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Effects of Concurrent Administration of Meloxicam on Pharmacokinetic Parameters of Enrofloxacin in Turkeys

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Abstract

The pharmacokinetic studies of enrofloxacin was conducted in eighteen turkeys (1 to 1.5 years age) weighing between 3 to 4 kg following single i.v. dose (10 mg/kg b.w.) alone and with meloxicam (1 mg/kg b.w.). Quantitative estimation of enrofloxacin and meloxicam was done by high performance liquid chromatography. The maximum concentration of drug in plasma (Cp_{max}) of enrofloxacin with meloxicam (8.42 ± 0.40 µg/ml) was not significantly different from that of enrofloxacin alone (9.68 ± 0.44 µg/ml). Pharmacokinetic parameters of enrofloxacin alone (C°p =10.38±0.43 µg/ml, $t_{½}\beta$ =2.73±0.12 h, MRT = 3.65±0.21 h, Cl_{B} =8.41±0.66 ml/kg/min, Vd_{area} =1.95±0.08 L/kg) as compared to when it was administered with meloxicam (C°p =9.35±0.62 µg/ml, $t_{½}\beta$ =2.70±0.13 h, MRT =3.73±0.18 h, Cl_{B} =9.79±0.84 ml/kg/min, Vd_{area} =2.26±0.15 L/kg) in turkeys did not differ significantly.

The $t_{½}\beta$ of meloxicam with enrofloxacin (2.50±0.08 h) was significantly shorter as compared to meloxicam alone (3.03±0.18 h). Based on pharmacokinetic studies ENR may be injected at dose rate of 4.5 mg/kg i.v. at an interval of 20.38 h in turkeys.

Keywords: Pharmacokinetics; Enrofloxacin; Meloxicam; Interaction; Intravenous; Turkeys

Introduction

Enrofloxacin is 2nd generation fluroquinolone developed exclusively for veterinary use [1,2]. It possess broad spectrum activity and is effective against many gram-negative organisms such as *Escherichia coli*, *Salmonella, Klebsiella, Pasteurella, Proteus, Haemophilus, Compylobactor* and *Pseudomonas* and gram-positive bacteria like *Streptococcus*, *Staphylococcus, Clostridium, Erysipelothrix* and *Mycoplasma*. Enrofloxacin penetrates well into different tissues and has relatively slower elimination. Microbial resistance to their action does not develop rapidly [3].

Meloxicam is a safer non steroidal anti-inflammatory drug (NSAIDs) of oxicam class because it specifically inhibits cyclooxygenase -2 and has a superior gastrointestinal tolerability [4]. Its therapeutic index is six to twenty times more than other NSAIDs [5]. The meloxicam cause analgesia by suppressing generation of prostaglandin via inhibition of cyclooxygenase I and II enzyme [6]. It has no effect on platelet aggregation or renal prostaglandin synthesis and show sparing action on cyclooxygenase -1 [7,8]. Meloxicam is metabolized to four biologically inactive metabolites [9] and are equally excreted in urine and faeces. Meloxicam is used as anti-inflammatory, analgesic, antipyretic and prescribed with antibacterial agents. There are evidences that administration of two drugs together interact and can affect the pharmacokinetic parameters of each other and may affect the cure of diseases. It is possible that meloxicam may have some effect on the kinetic profile of enrofloxacin due to interaction which can increase or decrease the dose of each other. The pharmacokinetic parameters of ENR are available in other species of animals but there is paucity of such studies in turkeys. Therefore, the present work was designed to study the pharmacokinetic studies of enrofloxacin and its interaction with meloxicam in turkeys.

