ABSTRACT
Pharmacokinetics of enrofloxacin (Fortius® - Virbac Animal Health India Pvt. Ltd., Mumbai, India) was studied in five albino rats following intraperitoneal (i.p.) administration (5 mg/kg). Estimation of enrofloxacin in plasma was analyzed by microbiological assay technique (cylinder plate diffusion method) using E. coli (ATCC 25922) as the test organism. Kinetic parameter of enrofloxacin was calculated by using one-compartment open model. Therapeutic concentration of 0.12 µg/ml was maintained up to 72 h and the drug was also detectable up to 72 h. Absorption half life ($t_{1/2}^{Ka}$), elimination half life ($t_{1/2}^{β}$), mean residence time (MRT), Volume of distribution during area under curve ($V_{d_{area}}$) and total body clearance ($Cl_{B}$) of 5.83 ± 1.24 h, 42.84 ± 2.43 h, 66.87 ± 2.48 h, 6.76 ± 0.30 l/kg and 1.87 ± 0.18 ml/kg/min, respectively were obtained for enrofloxacin in albino rats. The in vitro protein binding percent of enrofloxacin in albino rats ranged from 37% to 44% with average of 41.23 %. The AUC/MIC$_{90}$ for a successful clinical/microbiological outcome of >100–125 was achieved at MIC$_{90}$ of 0.25 µg/ml and optimal $C_{P}^{O}$/MIC (>10) was attained at MIC$_{90}$ of 0.125 µg/ml in albino rats. The highest enrofloxacin MIC$_{90}$ of bacteria that fulfills the minimum AUC/MIC ratio (>100) for the present dosage regimen is 0.25 µg/ml. To achieve the optimal $C_{P}^{O}$/MIC (>10), the present dosing regimen would allow an MIC$_{90}$ of 0.125 µg/ml for Gram-negative and Gram-positive pathogens. For maintaining therapeutic concentration of 0.125 µg/ml, a loading dose (D*) of around 3 mg/kg and maintenance dose (D$_{0}$) of 2 mg/kg may be used at the dosage interval (τ) of 72 h for treating systemic infections in albino rats.

Key words: Disposition kinetics, in vitro plasma protein binding, enrofloxacin, albino rats.

INTRODUCTION
Enrofloxacin [1-cyclopropyl-7- (4-ethyl-1-piperazinyl) - 6- fluoro - 1, 4 –dihydro – 4 – oxo – 3- quinoline carboxylic acid] is a recent fluorinated quinolone carboxylic acid derivatives developed exclusively for veterinary use [1]. It effectively penetrates all organs...
and tissues and the distribution pattern is more or less similar in all species. In different species, enrofloxacin is de-ethylated to ciprofloxacin \textit{in vivo} \cite{2}, which is also a potent antimicrobial agent used in human medicine \cite{3}. Both enrofloxacin and ciprofloxacin are bactericidal at very low concentrations for a broad spectrum of gram-negative and gram-positive bacteria as well as mycoplasmas \cite{4}. Pharmacokinetic studies of enrofloxacin in healthy albino rats was carried out to obtain the detailed pharmacokinetic data and so as to derive appropriate dosage regimen of enrofloxacin to treat various systemic infections.

MATERIALS AND METHODS

Experimental animals

Five clinically healthy adult albino rats of either sex weighing between 200 to 250 g body weights were used. The rats were kept in colony cage and maintained under hygienic condition in the department of veterinary pharmacology and toxicology and provide standard rodent diet as well as \textit{ad libitum} clean drinking water with the help of rodent drinking bottle. All animals were kept under the same experimental conditions with natural day and night cycle. The animals did not receive any drug treatment before the study. The study was approved by instutional ethical committee of College of Veterinary Science and Animal Husbandry, Mhow, Madhya Pradesh, India.

Dosage forms

Enrofloxacin (Fortius\textsuperscript{®} - 10\%) - an injectable single application commercial preparation containing enrofloxacin in concentration of 100 mg/ml marketed by Virbac Animal Health India Pvt. Ltd., Mumbai, India was used in the present study. Enrofloxacin (5 mg/kg, i.p.) was given in each of the five albino rats.

