INTERNATIONAL JOURNAL OF ADVANCED BIOLOGICAL RESEARCH

www.scienceandnature.org

# BIOAVAILABILITY STUDY OF THREE COMMERCIAL PREPARATIONS OF 10% ENROFLOXACIN THROUGH INTRAMUSCULAR ROUTE IN GOATS

[a]Gond; V.K., [a]Gangwar, S.K. & [b]Jayachandran, C.
[a]Animal Production Research Institute ( APRI), Dr. R.P.C.A.U., Pusa, Samastipur, Bihar
[b]Department of Veterinary Pharmacology & Toxicology Bihar Veterinary College, Patna.

**ABSTRACT**
A comparative bioavailability of three brands of 10% enrofloxacin was determined after single intramuscular (I.M) administrations @ 5mg/kg body weight to 5 healthy female goats. Blood was sampled before and after drug administration for 24 hours. Plasma enrofloxacin concentrations were analyzed by using high performance liquid chromatography (HPLC) method. Pharmacokinetics was best described by one compartment open model through I.M route respectively. Peak plasma concentration ($C_{max}$), 5.35 ±0.87, 1.94 ±0.16 and 3.34 ±0.77 µg/ml were obtained in brand I, II, III respectively. The drug was present significantly at lower concentration in brand II (0.07 ±0.02) as compared to brand I (1.58 ± 0.41 µg.ml$^{-1}$) and Brand III (0.42 ± 0.21) at 0.042 h. Similarly, brand II shows lower concentrations upto 12 h. The drug maintained its therapeutic concentration (≥ 0.125 µg.ml$^{-1}$) up to 12 h in all three brands I, II, III. The bioavailability (F %) of brand I (84.46 ±10.12) is significantly higher as compared to brand III (50 ±11.84), but more or less similar to brand II (64.80 ± 7.64).

**KEY WORDS:** Enrofloxacin, Bioavailability, Antibacterial, Brand, HPLC, Goats.

## INTRODUCTION

Bioavailability is the rate and extent to which a drug enters the systemic circulation unchanged following administration by any route. The formulation of the dosage form and route of administration affect the bioavailability (F %) of a drug and may there by influence the intensity and duration of the pharmacological effect. The rate of absorption can be obtained from the peak plasma concentration ($C_{max}$) and the time to reach peak concentration ($t_{max}$), based on the measured plasma concentration time data. Any drug when given through intravenous route is 100% bioavailable but when administered by extra-vascular route (intramuscular, subcutaneous, oral *etc.*), bio-availability differs significantly due to differences in absorption rate as well as amount of absorption.

Enrofloxacin (ENR) is a third generation fluoroquinolone, exclusively for veterinary use against septicaemia, respiratory tract, urinary tract, soft tissues, bone and joint infection *etc*. (Sanjib *et al.*, 2005). It is potent inhibitor of DNA-gyrase enzyme and is highly effective against many organism that are resistant to β-lactamase, amino-glycosides, macrolides, tetracyclines, folic acid antagonist *etc*. (Bauditz, 1987; Elmas *et al.*, 2000). It has excellent bioavailability with superior pharmacokinetic profile and rapidly absorbed and well distributed throughout the body following oral and intramuscular administration in animals. 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 increase availability 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 compared with each other with the respect of pharmacokinetics parameters.

## MATERIALS & 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. 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 was administered in each of five female healthy goats through Intramuscular routes and an interval of 15day 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 %

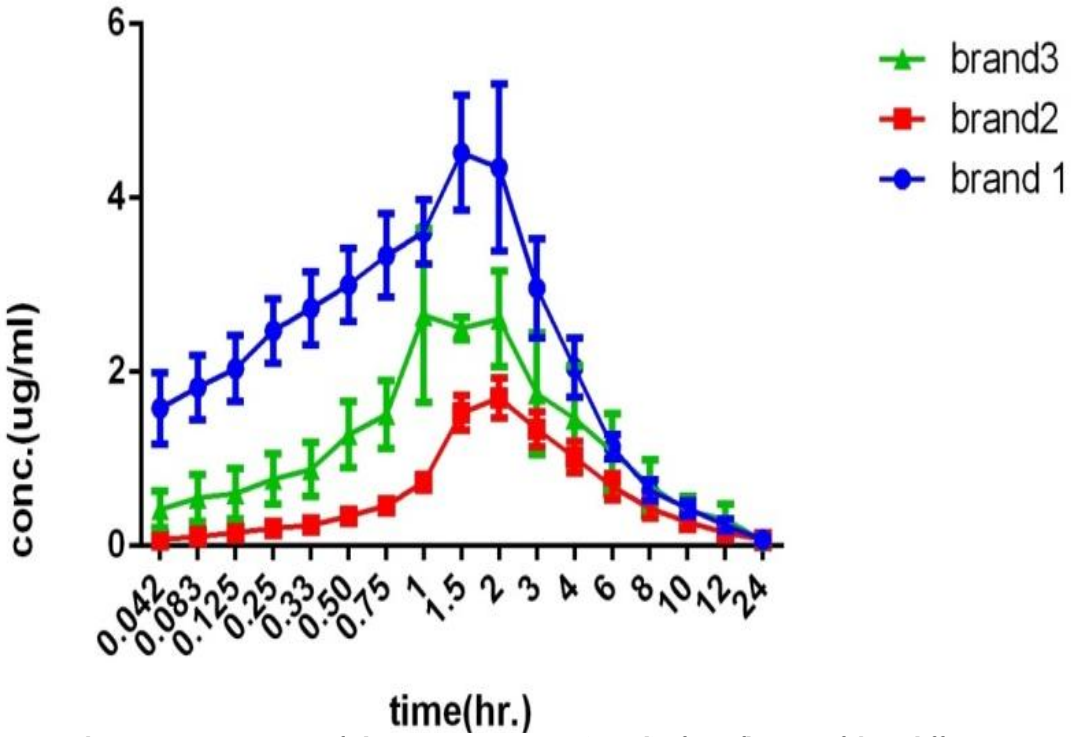
enrofloxacin in plasma were estimated by HPLC method described by Nielsen and Gyrd-Hansen (1997) and Kung *et al*. (1993) .The experimental data were analysed by using two compartment open model (Notari, 1980). For one compartment open model, the concentration of the drug in plasma at any time is obtained from the formula:

