats, the peak plasma concentration (Cmax) was observed 4.48±0.19 µg ml^{-1} which was not significantly higher and almost comparable to the Cmax 5.1±0.51 µg ml^{-1} observed in only cefquinome administered goats. Following co-administration of cefquinome with flunixin, no significant changes were observed in most of the pharmacokinetic parameters of cefquinome, except elimination half-life (t1/2β) and volume of distribution (Vdarea) which were significantly increased. The integration of pharmacokinetic and pharmacodynamics parameters suggested that the cefquinome at the dose rate of 2 mg kg^{-1} body weight intramuscularly can be administered with flunixin to treat bacterial infections with inflammatory conditions in goats.

Keywords: Disposition kinetic, microbiological assay, compartmental open model

Introduction
Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly indicated as an adjunct to antimicrobial therapy in veterinary practice for the treatment of infectious diseases. Cefquinome is a fourth generation aminothiazolyl cephalosporin with broad spectrum of activity against Gram-positive and Gram-negative bacteria, developed exclusively for veterinary use including food animals (Murphy *et al*., 1994) [16]. It has a broad spectrum of antibacterial activity with time dependent bactericidal effect, as shown by β-lactam antibiotics (Thomas *et al*., 2006) [7]. In ruminants, the use of NSAIDs is associated with the treatment of pain, mastitis, pneumonia and inflammatory conditions (Pugh, 1991; Ziv, 1992; Deleforge *et al*., 1994) [20, 32, 7]. Amongst Non-steroidal anti-inflammatory drugs, Flunixin, used for analgesic, antiphlogistic and antipyretic purposes in a variety of mammalian species. Flunixin acts via analgesic and anti-inflammatory mechanisms. Analgesic actions may involve blocking pain impulse generation via a peripheral action by inhibition of the synthesis of prostaglandins and possibly inhibition of the synthesis or actions of other substances, which sensitize pain receptors to mechanical or chemical stimulation. Flunixin may act peripherally in inflammed tissue, probably by inhibiting the enzyme cyclooxygenase to decrease the formation of precursors of prostaglandins, and possibly by inhibiting other local mediators of the inflammatory response (Lees and Higgins, 1985) [14]. Various pharmacokinetic interactions between antimicrobials and NSAIDs have been described (Singh *et al*., 2008; Dumka *et al*., 2010; Abo-El-Sooud and AL- Anati, 2011; Ranjan *et al*., 2011; Ali and Mohiuddin, 2012; Patel *et al*., 2012a; Patel *et al*., 2012b) [24, 8, 1, 22, 4, 17, 18].

There is less information available on the influence of the co-administration of flunixin on the pharmacokinetics of cefquinome in animals. So, the present study was conducted to investigate the influence of flunixin on the pharmacokinetics of cefquinome in goats.

Materials and Methods

Experimental animals

The study was conducted on five apparently healthy Marwari male goats of 8 – 10 month of age (Weight between 25-30 kilograms). The experiment was conducted at the Livestock Research Station, Kodamdesar, Rajasthan University of Veterinary and Animal science, Bikaner. During this period they were subjected to clinical examination in order to exclude the possibility of any disease. The animals were then housed in separate pens and maintained on concentrate, green fodder and water adlibitum. The experimental protocol for general procedure and use of animals for conducting the present study has been reviewed and approved by the Institutional Animal Ethics Committee (IAEC) and submitted to CPCSEA.

Drugs and test organism

Cefquinome sulphate injection (25 mg ml -1;Cobactan 2.5%, MSD Healthcare) was purchased from local market. Flunixin injection (Flunimeg, Zydus Animal Health) was purchased from local market. MTCC equivalent (MTCC 1541) of Micrococcus luteus (ATCC 9341) as the test organism used in microbiological assay work for the present study, were procured from institute of Microbial Technology (IMTECH), Chandigarh, India.

Experimental protocol

The study was carried out in cross-over design, with a minimum of 15 days of washout period. Cefquinome sulphate injection was administered intramuscularly on gluteal muscle at the dose rate of 2 mg kg^{-1} body weight. The dosage level of cefquinome employed in the present study was comparable to the dose of cefquinome used by previous workers in goat (Dumka *et al*., 2013) [9] and sheep (Uney *et al*., 2011) [28]. Blood samples were collected in test tubes containing EDTA, immediately before administration of cefquinome (0 h) and at 0.08, 0.16, 0.33, 0.5, 0.75, 1.0, 1.5, 2, 4, 6, 8, 10, 12 and 24 h after administration of the drug. Following a washout period of 21 days, Cefquinome sulphate injection at the dose rate of 2 mg kg^{-1} body weight intramuscularly and flunixin injection at the dose rate of 2.2 mg kg^{-1} body weight intravenously were administered simultaneously. Blood samples were collected before administration of cefquinome and flunixin (0 h) and at same time intervals mentioned above after administration of the drugs. Blood samples were centrifuged at 3000 rpm for 15 min to separate the plasma. Plasma samples were stored at −20 °C until assayed.

