Int.J.Curr.Microbiol.App.Sci (2018) Special Issue-7: 5200-5204

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Special Issue-7 pp. 5200-5204**
Journal homepage: http://www.ijcmas.com

Original Research Article

Comparative Pharmacokinetics of Three Commercial Preparations of 10% Enrofloxacin Following Intravenous Administration in Goats

V. K. Gond[1*] and C. Jayachandran[2]

[1]Department of Animal Husbandry and Veterinary Science, T.C.A., Dholi, Muzaffarpur- 843121, India
[2]Department of veterinary pharmacology and Toxicology B.V. C., Patna-14, India
**Corresponding author*

A B S T R A C T

A comparative pharmacokinetics of three brands of 10% enrofloxacin was determined after single intravenous (I.V) administrations @5mg/kg body weight to 5 healthy female goats. Blood was sampled before and after drug administration at 0.042, 0.083, 0.125, 0.333, 0.5, 0.75 min and 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 24h. Plasma enrofloxacin concentrations were analyzed by using high performance liquid chromatography (HPLC) method. The drug was present significantly at lower concentration in brand II (8.26 ± 0.66) as compared to brand I (17.08 ± 1.92 $\mu g.ml^{-1}$) and Brand III (14.11 ± 2.91) at 0.042 h. Similarly, brand II shows lower concentrations upto 0.333 h and at 3 & 24 h. The drug maintained its therapeutic concentration (≥ 0.125 $\mu g.ml^{-1}$) up to 12 h in brand I and II while it was present up to 24 h in brand III. The distribution half-life ($t_{1/2}$ α) were noted with mean value of 0.33 ± 0.08, 0.46 ± 0.03, 1.12 ± 0.63 h of Brand I,II,III respectively. The elimination half-life ($t_{1/2}$ β) were noted 3.93 ± 0.46, 4.04 ± 0.53, 4.56 ± 1.2 h of Brand I, II, III respectively. Many of the kinetic parameters like distribution half-life ($t_{1/2}$ α), elimination half-life ($t_{1/2}$ β), area under curve (AUC), area under first moment curve (AUMC), mean residential time (MRT), tissue to plasma concentration ratio (T ≈ P) and various values of volume distribution do not differ significantly between the three different brands. Three different brands of enrofloxacin along with same strength manufacture by different pharmaceuticals companies not differ significantly.

Keywords

Enrofloxacin, Bioavailability, Antibacterial, Brand, HPLC, Goats

Introduction

Enrofloxacin is a third generation fluoroquinolone carboxylic acid derivative, developed exclusively for veterinary use against septicaemia, respiratory tract, urinary tract, soft tissues, bone and joint infection etc. (Sanjib *et al.*, 2005). Enrofloxacin is potent inhibitor of DNA-gyrase enzyme and is highly effective against many organisms that are resistant to B-lactamase, aminoglycosides, macrolides, tetracyclines, folic acid antagonist etc. (Bauditz, 1987; Elmas *et al.*, 2000). Enrofloxacin has the additional benefit of being metabolized (de-ethylated) to ciprofloxacin that also exerts potential antimicrobial activity at very low concentration (Tyezkowska *et al.*, 1989; Flammer *et al.*, 1989). Enrofloxacin and ciprofloxacin are bactericidal and both are expected to act synergetically against gram-negative and gram-positive bacteria and Mycoplasma (Hooper and Wolfson, 1991).

Because of high prevalence of enrofloxacin sensitive bacterial infection and high cost of the pioneer product, there has been tremendous increase in the use of other brand of enrofloxacin with increased availability and use of generic enrofloxacin product from different pharmaceutical companies, practitioner are faced with dilemma of therapeutic failure and side effects following the use of some of these array of multisource product in the market. Since these clinical condition results in great economic losses to farmer and the pioneer formulations and few brand have severally proven effective. Keeping in view of above facts the present study was undertaken and compare with each other with the respect of pharmacokinetics parameters.

Materials and Methods

Five clinically healthy female goats of 17-20 kg body weight were used in the present study. The goats were housed in the animal shed with concrete floor in the Department of Veterinary Pharmacology and toxicology, Bihar Veterinary College Patna-14. The goats were maintained on dry fodder concentrate and green grasses apart from routine grazing of about 4 to 5 hours. Deworming was done a fortnight prior to the experiment with Analgon (albendazole) 5 $mg.kg^{-1}$ body weight. Three commercial preparation of 10% enrofloxacin of different pharmaceuticals companies were administered @ 5mg kg^{-1}. First commercial product of enrofloxacin (ENR) was administered in each of five female healthy goats through intravenous routes and an interval of 15 day respectively, was allowed to elapse before administration of next dose of the drug. After conducting the kinetic study of first commercial product, the next two commercial products was administered in the same goats alternately, wash out period of 15 days was allowed before each administration by the above noted routes. The biological samples (plasma) were collected at 0.042, 0.083, 0.125, 0.333, 0.5, 0.75 min and 1, 1.5, 2, 3, 4, 6, 8, 10, 12 and 24 h. Concentration of different commercial preparation of 10 % enrofloxacin in plasma were estimated by HPLC method described by Nielsen and Gyrd-Hansen (1997) and Kung *et al.,* (1993). The experimental data were analysed by using two compartment open model (Notari, 1980). For two compartment open model, the concentration of the drug in plasma at any time is obtained from the formula:

$C_p = A_e^{-\alpha t} + B_e^{-\beta t}$ (Two compartment model),

Where Cp is the drug concentration in plasma at time, t.

Results and Discussion

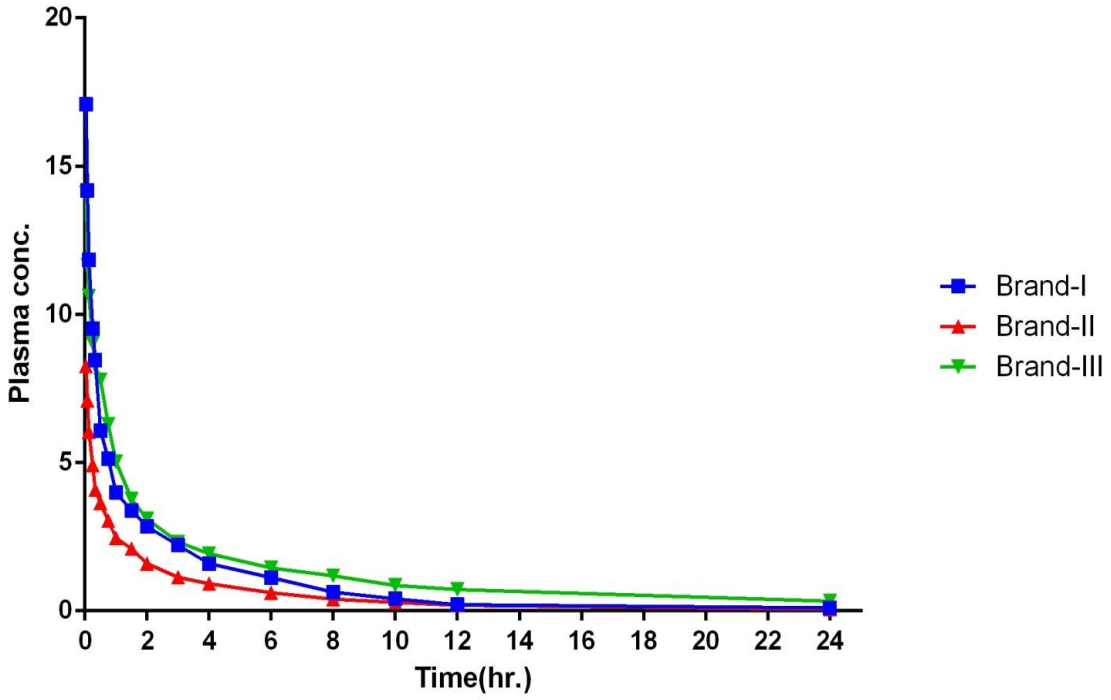
The drug was present significantly at lower concentration in brand II (8.26 ± 0.66) as compared to brand I (17.08 ± 1.92 $\mu g.ml^{-1}$) and Brand III (14.11 ± 2.91) at 0.042 h. Similarly, brand II shows lower concentrations upto 0.333 h and at 3 and 24 h. The drug maintained its therapeutic concentration (≥ 0.125 $\mu g.ml^{-1}$) up to 12 h in brand I and II while it was present up to 24 h in brand III. In contrast, Nitesh kumar *et al.,* (2003) showed that enrofloxacin appeared in plasma of all animals at 0.042 h and was detectable only upto 12 h when enrofloxacin was administered in buffalo calves at the dose rate of 4mg/kg body weight. Elmas *et al.,* (2001) showed that enrofloxacin appeared upto 24 h at effective concentration in goat after i.v. administration. The distribution rate constant (α) and distribution half-life ($t_{1/2}\ \alpha$) were noted with mean value of 2.49 ± 0.39, 1.54 ± 0.14, 1.30 ± 0.39 h h^{-1} and 0.33 ± 0.08, 0.46 ± 0.03, 1.12 ± 0.63 h of Brand I, II, III Respectively.