Experimental design

The animals were individually weighed immediately before administering the drug in order to determine the precise dose. Enrofloxacin (5 mg/kg) was injected intraperitoneally in each albino rats and blood samples (approx.0.5 ml) were withdrawn from the infra orbital sinus through an inner medial canthus of eye into heparinised glass centrifuge tubes before and at 0.083, 0.25, 0.50, 0.75, 1, 1.5, 2, 4, 6, 8, 12, 24, 48 and 72 h post drug administration. Blood samples were centrifuged at 3000 r.p.m. for 15 min at room temperature in order to separate plasma and kept at - 4\(^\circ\)C until analysis, which was usually done on the day of collection.
Analytical method

The plasma samples were assayed by a standard microbiological assay technique \cite{5} using *Escherichia coli* (ATCC 25922) as the test organism. The six wells, 8 mm in diameter, were cut at equal distances into a (120 × 120 mm) petriplate containing 25 ml of seeded agar. The test organism was grown in nutrient broth for 1/2 to 1 hour at 37°C until the growth was seen (turbid by naked eye). Enrofloxacin assay plates were flooded with the broth containing the organism and excess broth was drained out after some time. The plates were dried in the incubator at 37°C for a period of about an hour. The wells were filled with the test samples and/or an enrofloxacin standard solution (prepared from a commercial solution). Standard curve of enrofloxacin was prepared in pooled antibacterial-free plasma. The standards and samples were tested in triplicate. The plates were kept at room temperature for 2 h before being incubating at 37°C for 18 h. The mean inhibition zone diameters were measured and the concentrations in the plasma samples were calculated from the standard curve. The standards were included in each assay plate in order to compensate for any plate-to-plate variations. There was a linear relationship between the zone of inhibition and the logarithm of the plasma enrofloxacin concentration with a correlation coefficient of 0.99. The reproducibility of this method was excellent and the inter-assay variability was < 5%. The limit of quantitation was 0.04 μg/ml. A standard curve was considered acceptable if the quality control samples were within 15% of the nominal concentration.

Pharmacokinetic analysis

The plasma concentration-time profile of enrofloxacin plotted on a semi-logarithmic scale after intraperitoneal administration in each animal was used to establish various disposition kinetic determinants and mean kinetic variables were obtained by averaging the variables calculated for individual animals.

The log plasma drug concentrations versus time profile for each rat were analyzed according to the computed least square regression technique. The kinetic parameters were calculated manually by applying one-compartment open model as described \cite{6}. The concentration of the drug in plasma at any time is obtained by the following formula (Eqn. 1):

\[
C_p = B e^{\beta t} - A e^{-K_a t}
\]  
(Eqn. 1)
where, $C_p$ is the plasma level of enrofloxacin at time $t$ and $e$ represents the base of natural logarithm, $A'$ and $B$ are the extrapolated zero-time intercepts of the absorption and elimination phases, respectively, $K_a$ and $\beta$ are the absorption and elimination rate constants, respectively.

The ultimate objective of present disposition study was to compute dosage regimen of enrofloxacin in albino rats for the treatment of infectious diseases. Appropriate loading ($D^*$) and maintenance ($D_0$) dose for maintaining minimum therapeutic concentration ($C_p^{\infty \text{min}} = \text{MIC}$) of 0.125, 0.25 and 0.5 $\mu$g/ml at desired dosage interval ($\tau$) of 24, 48 and 72 h were also derived$^{[7]}$ as per the following equation (Eqn. 2 & 3):

$$D^* = C_p^{\infty \text{min}} . V_{d\text{area}} . (e^{\beta \cdot \tau})$$  
(Eqn. 2)

$$D_0 = C_p^{\infty \text{min}} . V_{d\text{area}} . (e^{\beta \cdot \tau} - 1)$$  
(Eqn. 3)

### Protein binding

Drug concentration of 1, 2, 3, 4 and 5 $\mu$g/mL were added to the plasma of albino rats and binding of enrofloxacin was determined in vitro based on the diffusion of free antibiotic into the agar medium$^{[8]}$. The concentration of enrofloxacin in phosphate buffer and plasma were estimated by microbiological assay. The differences in the diameters of the inhibition zones between the solutions of the drugs in the buffer and plasma samples were calculated.