Drug bioassay

Cefquinome concentrations in plasma samples were estimated by microbiological assay method using MTCC equivalent (MTCC 1541) of Micrococcus luteus (ATCC 9341) (Arret *et al*., 1971; El Badawy *et al*., 2015) [5, 10]. Six equidistant identical (6.0±0.1 mm) wells were punched in the solidified media in petri plates using a punching machine. The wells were charged with the test samples/cefquinome standard in triplicates. The petri plates were incubated at 30 degree C for 24 h. In test sample plates, three alternate wells out of six were filled with reference concentration of the drug which gives a clear zone of inhibition of 16-18 mm so as to minimize the plate to plate variation in zones of inhibition. Zones of inhibition were measured using a Vernier calliper and the mean of triplicate samples was taken and compared with that of reference standard(s) to obtain the concentration of cefquinome in test samples. Minimum sensitivity of the assay method was 0.20 µg ml^{-1}.

Pharmacokinetic analysis

The plasma cefquinome concentration time profile of each animal following intramuscular administration of cefquinome alone and when co administered with flunixin were used to determine the pharmacokinetic variables describing the absorption, distribution and elimination characteristics of cefquinome in goats. To determine the different disposition kinetic variables, plasma drug concentration–time data were analyzed by employing the compartmental (Gibaldi and Perrier, 2007; Baggot, 2001) [12, 6] and non-compartmental (Yamoka *et al*., 1978; Gibaldi and Perrier, 2007) [30, 12] pharmacokinetic models.

Statistical analysis of data

The data generated in the present studies were subjected to statistical analysis by employing student's 't' test using MS Excel (2007).

Results and Discussion

No adverse effects or toxic manifestations were observed to cefquinome IM injection alone or co-administered with flunixin in goats. Plasma cefquinome concentrations at different time intervals following intramuscular administration of cefquinome alone and co-administered with flunixin in goats is presented as semi logarithmic plot in Figure-1 and Figure-2 respectively. Following intramuscular administration of cefquinome at the dose rate of 2 mg kg^{-1} body weight in goats, the plasma concentration of cefquinome was quickly raised well above minimum inhibitory concentration (MIC) against pathogens (Ahmad *et al*., 2015) and found 0.72±0.28 µg ml^{-1} was observed at 0.08 h after drug administration. The peak plasma concentration (Cmax) was observed 5.10±0.51 µg ml^{-1} at 1.00 h post administration of cefquinome intramuscularly in goats at 2 mg kg^{-1} body weight. In the present study, the higher peak plasma concentration (Cmax) was observed than in 4.36±0.10 µg ml^{-1} at 0.75 h in sheep (Rana *et al*., 2015) [21], 4.84±0.23 µg ml^{-1} at 1.50 h in goat (Dumka *et al*., 2013) [9], 4.01±0.57 µg ml^{-1} in piglets (Li *et al*., 2008) [15], and 4.83 µg ml^{-1} at 0.43 h in dog (Zhou *et al*., 2015) [33] administered cefquinome intramuscularly at the same dose. However, the Higher value of the Cmax like 9.05±0.06 µg ml^{-1} at 0.95 h in rabbits (Shalaby *et al*., 2014) [23] and 9.38±1.69 µg ml^{-1} at 0.38 h in duck (Yuan *et al*., 2011) [31]. Cmax achieved earlier in sheep (Rana *et al*., 2015) [21], dog (Zhou *et al*., 2015) [33], rabbit (Shalaby *et al*., 2014) [23] and duck (Yuan *et al*., 2011) [31]. While later in goats (Dumka *et al*., 2013) [9] and camel (AlTaher, 2010) [3].