Table.1 Pharmacokinetics parameters of three commercial preparation (Brand I, Brand II, Brand III) of 10% enrofloxacin following Single i/v dose of 5mg/kg (n=5)

Kinetics Parameters	Brand I	Brand II	Brand III
A ($\mu g.ml^{-1}$)	$12.07^{a} \pm 1.25$	$4.80^{b} \pm 0.54$	$6.15^{ab} \pm 2.11$
B ($\mu g.ml^{-1}$)	$3.46^{a} \pm 0.37$	$1.95^{b} \pm 0.35$	$4.26^{a} \pm 1.13$
C_P^o ($\mu g.ml^{-1}$)	$15.53^{a} \pm 1.31$	$6.75^{b} \pm 0.56$	$10.40^{ab} \pm 2.65$
α (h^{-1})	$2.49^{a} \pm 0.39$	$1.54^{ab} \pm 0.14$	$1.30^{b} \pm 0.39$
$t_{1/2}\alpha$ (h)	$0.33^{a} \pm 0.08$	$0.46^{a} \pm 0.03$	$1.12^{a} \pm 0.63$
β (h^{-1})	$0.18^{a} \pm 0.02$	$0.18^{a} \pm 0.02$	$0.19^{a} \pm 0.03$
$t_{1/2}\beta$ (h)	$3.93^{a} \pm 0.46$	$4.04^{a} \pm 0.53$	$4.56^{a} \pm 1.24$
AUC ($mg.L^{-1}.h$)	$24.87^{a} \pm 2.39$	$14.11^{a} \pm 1.94$	$36.06^{a} \pm 12.66$
AUMC ($mg.L^{-1}.h^{2}$)	$113.33^{a} \pm 17.30$	$67.47^{a} \pm 13.73$	$325.84^{b} \pm 227.36$
MRT (h)	$4.58^{a} \pm 0.63$	$4.62^{a} \pm 0.53$	$6.52^{a} \pm 2.15$
K_{12} (h^{-1})	$1.34^{a} \pm 0.25$	$0.65^{b} \pm 0.07$	$0.48^{a} \pm 0.23$
K_{21} (h^{-1})	$0.72^{a} \pm 0.14$	$0.57^{a} \pm 0.09$	$0.67^{a} \pm 0.16$
Kel (h^{-1})	$0.61^{a} \pm 0.05$	$0.49^{a} \pm 0.05$	$0.35^{a} \pm 0.11$
$T \approx P$	$2.59^{a} \pm 0.36$	$1.87^{ab} \pm 0.39$	$0.91^{b} \pm 0.43$
Vd_{area} ($L.kg^{-1}$)	$1.22^{a} \pm 0.14$	$2.14^{b} \pm 0.24$	$1.20^{a} \pm 0.41$
Cl_B ($ml.kg^{-1}min^{-1}$)	$3.63^{a} \pm 0.36$	$6.34^{b} \pm 0.84$	$3.43^{a} \pm 1.00$

Different superscripts denote significant difference (P <0.05)

Fig:-1, Mean ± SEM of Plasma Concentration(µg/ml) of enrofloxacin of three different commercial prepration in goats following single i.v. administration @5mg/kg b.wt.



This denotes the drug distributed rapidly in the body of goats. More or less similar $t_{1/2}\ \alpha$ of 0.21 ± 0.03 h in goat (Sudha kumari, 1998), 0.23 ± 0.05 h in pig (Anadon *et al.*, 1999) was noted, while higher $t_{1/2}\ \alpha$ of 0.68 h (Giguere *et al., 1996)* in horses was noted.

The elimination rate constant (β) and elimination half-life ($t_{1/2}\ \beta$) were noted 0.18 ± 0.02, 018 ± 0.02, 0.19 ± 0.03 h^{-1} and 3.93 ± 0.46, 4.04 ± 0.53, 4.56 ± 1.2 h of Brand I,II,III Respectively. This agreement with $t_{1/2}\beta$ of 4.02 to 4.70 h in goat (Elmas *et al.*, 2001), 3.30 h (Haritova *et al.,* 2003) and 3.73± 0.44 h (Mengozi *et al.,* 1996) in sheep. Many of the kinetic parameters like distribution half-life ($t_{1/2}\ \alpha$), elimination half-life ($t_{1/2}\ \beta$), area under curve (AUC), area under first moment curve (AUMC), mean residential time (MRT), tissue to plasma concentration ratio (T ≈ P) and various values of volume distribution do not differ significantly between the three different brands (Table 1). Some parameters like K_{12} show lower values in brand II and III, while Vd_{area} and Cl_B of brand II showed higher values as compared to brand I and III.

Pharmacokinetic study of three different commercial preparations of 10% enrofloxacin was conducted in five she goats following single intravenous injection @5mg/kg body weight. Many kinetics parameter are shows non- significant difference between three brands.