Materials and Methods

Experimental birds

Clinically 18 turkeys (either sex) of Instructional Varietal Bird farm, R.V.C. weighing between 3-4 kg (1 to 1.5 years) were used in this experiment. The birds were divided in to 3 groups (Group I- ENR alone, Group II – ENR + Meloxicam and Group III – Meloxicam alone) consisting of 6 birds in each group.The birds were kept in the experimental laboratory of Department of pharmacology & Toxicology and were provided standard ration and water *ad libtum*. The room temperature was maintained at 25°C (±5°C). The birds were dewormed with single oral dose of fenbendazole suspension @ 10 mg/kg b.w. 30 days prior to study.The protocol of the experiment was approved by Institutional Animal Ethics Committee of Ranchi Veterinary College, Ranchi.

Drugs used

(i) **Enrofloxacin:** Meriquin® 10% an injectable commercial preparation, containing 100 mg/ml enrofloxacin (w/v), marketed by Merind Pharmaceutical India was used. Enrofloxacin was injected at the dose rate of 10 mg/kg b.w. to each of the six turkeys by i.v. route.

(ii) **Meloxicam:** Melonex® an injectable commercial preparation, containing 5 mg/ml meloxicam, marketed by Intas Pharmaceutical Limited,Ahmedabad, Gujrat, India was used. Meloxicam was injected at the dose rate of 1 mg/kg b.w. to each of the six turkeys by i.v. route.

Collection of blood samples

Blood samples were collected from turkeys after i.v. administration

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of enrofloxacin alone and with meloxicam at predetermined time intervals at 0, 0.04, 0.08, 0.16, 0.25, 0.50, 0.75, 1, 2, 3, 4, 6, 8, 12, 24 and 48 h by wing venipuncture in heparinized test tube. Heparin was used at the dose rate of 20µl (1% w/v solution) for 1 ml of blood. Plasma was separated by centrifugation at 3000 rpm for 20 minutes and was kept in refrigerator at 4°C till analysis. The analysis was always done within 24 h of sample collection.

Estimation of enrofloxacin

Estimation of enrofloxacin was carried out by modified methods of Anadon et al. [10]. 0.5 ml of plasma was taken in a centrifuge tube and 1ml of acetonitrile was added and mixed vigorously for 1 min by vortex mixer. The whole aliquot was centrifuged at 3000 rpm for 10 min and was filtered with Whatman no.1 filter paper (70mm) and 20µl of the filtrate was injected to the HPLC.

Estimation of meloxicam

Estimation of Meloxicam was carried out by modified method of Shukla et al. [11]. 0.5 ml of plasma was taken in a centrifuge tube and 0.5 ml of acetonitrile was added and mixed vigorously for 1 min by vortex mixture. The whole aliquot was centrifuged at 5000 rpm for 15 min, then 0.5 ml of supernatant was taken in centrifuge tube and 0.5 ml of HPLC grade water was added and mixed vigorously for 1 min by vortex mixture. The whole aliquot was centrifuged at 5000 rpm for 15 min, then it was filtered with Whatman no.1 filter paper (70 mm) and 20 µl of the filtrate was injected to the HPLC.

Preparation of mobile phase

(i) **Enrofloxacin:** 50 ml acetic acid, 100 ml acetonitrile, 50 ml methanol and 1 ml triethylamine (0.1%) were taken, then HPLC grade water was added to make 1000 ml and at last the pH of whole mixture was maintained at 3 by adding triethylamine.

(ii) **Meloxicam:** Water and acetic acid were taken in ratio of 99:1 v/v and from this 65% of mixture was taken and 35% of acetonitrile was added. At last HPLC grade water was added to make 1000 ml and at last the pH of whole mixture was maintained at 6 by adding triethylamine.

Experimental condition of apparatus

Cecil 4100 (Mtd. By Cecil instrumentation, Cambridge, England) liquid chromatograph coupled with variable wavelength UV/VIS detector attached with an integrator and LichroCART catridge column was used. Injection of samples were done by 25 µl loop Hamilton syringe.

(i) **Enrofloxacin:** Mobile phase : As mentioned above.

Λvalue : 280 nm

Flow rate : 1ml/min

Temperature of oven : 40˚C

(ii) **Meloxicam:** Mobile phase : As mentioned above.