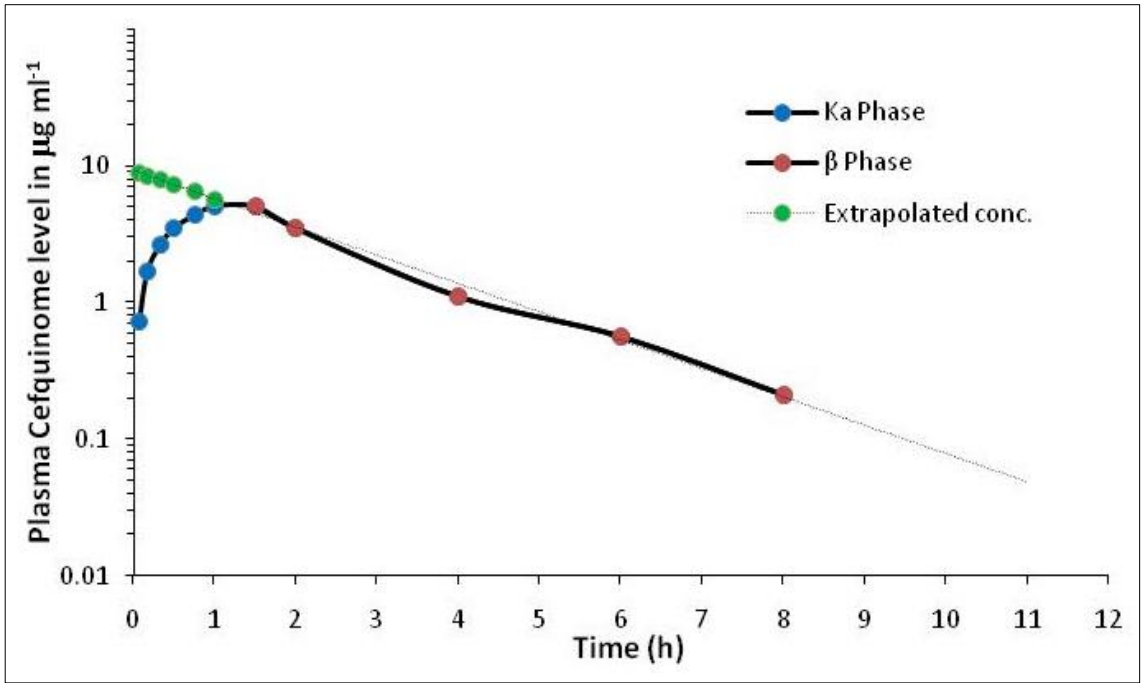

Fig 1: Semilogarithmic plot of mean (n=5) plasma concentration versus time curve of cefquinome given intramuscularly in goats at the dose of 2 mg kg^{-1} body weight. The points reflecting elimination / β phase (=) and absorption / Ka phase (=) are shown on the curve. The extrapolated plasma concentration values (=) obtained from the method of residuals are also reflected along with the linear regression line going up to zero time intercept