### Pharmacodynamic efficacy / Efficacy predictors

Clinical and microbiological outcomes of enrofloxacin therapy can be predicted by the site of infection and in terms of pharmacokinetic – pharmacodynamic (PK/PD) relationships based on $C_{\text{max}}$ : MIC and the AUC : MIC ratio$^{[9]}$. The pharmacodynamic efficacy of enrofloxacin was determined by calculating $\frac{C_{p}^{O}}{\text{MIC}_{90}}$ and AUC/MIC ratios following i.p. administration of drugs. In order to calculate the PK/PD efficacy predictors hypothetical MIC values were used. The minimum therapeutic concentration (MIC$_{90}$) value of enrofloxacin for different species of microorganisms ranged between 0.001 to 1.0 $\mu$g/ml$^{[10]}$. Keeping in mind the synergistic effect of the body immune system and other in vivo factors as well as to cover most of the susceptible organisms, the MIC$_{90}$ of 0.125, 0.25 and 0.5 $\mu$g/ml are taken into consideration. In the
present investigation, a MIC\textsubscript{90} of 0.125 µg/ml of enrofloxacin was taken into consideration for discussion.

**RESULTS**

Clinical examination of all animals before and after each trial did not reveal any abnormalities. No serious adverse events of enrofloxacin were observed throughout the study. The plasma concentrations (µg/ml) of enrofloxacin at different time interval in albino rats following single intraperitoneal administration of enrofloxacin (5 mg/kg, b.wt.) were depicted in Figure 1. Enrofloxacin concentrations were present in plasma from 0.083 to 72 h. The mean peak plasma concentration of enrofloxacin was observed 2.66 ± 0.03 µg/ml at time intervals of 1 h and plasma concentrations gradually declined up to 72 h. The minimum therapeutic concentration (≥ 0.125 µg/ml) of enrofloxacin was maintained throughout from 0.083 to 72 h.

![Figure 1](image)

**Figure 1**

Plasma concentrations (µg/ml) of enrofloxacin in albino rats

The values of different kinetic parameters of enrofloxacin such as the absorption rate constant (Ka) and absorption half-life (t\textsubscript{1/2} Ka) of enrofloxacin was noted to be 0.157 ± 0.05 h\textsuperscript{-1} and 5.83 ± 1.24 h, respectively and the elimination rate constant (β), elimination half life (t\textsubscript{1/2} β), area under curve (AUC), area under first moment curve
(AUMC), mean residence time (MRT), volume of distribution at area under curve (Vd\text{area}) and total body clearance (Cl_B) of enrofloxacin were depicted in Table 1.

**Table 1:** shows kinetic parameters of enrofloxacin in albino rats calculated by one compartment open model following single intraperitoneal (i.p.) dose @ 5 mg/kg b.wt.

<table>
<thead>
<tr>
<th>PK parameters (Unit)</th>
<th>Enrofloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (µg/ml)</td>
<td>0.49 ± 0.05</td>
</tr>
<tr>
<td>B (µg/ml)</td>
<td>0.82 ± 0.01</td>
</tr>
<tr>
<td>C_p^0 (µg/ml)</td>
<td>1.31 ± 0.04</td>
</tr>
<tr>
<td>Ka (h\text{^{-1}})</td>
<td>0.157 ± 0.05</td>
</tr>
<tr>
<td>t_{1/2} Ka (h)</td>
<td>5.83 ± 1.24</td>
</tr>
<tr>
<td>β (h\text{^{-1}})</td>
<td>0.016 ± 0.001</td>
</tr>
<tr>
<td>t_{1/2} β (h)</td>
<td>42.84 ± 2.43</td>
</tr>
<tr>
<td>AUC (µg/ml.h)</td>
<td>46.44 ± 4.39</td>
</tr>
<tr>
<td>AUMC (µg/ml.h^2)</td>
<td>3141.93 ± 396.79</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>66.87 ± 2.48</td>
</tr>
<tr>
<td>K_{12} (h\text{^{-1}})</td>
<td>0.039 ± 0.01</td>
</tr>
<tr>
<td>K_{21} (h\text{^{-1}})</td>
<td>0.110 ± 0.04</td>
</tr>
<tr>
<td>Kel (h\text{^{-1}})</td>
<td>0.024 ± 0.002</td>
</tr>
<tr>
<td>Fc</td>
<td>0.691 ± 0.01</td>
</tr>
<tr>
<td>T ≈ P</td>
<td>0.465 ± 0.03</td>
</tr>
<tr>
<td>Vd_C (L/kg)</td>
<td>3.83 ± 0.14</td>
</tr>
<tr>
<td>Vd_B (L/kg)</td>
<td>6.08 ± 0.07</td>
</tr>
<tr>
<td>Vd\text{area} (L/kg)</td>
<td>6.76 ± 0.30</td>
</tr>
<tr>
<td>Vd\text{SS} (L/kg)</td>
<td>5.21 ± 0.17</td>
</tr>
<tr>
<td>Cl_B (ml/kg/min)</td>
<td>1.87 ± 0.18</td>
</tr>
</tbody>
</table>