$C_p = A_e^{-\alpha t} - B_e^{-\beta t}$……. (One compartment model), Where Cp is the drug concentration in plasma at time, t¨

Bioavailability (F %) of three commercial preparation following intramuscular administration was determined by the ratio between AUC (i.m.) and AUC (i.v.) for each goats as– F═ (AUC) i.m. / (AUC) i.v. ×100.

**RESULTS & DISCUSSION**

The drug was present significantly at lower concentration in brand II (0.07 ±0.02) as compared to brand I (1.58 ± 0.41 µg.ml$^{-1}$) and Brand III (0.42 ±0.21) at 0.042 h. Similarly, brand II shows lower concentrations upto 12 h. The drug maintained its therapeutic concentration (≥ 0.125 µg. ml$^{-1}$) up to 12 h in all three brands I, II, III. Elmas *et al.* (2001) noted more or less similar value of 0.09 mg.ml$^{-1}$ at 24 h after i.m. injection of enrofloxacin (5mg.kg$^{-1}$) in goat. Calculation of kinetic parameters of enrofloxacin of three different commercial preparations *i.e*. Brand is done by one-compartment open model after i.m. administration (5mg.kg$^{-1}$). The mean extrapolated zero time concentration of the drug in plasma during absorption phase (A) is noted to be non-significant for all the three brands whereas during elimination phase (B) brand I shows significantly higher value as compared to brand II. Many of the kinetic parameters like absorption rate constant (Ka), elimination rate constant (β), absorption half-life ($t_{1/2}$ Ka), elimination half-life ($t_{1/2}$ β), area under curve (AUC), area under first moment curve (AUMC), mean residential time (MRT), mean absorption time (MAT), maximum concentration ($C_{max}$), time to reach maximum concentration ($t_{max}$) and total body clearance ($Cl_B$) do not differ significantly between the three different brands. More or less similar $t_{1/2}$ Ka of 0.25 h (Elmas *et al.*, 2001) after i.m. injection of enrofloxacin in goat was noted. In contrast, 0.26 h in breeding bull (Verma *et al.*, 1999) and 0.36 h (Abdel-Aziz *et al.*, 1997) in chickens were noted after i.m. injection of enrofloxacin. More or less similar $t_{1/2}$ β of 3.87 h (Haritova *et al.*, 2003) after i.m. injection of enrofloxacin in sheep and 4.00 to 4.71 h (Elmas *et al.*, 2001) in goat were noted. Some parameters like $Vd_B$ and $Vd_{area}$ of brand I show significantly lower values as compared to brand II. More or less similar $Vd_{area}$ of 1.42 L.kg$^{-1}$ (Rao *et al.*, 2001) after i.m. administration of enrofloxacin in goat was noted. The bioavailability (F%) showed significantly higher in brand I (84.46 ± 10.12) as compared to lower value of brand III (50.00 ± 11.84) but brand II (64.80 ±7.64) showed non-significant difference as compare to brand I & III. More or less similar bioavailability (F %) of 90% (Elmas *et al.*, 2001) in Angora goat after i.m. injection of enrofloxacin was obtained. The value of 75.35% (Haritova *et al.*, 2003) and 85.28 ±3.40 % (Mengozzi *et al.*, 1996) after i.m. injection of enrofloxacin in sheep were also noted.