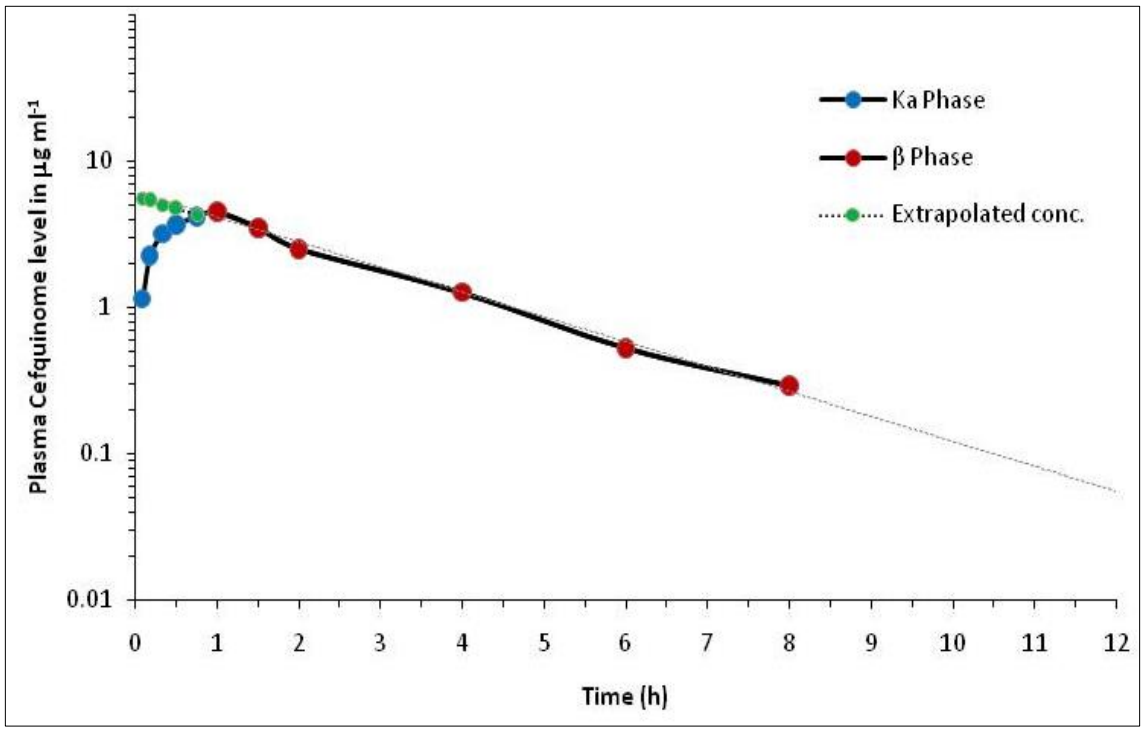

Fig 2: Semilogarithmic plot of mean (n=5) plasma concentration versus time curve of cefquinome given intramuscularly at the dose of 2 mg kg^{-1} body weight to goats co-administered flunixin intravenously at the dose of 2.2 mg kg^{-1} body weight. The points reflecting elimination / β phase (=) and absorption / Kaphase (=) are shown on the curve. The extrapolated plasma concentration values (=) obtained from the method of residuals are also reflected along with the linear regression line going up to zero time intercept

In the present study, following intramuscular administration of cefquinome in flunixin pretreated goats, the peak plasma concentration (Cmax) was observed 4.48±0.19 µg ml^{-1} which was not significantly higher and almost comparable to the Cmax 5.1±0.51 µg ml^{-1} observed in only cefquinome administered goats. Similarly, no significant alteration in Cmax of cefquinome following co-administration with meloxicam in sheep was found by Tiwari *et al.* (2015) [25] which supports the present study. However in contrast to present study, a significant increase in peak plasma concentration (Cmax) of cefquinome was observed in tolfenamic acid co-administrated sheep (4.73±0.05 µg ml^{-1}) as compared to cefquinome alone treated sheep (4.36±0.10 µg ml^{-1}) by Rana *et al.* (2015) [21]. Likewise EL-Hewaity (2014) [11] also reported a significant increase in Cmax in goats following cefepime coadministration with flunixin as

compared to cefepime alone treated goats. Similarly, Cmax of cefepime was also found higher in ketoprofen administered sheep than Cmax observed in cefepime alone (Patel *et al*., 2012b) [18]. Likewise Singh *et al*. (2008) [24] also reported significantly higher Cmax value of ceftriaxone given with the paracetamol as compared to ceftriaxone alone treated animals. Whereas the lower value of Cmax of ceftriaxone was found when coadministered with paracetamol (19±0.32 µg ml^{-1}) in comparison ceftriaxone alone treated goats (45.6±0.19 µg ml^{-1}) in findings of Jimoh *et al*. (2011) [13] The disposition kinetics of cefquinome in goats could be described by one compartment open model considering the plasma concentration versus time semi logarithmic curve. Disposition of cefquinome has been described with one compartment open model in goats (Dumka *et al*., 2013) [9], camel (Al-Taher, 2010) [3], dog (Zhou *et al*., 2015) [33] but two- compartment open model in sheep (Tohamy, 2011) [27], piglets (Li *et al*., 2008) [15] and duck (Yuan *et al*., 2011) [31]. The comparative pharmacokinetic parameters were generated following intramuscular administration of cefquinome alone and co-administered with flunixin and subjected to statistical analysis using students's 't' test using MS Excel (2007), are depicted in the table 1.

Table 1: Pharmacokinetic parameters of cefquinome (2 mg kg^{-1}) following a single dose, intramuscular administration alone and in combination with flunixin (2.2 mg kg^{-1}) treated goats (Mean±SE, n = 5) employing one compartment open model

Pharmacokinetic parameters	Units	Mean±S.E.	
		Cefquinome alone	Cefquinome with Flunixin
Ka	h-1	2.67±0.52	3.49±0.31
t1/2Ka	h	0.29±0.04	0.21±0.02
β	h-1	0.47±0.01	0.38±0.02**
t1/2β	h	1.48±0.04	1.85±0.12*
Cmax(obs)	µg ml^{-1}	5.39±0.38	4.57±0.19
tmax(obs)	h	1.15±0.15	0.95±0.05
AUC	µg ml^{-1}h	14.44±0.82	13.67±0.57
AUMC	µg ml^{-1}h2	38.19±2.45	34.35±4.13
MRT	h	2.64±0.07	2.56±0.36
Vdarea	L kg^{-1}	0.29±0.02	0.42±0.042**
Cl'	ml kg^{-1}h-1	140.33±8.09	147.41±6.44

NS: Non-significant;*: Significant at P< 0.01 (99% confidence level)

Following intramuscular administration of cefquinome with flunixin in goats most of the pharmacokinetic parameters were not significantly altered in comparison to goats administered cefquinome alone except elimination half-life (t1/2β) and volume of distribution (Vdarea).