Λvalue : 355 nm

Flow rate : 0.8 ml/min

Temperature of oven : 35˚C

Calculation of pharmacokinetic parameters

The pharmacokinetic parameters of enrofloxacin and meloxicam were calculated by computerized programme (Pharmkit) based on the formula [12-14].

Calculation of dosage regimen

The dose of enrofloxacin (mg/kg, b. w.) was calculated by standard method Shargel and Andrew [15].

$Cp_{max} = (Dose/Vd)/1\text{-}e^{-k.r}$

Dosage interval of enrofloxacin was also calculated based on the method described by Shargel and Andrew [15].

$Cp_{max}/Cp_{min} = 1/e^{-k.r}$

Statistical analysis

The statistical comparision of important pharmacokinetic parameters were done as per statistical method of Snedecor and Cochran [16]. Quantitative data were analysed, using the independent t-test.

Result

The comparative mean pharmacokinetic parameters of enrofloxacin with and without meloxicam are presented in Table 1. The mean value of C^0p of ENR alone and with meloxicam were 10.38±0.43 µg/ml and

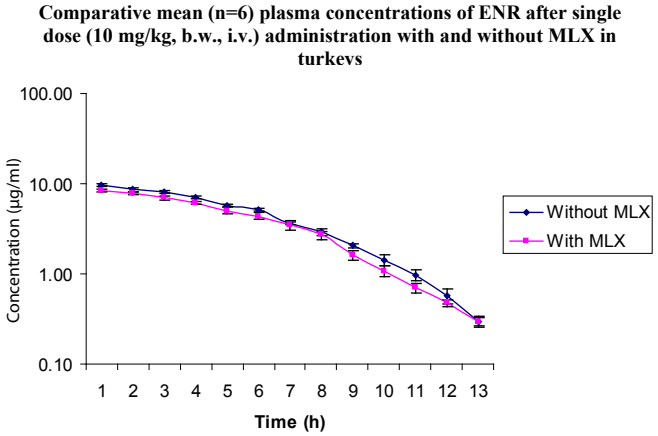

Figure 1:

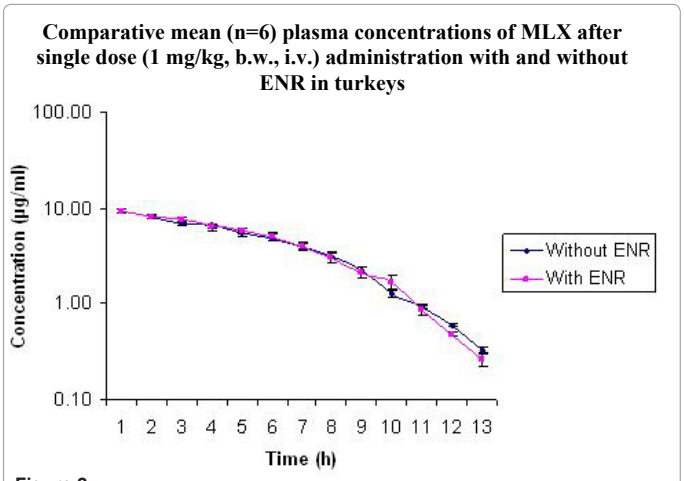

Figure 2:

Kinetic Parameters	Without meloxicam	With meloxicam	t-value
A(µg/ml)	5.59±0.26	4.97±0.29	1.48 NS
B(µg/ml)	4.79±0.25	4.38±0.35	0.88 NS
C^0p(µg/ml)	10.38±0.43	9.35±0.62	1.26 NS
α(h^{-1})	2.22±0.21	2.97±0.51	1.24 NS
β(h^{-1})	0.26±0.01	0.26±0.01	0.28 NS
$t_{½}$α(h)	0.27±0.05	0.23±0.05	0.51 NS
$t_{½}$β(h)	2.73±0.12	2.70±0.13	0.15 NS
AUC(mg/L.h)	20.51±1.47	17.72±1.40	1.26 NS
AUMC(mg/L.h)	76.56±8.99	66.94±7.16	0.76 NS
MRT(h)	3.65±0.21??	3.73±0.18	0.27 NS
Cl_B(ml/kg/min)	8.41±0.66	9.79±0.84	1.19 NS
Vd_{area}(L/kg)	1.95±0.08	2.26±0.15	1.65 NS
K_{12}(h^{-1})	0.84±0.12	1.22±0.26	1.20 NS
K_{21}(h^{-1})	1.15±0.08	1.51±0.23	0.32 NS
K_2(h^{-1})	0.48±0.03	0.50±0.02	0.41 NS
T/P	0.91±0.06	0.94±0.06	0.28 NS