**GRAPH 1** Showing mean ± S.E.M. of plasma concentrations (µg/ml) of enrofloxacin of three different commercial prepration in goats following single intramuscular dose of 5mg.kg$^{-1}$

**TABLE 1**: Kinetic parameters of Enrofloxacin of three different commercial preparations in goats calculated by one-compartment open model following single intramuscular dose of 5mg.kg$^{-1}$

| Parameter (Unit) | Intramuscular Route | | |
|---|---|---|---|
| | Brand I | Brand II | Brand III |
| A (μg.ml$^{-1}$) | 4.17 ± 0.58$^{a}$ | 2.43 $^{a}$ ± 0.44$^{a}$ | 4.00$^{a}$ ± 1.15$^{a}$ |
| B (μg.ml$^{-1}$) | 5.08$^{a}$ ± 0.47$^{a}$ | 2.16$^{b}$ ± 0.43$^{b}$ | 4.05 $^{ab}$ ± 1.35 |
| Ka (h$^{-1}$) | 2.45 $^{a}$ ± 0.35 | 1.23 $^{a}$ ± 0.24 | 1.87 $^{a}$ ± 0.90 |
| $t_{1/2}$ Ka (h) | 0.31 $^{a}$ ± 0.04 | 0.66 $^{a}$ ± 0.13 | 0.83 $^{a}$ ± 0.31 |
| β (h$^{-1}$) | 0.23 $^{a}$ ± 0.02 | 0.19 $^{a}$ ± 0.04 | 0.21$^{a}$ ± 0.05 |
| $t_{1/2}$ β (h) | 3.10 $^{a}$ ± 0.34 | 4.25 $^{a}$ ± 0.71 | 3.84$^{a}$ ± 0.55 |
| AUC (mgL$^{-1}$h) | 19.04 $^{a}$ ± 1.84 | 9.29 $^{a}$ ± 1.81 | 14.62 $^{a}$ ± 3.80 |
| AUMC (mg.L$^{-1}$.h$^{2}$) | 105.19$^{a}$ ± 22.02 | 71.23$^{a}$ ± 17.52 | 98.72$^{a}$ ± 32.99 |
| MRT (h) | 5.54$^{a}$ ± 1.13 | 7.22$^{a}$ ± 0.86 | 6.52$^{a}$ ± 0.83 |
| MAT (h) | 2.61$^{a}$ ± 0.98 | 2.70$^{a}$ ± 0.92 | 2.61$^{a}$ ± 1.26 |
| $C_{max}$ (μg.ml$^{-1}$) | 5.35$^{a}$ ± 0.87 | 1.94$^{b}$ ± 0.16 | 3.34$^{ab}$ ± 0.77 |
| $T_{max}$ (h) | 1.60$^{a}$ ± 0.09 | 1.80$^{a}$ ± 0.12 | 1.15$^{a}$ ± 0.15 |
| $Vd_{R}$ (L.kg$^{-1}$) | 1.01$^{a}$ ± 0.07 | 2.75$^{b}$ ± 0.56 | 1.89$^{ab}$ ± 0.50 |
| $Vd_{area}$ (L.kg$^{-1}$) | 1.21 $^{a}$ ± 0.15 | 3.52 $^{b}$ ± 0.48 | 2.30 $^{ab}$ ± 0.55 |
| $Cl_{B}$ (mg.kg$^{-1}$.min) | 4.53 $^{a}$ ± 0.43 | 10.90 $^{a}$ ± 2.59 | 6.84 $^{a}$ ± 1.16 |
| F (%) | 84.46 $^{a}$ ± 10.12 | 64.80 $^{ab}$ ± 7.64 | 50.00 $^{b}$ ± 11.84 |

Different superscripts denote significant (P<0.05)

## CONCLUSION

Pharmacokinetic and bioavailability study of three different commercial preparations of 10% enrofloxacin was conducted in five goats following single intramuscular (i.m) injection @ 5mg/kg$^{-1}$ body weight. The bioavailability (F %) values differ from brand to brand and this may be due to different physio-chemical properties of the brands and such other factors. The therapeutic concentration was maintained >12 hrs. in all the three brands. So on above facts all the three brands of enrofloxacin may be administered intramuscular route at the dose rate of 5mg/kg$^{-1}$ body weight every 12 hrly for treating systemic as well as local infection in goats.

## REFERENCES


Abdal-Aziz, M.I., Aziaz, M.A., Soliman, F.A., Afify, N.A. (1997) Pharmacokinetic evaluation of enrofloxacin in chickens, *Br Port Sci.* **38** (5): 614.

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

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, A.L., Yazar, E., Yarsan, E. (2001) Pharmacokinetics of enrofloxacin after intravenous and intramuscular administration in Angora Goats. *Can J. Vet. Res.* **65** (1): 64-7.

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

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

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

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

Rao, G.S., Ramesh, S., Ahmad, A.H., Tripathi, H.C., Sharma, L.D. and Malik, J.K. (2001) Pharmacokinetics of enrofloxacin and its metabolite ciprofloxacin after intramuscular administration of enrofloxacin in goats. *Vet. Res. Com.* **25**: 197-204.

Verma, H.K., Pangawkar, G.R., Chaudhary, R.K. and Srivastava, A.K. (1999) Pharmacokinetics and dosage regimen of enrofloxacin in buffalo bulls after intramuscular administration. *Vet. Res. Com.* **23** : 501-5.