The absorption half-life (t1/2ka) of cefquinome co administration with flunixin in goats was found to be 0.21±0.02 h which is almost similar to t1/2ka 0.29±0.04 h observed in cefquinome alone, suggesting co-administration of flunixin does not alter the absorption of cefquinome in goats. Similarly, no singnificant alteration was observed in absorption half-life (t1/2ka) of cefquinome (0.15±0.01h to 0.16±0.01 h) in goats when co-administration with the meloxicam (Tiwari *et al*., 2015) [25] which was in support to present study. Likewise, El-hewaity (2014) [11] also reported no significant alteration in t1/2ka of cefepime (0.25±0.02 h to 0.28±0.03 h) in goats when co-administration with the flunixin. Also no significant alteration in t1/2ka of cefepime (0.27±0.05 h to 0.18±0.02 h) was observed when coadminstered with ketoprofen in goats (Patel *et al*., 2012a) [17]. Similar result was found regarding absorption half-life (t1/2ka) of cefepime (0.17±0.01 h to 0.18±0.01 h) in cow calves when co-administered with ketoprofen (Patil *et al*., 2012) [19]. Likewise, Singh *et al*. (2008) [24] also reported no singnificant alteration in t1/2ka value of ceftriaxone (0.23±0.03 h to 0.21±0.02 h) in cross bred calves when co-administration with paracetamol which also support the present study.

In contrast to present study, Jimoh *et al*. (2011) [13] reported significant decrease in the t1/2ka value of ceftriaxone in goats co-administered with paracetamol (0.17±0.02 h) in comparison to given ceftriaxone (0.51±0.004h) alone. Rana *et al*. (2015) [21] also reported significant decrease in t1/2ka of cefquinome co-administration with flunixin (0.26±0.01) in comparison to given cefquinome (0.61±0.10 h) alone. However, the significant increase t1/2ka value of cefepime (0.16±0.01 h to 0.22±.001 h) was reported in sheep when co-administered with ketoprofen (Patel *et al*., 2012b) [18].

The elimination half-life (t1/2β) of cefquinome coadministration with flunixin in goats was found 1.85±0.12 h which is significantly higher to the t1/2β 1.48±0.04 h observed in cefquinome alone treated goats. Similar significant increase in the value of t1/2β of ceftizoxime was found in cross bred calves when co-administration with paracetamol (4.08±0.54 h) in comparison to given cetizoxime alone (1.44±0.12 h) by Singh *et al*. (2008) [24] which supports the present study.

Similarly, Jimoh *et al*. (2011) [13] also reported the higher t1/2β in goat given ceftriaxone co-administration with paracetamol (5.34±1.85 h) in comparison to given ceftriaxone (0.58±0.02 h) alone which also supports the present study. However, no significant alteration found in t1/2β of cefquinome coadministration with tolfenamic acid (9.00±0.51 h) in comparison to given cefquinome alone (12.29±2.62 h) by Rana *et al*. (2015) [21]. Significant alteration in t1/2β of cefepime was also not found in calves when co-administrated with ketoprofen (5.36±0.19 h) in comparision to given cefepime (5.15±0.09 h) alone (Patil *et al*., 2012) [19]. No alteration in t1/2β of cefquinome in goats was found when coadministration with meloxicam (1.60±0.05 h) in comparison to given cefquinome (1.75±0.08 h) alone (Tiwari *et al*., 2015) [25]. Similarly, no significant alteration in t1/2β of cefepime was found in goats when co-administration with ketoprofen (5.32±0.19 h) in comparison to given cefepime (5.13±0.2 h) alone (Patel *et al*., 2012a) [17].

The area under the curve (AUC) of cefquinome when coadministration with flunixin in goats was 13.67±0.57 µg ml^{-1} h which is almost similar to the AUC observed in goats given cefquinome alone 14.44±0.82 µg ml^{-1} h. Similarly no significant alteration was found in the AUC of cefquinome in sheep when co-administration with tolfenamic acid (17.52±0.14 µg ml^{-1} h) in comparison to cefquinome given (16.65±0.57 µg ml^{-1} h) alone (Rana *et al*., 2015) [21]. Likewise, no significant alteration found in the AUC of cefquinome in goats when co-administration with meloxicam (17.16±0.14 µg ml^{-1} h) in comparison to cefquinome given (18.49±0.74 µg ml^{-1} h) alone (Tiwari *et al*., 2015) [25]. Similarly Patel *et al*. (2012a) [17] also found no significant alteration in the AUC of cefepime in goats when co-administration with the ketoprofen (149.75±13.1 µg ml^{-1} h) in comparison to cefepime given (139.08±10.28 µg ml^{-1} h) alone. Patel *et al*. (2012b) [18] also found no significant

alteration in sheep when cefepime coadministered with ketoprofen (162.37±14.47 µg ml^{-1} h) in comparison to cefepime given (153.63±10.16 µg ml^{-1} h) alone.