NS=Non Significant

Table1: Comparative mean pharmacokinetic profile of ENR after single dose (10mg/kg) i.v. administration with and without MLX (1mg/kg, i.v.) in turkeys.

Kinetic Parameters	Without ENR	With ENR	t-value
A(µg/ml)	5.61±0.42	6.43±0.55	1.07 NS
B(µg/ml)	4.38±0.43	5.39±0.56	1.32 NS
C^0p(µg/ml)	9.99±0.74	11.81±1.08	1.27 NS
α(h^{-1})	4.80±1.45	4.38±0.69	0.24 NS
β(h^{-1})	0.23±0.01	0.28±0.01	2.57*
$t_{½}$α(h)	0.36±0.17	0.11±0.03	1.30 NS
$t_{½}$β(h)	3.03±0.18	2.50±0.08	2.39*
AUC(mg/L.h)	20.74±0.92	20.21±1.96	0.22 NS
AUMC(mg/L.h)	81.87±4.06	69.67±7.31	1.33 NS
MRT(h)	3.95±0.10	3.44±0.11	3.19**
Cl_B(ml/kg/min)	0.81±0.04	0.87±0.08	0.57 NS
Vd_{area}(L/kg)	0.21±0.01	0.19±0.02	0.87 NS
K_{12}(h^{-1})	2.50±0.72	1.98±0.38	0.58 NS
K_{21}(h^{-1})	2.28±0.64	2.11±0.32	0.21 NS
K_2(h^{-1})	0.47±0.03	0.56±0.02	2.14 NS
T/P	2.85±1.57	1.06±0.09	1.04 NS

NS=Non Significant, *P<0.05,**P<0.01

Table2: Comparative mean pharmacokinetic profile of MLX after single dose (1 mg/kg) i.v. administration with and without ENR (10 mg/kg, i.v.) in turkeys.

9.35±0.62 µg/ml respectively. The mean value of β of ENR alone and with meloxicam were 0.26±0.01 h^{-1} and 0.26±0.01 h^{-1} respectively.The mean value $t_{½}$β without meloxicam was 2.73±0.12 h and 2.70±0.13 h with meloxicam. The mean value of kinetic parameters of ENR i.e. AUC, MRT, Cl_B and Vd_{area} were 20.51±1.47 mg/L.h, 3.65±0.21 h, 8.41±0.66 ml/kg/min and 1.95±0.08 L/kg respectively in turkeys without meloxicam. The values of above parameters of ENR were 17.72±1.40 mg/L.h, 3.73±0.18 h, 9.79±0.84 ml/kg/min and 2.26±0.15 L/kg respectively in turkeys with meloxicam.

The mean comparative pharmacokinetic parameters of meloxicam in plasma of turkeys with and without enrofloxacin are presented in Table 2. The mean value of C^0p was 9.99±0.74 µg/ml in turkeys without enrofloxacin and above parameter was 11.81±1.08 µg/ml in turkeys with enrofloxacin. The mean value of β of meloxicam without enrofloxacin was 0.23±0.01 h^{-1} and with enrofloxacin was 0.28±0.01 h^{-1} in turkeys. The mean value of $t_{½}$β of meloxicam in without enrofloxacin was 3.03±0.18 h and this value was 2.50±0.08 h in turkeys with enrofloxacin (see supplementary data).