Where, A = zero time intercept for distribution phase; B = zero time intercept for elimination phase; C_p^0 (µg/ml) = theoretical zero time concentration (A+B); Ka = absorption rate constant; t_{1/2} Ka = absorption half life; β = elimination rate constant; t_{1/2} β
IC VALUE – 4.01

\[ t = \text{elimination half life}; \text{AUC} = \text{total area under plasma drug concentration curve}; \text{AUMC} = \text{area under first moment curve}; \text{MRT} = \text{mean residential time}; K_{12} = \text{rate constant of drug transfer from central compartment to peripheral compartment}; K_{21} = \text{rate constant of drug transfer from peripheral to central compartment}; K_{el} = \text{rate constant of drug elimination from central compartment}; F_{c} = \text{fraction of drug available for elimination from central compartment}; T \approx P = \text{approximate tissue to plasma concentration ratio}; V_{d_{\text{area}}} = \text{apparent volume of distribution}; V_{d_{SS}} = \text{volume distribution at steady state}; C_{l_{B}} = \text{total body clearance.}

The dosage regimen to maintain the different levels of therapeutic concentrations in plasma for i.p. route in albino rats at different dosage intervals are presented in Table 2. For maintaining $C_p\infty$ min of $0.125 \mu g/ml$, the loading doses ($D^*$) were calculated to be $1.87 \pm 0.16$ and $2.80 \pm 0.30 \text{ mg/kg}$ while maintenance doses ($D_0$) were calculated to be $1.03 \pm 0.12$ and $1.96 \pm 0.26 \text{ mg/kg}$ at dosage interval ($\tau$) of 48 and 72 h, respectively. Likewise, $D^*$s and $D_0$s were derived for maintaining $C_p\infty$ min of $0.25$ and $0.5 \mu g/ml$ at $\tau$ of 48 and 72 h (Table 2).

**Table 2:** shows calculated dosage regimens of enrofloxacin in albino rats for intraperitoneal route.

<table>
<thead>
<tr>
<th>$C_p\infty$ min ($\mu g/ml$)</th>
<th>$\tau$ (h)</th>
<th>Dose (mg/kg)</th>
<th>Enrofloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>48</td>
<td>$D^*$</td>
<td>$1.87 \pm 0.16$</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>$D_0$</td>
<td>$1.03 \pm 0.12$</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>$D^*$</td>
<td>$2.80 \pm 0.30$</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>$D_0$</td>
<td>$1.96 \pm 0.26$</td>
</tr>
<tr>
<td>0.25</td>
<td>48</td>
<td>$D^*$</td>
<td>$3.75 \pm 0.32$</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>$D_0$</td>
<td>$2.06 \pm 0.25$</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>$D^*$</td>
<td>$5.60 \pm 0.59$</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>$D_0$</td>
<td>$3.91 \pm 0.52$</td>
</tr>
<tr>
<td>0.50</td>
<td>48</td>
<td>$D^*$</td>
<td>$7.50 \pm 0.64$</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>$D_0$</td>
<td>$4.12 \pm 0.49$</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>$D^*$</td>
<td>$11.21 \pm 1.19$</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>$D_0$</td>
<td>$7.83 \pm 1.05$</td>
</tr>
</tbody>
</table>

Where,
$D^*$ = Loading dose, $D_0$ = Maintenance dose, $\tau$ = Dosage interval, $C_p\infty$ min = Minimum therapeutic concentration in plasma (MIC).
The individual PK/PD ratios for the assumed MIC\textsubscript{90} values for enrofloxacin are summarized in Table 3. The threshold AUC/MIC\textsubscript{90} for a successful clinical/microbiological outcome of >100–125 was achieved at MIC\textsubscript{90} of 0.25 µg/ml and optimal C\textsuperscript{O}\textsubscript{p}/MIC (>10) was attained at MIC\textsubscript{90} of 0.125 µg/ml in albino rats. The highest enrofloxacin MIC\textsubscript{90} of bacteria that fulfills the minimum AUC/MIC ratio (>100) for the present dosage regimen is 0.25 µg/ml. To achieve the optimal C\textsuperscript{O}\textsubscript{p}/MIC (>10), the present dosing regimen would allow an MIC\textsubscript{90} of 0.125 µg/ml for Gram-negative and Gram-positive pathogens.