So on above fact we conclude that three different commercial preparations of enrofloxacin along with same strength manufacture by different pharmaceuticals companies not differ significantly. Enrofloxacin may be administered i.v. at the dose rate of 5mg/kg body weight every 12 hourly for treating systemic as well as local infection in goats.

References

Anadon, A., Martinez-Larranaga, M. R., Diaz, M. J., Fernandez- Cruz, M. L., Martinez, M. A., Frejo, M. T., Martinez, M., Iturbe, J. and Tafur, M. 1999. Pharmacokinetic variables and tissue residues of enrofloxacin and ciprofloxacin in healthy pigs. *Am. J. Vet. Res.* 60: 1377-82.

Bauditz, 1987; Bauditz, R. (1987): Results of clinical studies with Baytril TM. Poult. *Vet. Med. Rev.*, 2: 130-136.

Elmas *et al., 2*000: Elmas, M., Yazar, E., Tras, B., Bas, A.L. and Eryavuz, A. (2000): Pharmacokinetics and oral Bioavailability of enrofloxacin in faunated & defaunated Angora goats.*Revue Med. Vet*., 6(151): 507-510.

Elmas M, Traso, Kaya S, Bas AL, Yazar E, Yarsan E., 2001. Pharmacokinetics of enrofloxacin after intravenous and intramuscular administration in Angora Goats. *Can J. Vet. Res.*

Flammer, K., Aucoin, D. P. and Whitt, D. A. 1991. Intramuscular and oral disposition of enrofloxacin in African grey parrots following single and multiple doses. *J. Vet. Pharmacol. Ther.* 14: 359-66.

Giguere, S., Sweeney, R.W. and Belanger, M. 1996. Pharmacokinetics of enrofloxacin in adult horses and concentration of the drug in serum, body fluids and endometrial tissues after repeated intragastrically administered doses. *Am. J. Vet. Res.* 57: 1025-30. 65(1): 64-7.

Giguere, S., Sweeney, R.W. and Belanger, M. 1996. Pharmacokinetics of enrofloxacin in adult horses and concentration of the drug in serum, body fluids and endometrial tissues after repeated intragastrically administered doses. *Am. J. Vet. Res.*

57: 1025-30.

Haritova A, Lashev L, Pashov D. 2003. Pharmacokinetic of enrofloxacin in Lactating sheep. *Res. Vet. Sci.* 74 (3): 241-5.

Hooper, D. C. and Wolfson, J. S. 1991. Fluoroquinolone antimicrobial agents. *New Eng. J. Med.* 7: 384-94.

Kung *et al.*, (1993): Kung, K., Riond, J. L. and Wanner, M. 1993. Pharmacokinetics of enrofloxacin and its metabolite ciprofloxacin after intravenous and oral administration of enrofloxacin in dogs. *J. Vet. Pharmacol. Ther*. 16: 462-68

Mengozzi, G., Intorre, L., Bertini, S. and Soldini, G. 1996. Pharmacokinetics of enrofloxacin and its metabolite ciprofloxacin after intravenous and intramuscular administration in sheep. *Am. J. Vet. Res.* 57: 1040-43.

Nielsen and Gyrd-Hansen (1997): Nielsen, P. and Gyrd-Hansen, N. 1997. Bioavailability of enrofloxacin after oral administration to fed and fasted pigs.*C.Pha rmacol. Toxicol.* 80: 246-50

Nitesh Kumar, Singh, S.D., Jayachandran, C. 2003. Pharmacokinetics of enrofloxacin and its active metabolite ciprofloxacin and its interaction with diclofenac after intravenous administration in buffalo calves. *The Vet. J.* 165: 302-6.

Notari, 1980: Notari, R.E. 1980. Biopharmaceutics and clinical pharmacokinetics. 3rd Edn. *Marcel Dekkar Inc*., New York.

Sanjib *et al.*, 2005: Sanjib, K., Chandana, C.B., Pritam, M. and Mohan, B. (2005): Pharmacokinetics stuies of enrofloxacin in Yak after intramuscular administration. *Ir. J. pharmacol. Therap*., 4(2): 91 – 94

Sudha Kumar, 1998. Pharmacokinetics of enrofloxacin and its interaction with paracetamol in goats. M.V. Sc. Thesis, Rajendra Agricultural University, Bihar, Pusa (Samastipur), India.

Tyczkowska, K., Hedeen, K. M., Aucoin, D. P. and Aronson, A. L. 1989. High performance liquid chromatographic method for the simultaneous determination of enrofloxacin and its primary metabolite ciprofloxacin in canine serum and prostatic tissue. *J. Chromatogr*. 493: 337-46.