The mean values of kinetic parameters of meloxicam i.e. AUC, MRT, Cl_B and Vd_{area} were 20.74±0.92 mg/L.h, 3.95±0.10 h, 0.81±0.04 ml/kg/min and 0.21±0.01 L/kg without enrofloxacin. The values of above parameters were 20.21±1.96 mg/L.h, 3.44±0.11 h, 0.87±0.08 ml/kg/min and 0.19±0.02 L/kg with enrofloxacin.

Discussion

The maximum plasma concentration (Cp_{max}) of enrofloxacin with meloxicam (8.42±0.40 µg/ml) was not significantly different from that of enrofloxacin alone (9.68±0.44 µg/ml). However, the effect of concurrent administration of enrofloxacin with meloxicam in febrile turkey could not be studied. Therefore, the further study on enrofloxacin in febrile turkey especially with meloxicam is required to pin-point its effect on the plasma levels . Tansakul et al. [17], similar to the finding of this study reported Cp_{max} of enrofloxacin (11.49±1.17µg/ml) after single dose (10 mg/kg, b.w.) after i.v. administration in healthy duck. It was observed that the plasma concentrations obtained after i.v. administration in turkeys with meloxicam (0.30±0.04 µg/ml) and without meloxicam (0.30±0.03 µg/ml) were much higher than the reported MIC values (0.01 to 2.0 µg/ml) [18,19]. Therefore, it is obvious

that enrofloxacin may combact infections caused by various susceptible pathogens in turkey if given in emergent conditions by i.v. route.

The mean Cp_{max} of meloxicam with enrofloxacin (9.36±0.44 µg/ml) in turkeys was not significantly different from that observed in meloxicam alone (9.30±0.43 µg/ml). Result obtained indicate that enrofloxacin does not change the pharmacokinetic profile of meloxicam when both are given together.

The mean C°p of enrofloxacin with meloxicam (9.35±0.62 µg/ml) in turkeys was not significantly different from that observed after enrofloxacin alone (10.38±0.43 µg/ml). Ranjan [20] also reported that meloxicam at dose rate of 0.5 mg/kg b.w. i.v. alongwith ceftizoxime (25 mg/kg, b.w.) in healthy sheep did not show any significant change in the C°p of ceftizoxime. The results of C°p evidenced that enrofloxacin may be used alone or with meloxicam in emergent diseases of turkey.

The $t_{½}\beta$ of enrofloxacin with meloxicam (2.70±0.13 h) was almost similar to that without meloxicam (2.73±0.12 h) in turkeys. The results showed that $t_{½}\beta$ of enrofloxacin with and without meloxicam in healthy turkeys did not differ significantly. Kanemaki et al. [21]. reported almost similar $t_{½}\beta$ (3 h) in dog.

The mean MRT value of enrofloxacin with meloxicam (3.73±0.18 h) did not differ significantly when enrofloxacin was administered alone (3.65±0.21h). However, Ahmed et al. [22] reported a higher MRT (8.826±1.24h) of enrofloxacin after single dose (7.5 mg/kg, b.w.) i.v. administration in yak.

The mean Cl_B value of enrofloxacin with meloxicam (9.79±0.84 ml/kg/min) did not differ significantly as compared with enrofloxacin alone (8.41±0.66 ml/kg/min). It is obvious from the results obtained in this experiment that similar Cl_B values of enrofloxacin with and without meloxicam in turkeys could produce similar initial plasma levels after i.v. administration in turkeys. Single dose kinetics of rifampicin, isoniazid as well as their combination dosage forms as tablet and capsule has been carried out in humans. Significantly greater rate and extent of absorption was observed from rifampicin capsule alone as compared to the rifampicin levels from combination dosage forms [23].