**Table 3:** depicts efficacy predictors (C\textsuperscript{O}\textsubscript{p}/MIC and AUC/MIC) estimated for enrofloxacin in albino rats using different MIC values.

<table>
<thead>
<tr>
<th>MIC 0.125 (µg/ml)</th>
<th>MIC 0.25 (µg/ml)</th>
<th>MIC 0.5(µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C\textsuperscript{O}\textsubscript{p}/MIC</td>
<td>10.48</td>
<td>5.24</td>
</tr>
<tr>
<td>AUC/MIC</td>
<td>371.52</td>
<td>135.76</td>
</tr>
</tbody>
</table>

For calculations the applied values were: C\textsuperscript{O}\textsubscript{p} = 1.31 µg/ml, AUC = 46.44 µg/ml.h in albino rats.

**DISCUSSION**

In the current investigation, we measured the residual concentrations of enrofloxacin in the plasma of albino rats using the microbial inhibition test. The reasons that we selected the bioassay are: (a) the bioassay measures the total activity, which could be more useful for pharmacodynamic evaluations than HPLC \cite{11}; (b) congruent results between the data determined by the microbiological assay and those determined by HPLC \cite{12}; and (c) the bioassay method is precise, reproducible, and does not require specialized equipment or toxic solvents \cite{13}. For these reasons, the application of microbiological assay for measuring enrofloxacin concentration is suitable \cite{14}.

The minimum inhibitory concentration (MIC\textsubscript{90}) values of enrofloxacin for different species of microorganisms ranged between 0.001 to 1.0 µg/ml \cite{10}. Hence, in the present investigation, the dosage regimen of enrofloxacin was calculated at three different therapeutic levels (0.125, 0.25 and 0.5 µg/ml) and at two dosage intervals (48 and 72 h).
As compared to the present study, a shorter $t_{1/2}$ of $2.82 \pm 0.33$ h in goat\[^{15}\], $2.5$ h\[^{16}\] & $2.19$ h\[^{17}\] in rabbit and $2.4$ h\[^{18}\] & $3$ h\[^{19}\] in dog were reported after i.v. administration of enrofloxacin. However, a very lower $t_{1/2}$ of $0.734$ h (enrofloxacin) and $0.934$ h (ciprofloxacin)\[^{20}\], $0.734$ h\[^{21}\] and $1.7$ h\[^{22}\] were noted in cows after i.v. administration of enrofloxacin. A very lower $t_{1/2}$ of $1.97 \pm 0.23$ h was noted in buffalo bulls\[^{23}\] and very lower value of $0.74$ h (enrofloxacin) and $1.38$ h (ciprofloxacin) in goats were noted\[^{24}\]. The much higher $t_{1/2}$ of $42.84 \pm 2.43$ h obtained in the present study indicate comparatively the much slower removal of enrofloxacin from the body of albino rats as compared to above noted species. This is further supported by very lower value of rate constant of drug elimination from central compartment ($K_e$) obtained for enrofloxacin in albino rats ($0.024 \pm 0.002$ h\(^{-1}\)).

A volume of distribution of $0.6$ L/kg\[^{20,21}\] and $1$ L/kg\[^{22}\] in cows, $0.61 \pm 0.13$ L/kg in buffalo bulls\[^{23}\], $2$ L/kg\[^{25}\] and $0.77 \pm 0.11$ to $1.22 \pm 0.07$ L/kg\[^{26}\] and $2.3$ L/kg\[^{27}\] in horses, $2.49 \pm 0.43$ L/kg in foals\[^{28}\], $3.02 \pm 0.22$ L/kg in sheep\[^{29}\] and $2.34 \pm 0.54$ L/kg in goats\[^{15}\] were reported while a very high volume of distribution (Table 2) was noted in the present study. This may suggest that enrofloxacin may be distributed well in body tissues and fluids in albino rats than all above noted species, which may also be beneficial for treating systemic microbial infections in albino rats.

$Cl_B$ values of enrofloxacin were noted to be $1.87 \pm 0.18$ ml/kg/min in the present study. More or less similar $Cl_B$ values of $1.73$ ml/kg/min in foals\[^{28}\] and $1.50 \pm 2.33$ ml/kg/min in horses\[^{26}\] were noted for enrofloxacin. However, a very longer $Cl_B$ value of $27.1$ ml/kg/min in dogs\[^{18}\], $22.8 \pm 6.8$ mL/kg/min in rabbits\[^{17}\], $9.27 \pm 2.40$ ml/kg/min in sheep\[^{29}\] and $9.40 \pm 1.36$ ml/kg/min in goats\[^{15}\] were obtained after i.v. administration of enrofloxacin.