However in contrast to present study, Jimoh *et al*. (2011) [13] reported lower value of AUC in goats when ceftriaxone coadministered with paracetamol (42.14±2.11 µg ml^{-1} h) in comparison to ceftriaxone given alone (144.10±1.71 µg ml^{-1} h). While higher value of AUC in cross bred calves observed ceftizoxime co-administered with paracetamol (74.10±2.01 µg ml^{-1} h) in comparison to cetioxime given (39.2±2.09 µg ml^{-1} h) alone (Singh *et al*., 2008) [24].

The area under the moment curve (AUMC) of cefquinome when co-administration with flunixin in goats was (34.35±4.13 µg ml^{-1} h 2) which is comparably similar to the AUMC (38.19±2.45 µg ml^{-1} h 2) observed in cefquinome alone. Similarly, no alteration found in the AUMC of cefquinome in goats when co-administration with the meloxicam (41.44±1.27 µg ml^{-1} h 2) in comparison to cefquinome given (41.89±1.37 µg ml^{-1} h 2) alone (Tiwari *et al*., 2015) [25]. No significant alteration of AUMC were observed in calves when cefepime co-administered with ketoprofen (338.77±23.35 µg ml^{-1} h 2) in comparision to cefepime given (367.26±36 µg ml^{-1} h 2) alone (Patil *et al*., 2012) [19]. Patel *et al*. (2012b) [18] also reported no significant alteration in AUMC in sheep when cefepime coadministered with ketoprofen (1013.18±116.63 µg ml^{-1} h 2) in comparison to cefepime given alone (921.31±84.21 µg ml^{-1} h 2). Similar result regarding AUMC was observed in goats when cefepime co-administered with ketoprofen (999.19±92.37 µg ml^{-1} h 2) in comparison to cefepime given (880.54±121.27 µg ml^{-1} h 2) alone (Patel *et al*., 2012a). Whereas the AUMC significantly decrease in goats when ceftriaxone co-administered with paracetamol (313.50±6.156 µg ml^{-1} h 2) in comparison to ceftriaxone given (167.14±54.34 µg ml^{-1} h 2) alone (Jimoh *et al*., 2011) [13].

In present study, there is no significant alteration in mean residence time (MRT) of cefquinome when co-administration with flunixin in goats 2.56±0.36 h in comparison to the MRT 2.64±0.07 h observed in cefquinome alone. Similarly, no alteration found in the MRT of cefquinome in goats when coadministration with the meloxicam (2.44±0.06 to 2.25±0.05 h) in comparison to cefquinome given alone (Tiwari *et al*., 2015) [25] supporting present study. Likewise, no significant alteration of MRT were observed in calves when cefepime coadministered with ketoprofen in comparison to cefepime given alone (Patil *et al*., 2012) [19]. Patel *et al*. (2012b) [18] also reported no significant alteration in MRT values in sheep when cefepime coadministered with ketoprofen (6.17±0.19 h) in comparision to cefepime given (5.95±0.18) alone. Similar result regarding MRT was observed in goats when cefepime coadministered with ketoprofen (6.70±0.15 h) in comparision to cefepime given (5.97±0.53 h) alone (Patel *et al*., 2012a) [17]. Similarly no significant alteration of MRT were observed in sheep when cefquinome co-administered with tolfenamic acid (7.27±0.27 h) in comparision to cefquinome given (9.14±1.83 h) alone (Rana *et al*., 2015) [21].

The apparent volume of distribution (Vdarea) of cefquinome coadministered with flunixin in goats was 0.42±0.042 L kg^{-1} which is significantly higher to the volume of distribution of 0.29±0.02 L kg^{-1} observed in cefquinome alone. Significant alteration observed in the volume of distribution (Vdarea) of ceftizoxime following co-administration of meloxicam in sheep (Ranjan *et al*., 2011) [22]. However, Jimoh *et al*. (2011) [13] reported significant decrease in volume of distribution of ceftriaxone co-administered with paracetamol in goats. Whereas no significant alteration found in volume of distribution in goats when cefepime co-administered with ketoprofen (Patel *et al*., 2012a) [17]. Rana *et al*. (2015) [21] also found no significant changes in the volume of distribution when cefquinome co-administered with tolfenamic acid (1.48±0.08 L kg^{-1}) in comparison to cefquinome given alone (2.07±0.36 L kg^{-1}).