The mean Vd_{area} of enrofloxacin with meloxicam (2.26±0.15 L/kg) did not differ significantly as compared with enrofloxacin alone (1.95±0.08 L/kg).Result indicated that meloxicam did not hamper the pharmacokinetic profile of enrofloxacin when both were given together. Ahmed et al. [22] reported Vd_{area} (5.784±0.84 L/Kg) of ENR after single dose (7.5 mg/kg, b.w.) i.v. administration in yak. Similar Vd value (2.5±0.20 L/kg) has also been reported for ENR after i.v. administration (5 mg/kg) in ostrich [24]. The high Vd value of ENR with meloxicam obtained after i.v. administration (2.26±0.15 L/kg) indicated its good penetration into wide range of tissue in turkeys. The apparent value of volume of distribution of ENR in birds is reported to be variable, ranging between 1.49 to 3.9 L/kg.

The $t_{½}\beta$ of meloxicam with ENR (2.50±0.08 h) was significantly ($p<0.05$) shorter in healthy turkeys as compared to meloxicam alone (3.03±0.18). Baert and Backer [25] reported $t_{½}\beta$ of 3.21h after i.v. administration (0.5 mg/kg, b.w.) in chicken.

The mean MRT value of meloxicam with enrofloxacin (3.44±0.11 h) was significantly ($p<0.01$) lower in healthy turkeys as compared to meloxicam alone (3.95±0.10 h). Baert and Backer [25] also reported reported MRT value (4.41 h) of meloxicam similar to this study in chicken after i.v. administration (0.5 mg/kg, b.w.).

The mean Vd_{area} of meloxicam with enrofloxacin (0.19±0.02 L/kg) did not differ significantly as compared with meloxicam alone (0.21±0.01 L/kg). Baert et al. [26] also reported Vd_{area} equal to 0.58 L/kg of meloxicam alone in ostrich after i.v administration (0.5 mg/kg, b.wt.).

The mean Cl_B value of meloxicam with enrofloxacin (0.87±0.08 ml/kg/min) also did not differ significantly as copmpared with meloxicam alone (0.81±0.04 ml/kg/min). Results indicated that meloxicam did not affect the pharmacokinetic profile of enrofloxacin.

The mean AUC value of meloxicam with enrofloxacin (20.21±1.96 µg/L.h) did not differ significantly from meloxicam alone (20.74±0.92 mg/Lh). Busch et al. [27] reported AUC (24.1 mg/L.h) after i.v. administration in dog (0.2 mg/kg, b.w.).

Based on pharmacokinetic studies ENR may be injected at dose of 4.5 mg/kg b.w. i.v. at an interval of 20.38 h in turkeys.

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References

1. Altreuther P (1987) Data on chemistry and toxicology of Baytril. Vt Med Rev 2: 87-89.
2. Chu DTW, Fernandes PB (1989) Structure activity relationship of the fluroquinolones. Antimicrob Agent Chemother 33: 131-135.
3. Andriole VT (ed) (1998) The quinolones Academic Press, Inc; New York.
4. Sharma S, Sher P, Badve S, Pawar AP (2005) Adsorption of meloxicam on porous calcium silicate: Characterization and tablet formulation. AAPS Pharm Sci Tech 6: 618-625.
5. Engelhardt G, Thomae K (1996) Pharmacology of meloxicam, a new non steroidal anti-inflammatory drug with an improved safety profile through preferential inhibition of Cox-2. British J Rheumatology 35: 4-12.
6. Crandell DE, Mathews KA, Dyson DH (2004) Effect of meloxicam and carporofen on renal function when administered to healthy dogs prior to anaesthesia and painful stimulation. Am J Vet Res 65: 1384-1390.
7. Alencar MMA, Pinto MT, Oliveira DM, Pessoa AW.de.P.; Candido. I.A.; Gomes, C.V.; Coelho, H.S.M. and Rocha, M.F.G (2002) Evaluation of the pharmacologic ativity of meloxican on renal function in dogs. Ciencia Animal 12: 25-33
8. Vane JR, Botting RN (1995) New insight into the mode of action of anti-inflammatory drugs. Inflamm Res 44: 1-10.
9. Türck D, Roth W, Busch U (1996) A review of the clinical pharmacokinetics of meloxicam. Br J Rheumatol 35:13–16.
10. Anadon A, Martinez–Larranga MR, Diaz MJ, Bringas P, Martinez MA. (1995). Pharmacokinetics and residues of enrofloxacin in chicken. Am J Vet Res 56: 501-506.
11. Shukla M, Singh G, Sindhura BG, Telang AG. Rao GS, et al. (2007) Comparative plasma pharmacokinetics of meloxicam in sheep and goat following intravenous administration. Comp Biochem Physiol C Toxicol Pharmacol 145(4): 528-532.
12. Notari RE (1980) Biopharmaceutics and Clinical pharmacokinetics (3rdedn). Marcel Dekker, INC, New York.
13. Baggot JD (1977) Principles of drug disposition in domestic animals. The basis of Veterinary Clinical Pharmacology. (1stedn), W.B. Saunders company Philadelphia, London, Toranto.
14. Ruoff WW Jr, Sams RA (1985) Pharmacokinetics and bioavailability of cephalothin in horses and mares. Anim. J Vet Res 46 (10): 2085-2090.
15. Shargel L (1985) Applied biopharmaceutics and pharmacokinetics. Appletum Century (Raft), New York, Conneilicut, America.