Variation among species, breed, sex, age and different methods for estimation of drugs may contribute to the wide discrepancies in kinetic parameters as suggested by various workers\[^{30}\].

The major objective of the present study was to calculate and modify the dosage regimen of enrofloxacin. Enrofloxacin may be routinely used at the dose rate of $2.8$ mg/kg as loading dose ($D*$) and $2$ mg/kg as maintenance dose ($D_0$) for maintaining MIC
of 0.125 µg/ml at the dosage interval (τ) of 72 h for treating septicemia and any other systemic infections in albino rats. For treating severe infections (MIC = 0.25 and 0.5 µg/ml), the suggested D* and D₀ may be used (Table 3).

The *in vitro* protein binding percent of enrofloxacin in albino rats ranged from 37% to 44% with average of 41.23 %. The extent of binding of enrofloxacin to the plasma proteins of albino rats (41.23 %) in the present study was in accordance to the corresponding values of 36-45% for enrofloxacin\[22\] in cattle, 24-38% for levofloxacin in man\[31\] and 17.0 ± 1.2% in calves for levofloxacin\[32\] as well as 26% for danofloxacin\[33\], 17- 24% for orbifloxacin in horses\[34\] and 34.5% for moxifloxacin in lactating ewes\[35\] have been recorded. The drug was mainly bound to albumin, and the binding was fully reversible. This low degree of protein binding will not inhibit distribution of the drug to the interstitial fluid (the site of action for most antibacterial drugs), and interstitial fluid drug concentrations are expected to equal the plasma concentrations\[34\].

There is general consensus that the clinical and microbiological outcomes of fluoroquinolone treatment are favourable and selection of a mutant subpopulation is preventable if an AUC/MIC ≥ 100–125 and a C\(_{\text{max}}\)/MIC of 10 are achieved in Gram-negative infections\[36,37\]. For Gram-positive pathogens, the minimum required C\(_{\text{max}}\)/MIC is also 10, while the optimum AUC/MIC target values are still a topic of debate\[36\]. An AUC/MIC of 30–50 is claimed to be optimal in numerous studies performed mainly in *in vitro* or animal models \[38\]. Other studies conducted on different patient populations suggested a minimum AUC/MIC of 87-125 to achieve a favourable outcome and to avoid development of resistance regardless of whether the organism is Gram-positive or Gram-negative\[37\].

Considering the AUC/MIC\(_{90}\) and C\(_{\text{P}}^{0}\)/MIC\(_{90}\) ratios obtained in the present study, it can be stated that enrofloxacin administered intraperitoneally in the dosing schedule applied is efficacious against bacteria with MIC\(_{90}\) values under 0.125 µg/ml in albino rats. The high value of AUC/MIC\(_{90}\) (371.52) and C\(_{\text{P}}^{0}\)/MIC\(_{90}\) (10.48) obtained in the present study, provides support for excellent clinical and bacteriological efficacy of enrofloxacin in albino rats. In agreement with the present results, a C\(_{\text{max}}\)/MIC ratio of more than 10 has been reported following subcutaneous administration of both
danofloxacin and enrofloxacin in calves\textsuperscript{[39]}. The AUC/MIC ratio was higher in present study than the values of 76.6 reported for levofloxacin administered intramuscularly in calves\textsuperscript{[32]} and for other fluoroquinolones, 40.7 for marbofloxacin in cows\textsuperscript{[40]}. However, it is necessary to note that the numerical values of AUC/MIC\textsubscript{90} and \( C_{\text{max}}/\text{MIC}_90 \) used as a surrogate marker to predict optimal dosage, have been generated in experimental infections in laboratory animals or in human clinical trials\textsuperscript{[41]}.

**CONCLUSION**

In conclusion, the fact that general adverse reactions were not observed in any albino rats and favourable pharmacokinetic properties of enrofloxacin, such as long half-life and high bioavailability with wide penetration into different body fluids and tissues from blood, were found. Based on the calculated AUC/MIC\textsubscript{90} and \( C^0_{\text{p}}/\text{MIC}_90 \), a dosage of 3 mg/kg could be effective in albino rats \( \text{MIC}_90 \geq 0.125\mu\text{g/ml} \) following intraperitoneal route.

**ACKNOWLEDGEMENT**

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**REFERENCES**


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