The apparent clearance (Cl') of cefquinome co-administered with flunixin in goats was 147.41±6.44 ml kg^{-1} h-1 which is almost similar to 140.33±8.09 ml kg^{-1} h-1 observed in cefquinome alone.

Conclusion

The finding of the present study showed that no significant alteration in the major pharmacokinetic parameters of cefquinome were observed following its concomitant administration with flunixin in goats so flunixin at the dose rate of 2.2 mg kg^{-1} body weight intravenously can be successfully co-administered with cefquinome at the dose rate of 2 mg kg^{-1} intramuscular for combating bacterial infections with an inflammatory condition in goats. Flunixin coadministered with cefquinome in goats, cause no alteration in most of the pharmacokinetics parameters of cefquinome, requiring no revision of dosage regimen. As per general recommendation that T>MIC should be atleast 50% of the dosage interval for optimum bactericidal effect, a 12 h dosing interval at the rate of dose rate 2 mg kg^{-1} by intramuscular is recommended.

Acknowledgement

We thank Incharge, Livestock Research Station, Kodamdesar, Rajasthan University of Veterinary and Animal science, Bikaner and Prinncipal Investigator, AIRCP on genetic improvement of marwari goats in farmers' flocks, CVAS, Bikaner for their support during the research work by providing physical facility and animals to carry out this work.

References

1. Abo-EL-Sooud K, AL-Anati L. Pharmacokinetic study of flunixin and its interaction with enrofloxacin after intramuscular administration in calves. Vet. World. 2011;4(10):449-454.
2. Ahmad I, Hao H, Huang L, Sanders P, Wang X, Chen D *et al*. Integration of PK/PD for dose optimization of cefquinome against Staphylococcus aureus causing septicaemia in cattle. Front. Microbiol. 2015;6:588.
3. Al-Taher AY. Pharmacokinetics of cefquinome in camels. J Anim. Vet. Adv. 2010;9:848-852.
4. Ali T, Mohiuddin OA. *In vitro* interaction study of cefixime with diclofenac sodium, flurbiprofen, mefenamic acid and tiaprofenic acid. J Chem. Pharm. Res. 2012;4(6):2911-2918.
5. Arret B, Johnoson DP, Kirshaum A. Outline of details of microbiological assay of antibiotics: second revision. J Pharm. Sci. 1971;60:1489-1694.
6. Baggot JD. The Physiological Basis of Veterinary Clinical Pharmacology. Blackwell Science Ltd., UK; c2001. ISBN 0-632-05744-0.