16. Snedecor CW, Cochran WG (1994) Statistical methods. 6th edn. Iowa State Univ. Press, Ames, USA.

17. Tansakul N, Poapolathep A, Klangkaew N, Phaochoosak N, Passudaruk (2005) Pharmacokinetics and withdrawal times of enrofloxacin in ducks. *Kasetsart Journal Animal Sciences* 39: 235-239.

18. Scheer M (1987) Studies on the antimicrobial activity of baytril. *Vet Med Rev* 2:90-99.

19. Bauditiz R (1990) Enrofloxacin-clinical evaluation in several animals. In F. Simon.; Lwess; P. and Semjen, G, (eds). Veterinary Pharmacology, Toxicology and Therapy in Food producing animals. *(University of Vety. Sci. Unipharam Co. Ltd. Budopest);* 21-26.

20. Ranjan (2008) Pharmacokinetic studies of ceftizoxime and its interaction with meloxicam in healthy and febrile sheep. M.V.Sc. Thesis submitted to Birsa Agricultural University, Ranchi, Jharkhand, India.

21. Kanemaki N, Matsura K, Yashiro N, Takasu K, Ushirodo H (1995) Pharmocokinetics of enrofloxacin in dogs. *J Jap Vet Med Assoc* 48:957-959.

22. Ahmed FA, Sheikh IU, Saud N, Singh SK, Baruah, et al. (2006) *Indian journal of animal sciences*. National Research centre on Yak (ICAR); Dirang, Arunchal Pradesh, India.

23. Dosi BS, Bhate AD, Chauhan BL, Parkar TA, Kulkarni RD (1986). Pharmacokinetic interaction of oralrifampicin and isoniazid in normal subjects. Indian Drug 23: 672-676.

24. Lucas JJ, Codriguez C, Waxma S, Gonzalas F, De Viante ML,et al. (2004) Pharmacokinetics of enrofloxacin after single intravenous and intramascular administration in young domestic ostrich. *J Vet Pharmacol Ther* 27: 119-122.

25. Baert K, De Backer P (2003) Comparative pharmacokinetics of three non-steroidal anti-inflammatory drugs in five bird species. Comp Biochem Physiol C Toxical Pharmacol 134: 25-33.

26. Baert K, Nackaerts J, De Backer P (2002) Disposition of sodium salicylate; flumixin and meloxicam after intravenous administration in ostriches. (*Structhio Camelus) J Av Md and Surgery* 16: 123-128.

27. Bush U, Schmid J, Heinzel G, Schmaush H, Baierl J (1998) Drug Metabolism and disposition of meloxicam in animals and relevance to humans. Department of pharmacokinetics, Boehringer Ingelheim pharma KG, Drug Metab Dispos 26: 576-584.