7. Deleforge J, Thomas E, Davot JL, Boisrame B. A field evaluation of the efficacy of tolfenamic acid and oxytetracycline in the treatment of bovine respiratory disease. J Vet. Pharmacol. Ther. 1994;17:43-47.
8. Dumka VK, Sandhu HS, Rajput N. Plasma levels, pharmacokinetics and dosage regimen of intravenously administered galtifloxacin in buffalo calves (*Bubalus bubalis*) on coadministration with meloxicam. Brazilian J Vet. Res. Anim. Sci. 2010;47:461-467.
9. Dumka VK, Dinakaran V, Ranjan B, Rampal S. Comparative pharmacokinetics of cefquinome following intravenous and intramuscular administration in goats. Small Rumin. Res. 2013;113(1):273-277.
10. El-Badawy SA, Amer AM, Kamel GM, Eldeib KM, Constable PD. Comparative pharmacokinetics using a microbiological assay and high-performance liquid chromatography following intravenous administration of cefquinome in lactating goats with and without experimentally induced Staphylococcus aureus mastitis. Small Rumin. Res. 2015;133:67-76.
11. El-Hewaity M, Abd El Latif A, Soliman A, Aboubakr M. Comparative pharmacokinetics of cefquinome (Cobactan 2.5%) following repeated intramuscular administrations in sheep and goats. J Vet. Med; c2014. p. 1-5.
12. Gibaldi M, Perrier D. Pharmacokinetics. Edn 2, Marcel Dekker, New York (USA); c2007.
13. Jimoh OA, Bello SO, Etuk EU, Adeleye SA, Igbokwe VU. Comparative pharmacokinetics of intramuscular ceftriaxone co-administered with acetaminophen in healthy and infected Sokoto red goats. Int. J Pharmacol. 2011;7(5):623-628.
14. Lees P, Higgins AJ. Clinical pharmacology and therapeutic uses of nonsteroidal anti-inflammatory drugs in the horse. Equine Vet. J. 1985;17:83-96.
15. Li XB, Wu WX, Su D, Wang ZJ, Jiang HY, Shen JZ. Pharmacokinetics and bioavailability of cefquinome in healthy piglets. J Vet. Pharmacol. Ther. 2008;31(6):523-527.
16. Murphy SP, Erwin ME, Jones RN. Cefquinome (HR 111V). *In vitro* evaluation of a broad-spectrum cephalosporin indicated for infections in animals. Diagn. Microbiol. Infect. Dis. 1994;20:49-55.
17. Patel HB, Patel NN, Patel SD, Dewda S, Patel JH, Bhavsar SK, *et al*. Effect of ketoprofen co-administration or febrile state on pharmacokinetic of cefepime in goats. J Animals Vet. Adv. 2012a;7(1):46-53.
18. Patel NN, Patel HB, Patel SD, Patel JH, Bhavsar SK, Thaker AM. Effect of ketoprofen co-administration on febrile state on pharmacokinetic of cefepime in sheep. Vet. Arhiv. 2012b;82(5):473-481.
19. Patil AJ, Bhavsar SK, Patel HB, Patel NN, Patel SD, Dewda S, *et al*. Effect of Ketoprofen co-administration on Pharmacokinetics of Cefepime in Cow Calves. Intern. J Vet. Science. 2012;1(2):72-75.
20. Pugh DM. Allergy, anaphylaxis, inflammation, pain and shock, In: Brander, G.C., Pugh, D.M., Bywater, R.J., Jenkins, W.L. (Eds.), Vet. Applied Pharmacol. Therap. 5th ed. Bailliere Tindall, London; c1991. p. 124-148.
21. Rana MP, Sadariya KA, Thaker AM. Effect of tolfenamic acid co-administration on pharmacokinetics of cefquinome following intramuscular administration in sheep. Veterinarskiarhiv. 2015;85(3):283-292.
22. Ranjan A, Roy BK, Prasad R, Ranjan R. Meloxicam cotreatment alters pharmacokinetics of ceftizoxime in febrile sheep. Indian J Anim. Sci. 2011;81(2):152-154.
23. Shalaby MA, Goudah A, Gihan MK, Hassan AS. Disposition kinetics of cefquinome in healthy rabbits following intramuscular and oral administration. World J Pharm. Pharm. Sci. 2014;4(1):263-274.
24. Singh R, Chaudhary RK, Dumka VK. Influence of paracetamol on the pharmacokinetics and dosage regimen of ceftizoxime in cross bred calves. Israel J Vet. Med. 2008;63(3):72-76.
25. Tiwari S, Bhavsar S, Patel R, Patel LJ, Varia R, Modi FD *et al*. Effect of meloxicam co-administration and febrile state on pharmacokinetic of cefquinome in goats. J Vet. Pharmacol. Toxicol. 2015;14(2, 8):11.
26. Thomas E, Thomas V, Wilhelm C. Antibacterial activity of cefquinome against equine bacterial pathogens. J Vet. Microb. 2006;115:140-147.
27. Tohamy MA. Age-related intramuscular pharmacokinetics of cefquinome in sheep. Small Rumin. Res. 2011;99(1):72-76.
28. Uney K, Altan F, Elmas M. Development and validation of a high-performance liquid chromatography method for determination of cefquinome concentrations in sheep plasma and its application to pharmacokinetic studies. Antimicrob. Agents Chemother. 2011;55(2):854-859.
29. Winther L, Baptiste KE, Friis C. Antimicrobial disposition in pulmonary epithelial lining fluid of horses, part iii. Cefquinome. J Vet. Pharmacol. Therap. 2011;34(5):482-486.
30. Yamoka K, Nakaqawa T, Uno T. Statistical moments in pharmacokinetics. J Pharmacokinet. Biopharm. 1978;6(6):547-58.
31. Yuan L, Sun J, Wang R, Sun L, Zhu L, Luo Xand Liu Y. Pharmacokinetics and bioavailability of cefquinome in healthy ducks. Am. J Vet. Res. 2011;72(1):122-126.
32. Ziv G. Treatment of peracute and acute mastitis. In: Hinchcliff, K.W., Jernigan, A.D. (Eds.), The Veterinary Clinics of North America-Applied Pharmacology and Therapeutics II.W.B. Saunders Co, Philadelphia; c1992. p. 1- 15.
33. Zhou YF, Zhao DH, Yu Y, Yang X, Shi W, Peng YB, *et al*. Pharmacokinetics, bioavailability and PK/PD relationship of cefquinome for Escherichia coli in Beagle dogs. J Vet. Pharmacol Therap. 2015;38:543-548.