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Effect of tolfenamic acid on disposition kinetics of marbofloxacin on goats

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LIST OF ABBREVIATIONS

MFX	Marbofloxacin
TA	Tolfenamic acid
A	Zero-time intercept of the distribution slope
α	Distribution rate constant
B	Zero-time intercept of decline in serum concentration of drug
β	Elimination rate constant.
k_{10}	First-order elimination rate constant from central compartment.
k_{12}	Rate constant for passage from central to peripheral compartment.
k_{21}	Rate constant for passage from peripheral to central compartment.
k_{ab}	Absorption rate constant.
$t_{1/2\alpha}$	The distribution half-life.
$t_{1/2\beta}$	Elimination half-life.
$t_{1/2ab}$	Absorption half-life.
T_{max}	The time at which the maximum concentration of drug was reached after extra vascular administration (h).
C^0	Plasma drug concentration at t=0(Immediately) following drug administration.
C_{max}	Maximum serum concentration of drug in blood after extravascular administration (μg/ml).
Cl	Total body clearance.
CL_2	Inter-compartmental clearances.
V_1	Apparent volume of central compartment.
V_2,	Apparent volume of peripheral compartment.
V_{dss}	Volume of distribution at steady state.
AUC_{0-t}	Area under the [plasma drug concentration versus time] curve.
$AUC_{0-\infty}$	Total area under the concentration–time curve from zero to infinity.
AUMC	Area under the first moment curve.
MRT	Mean residence time.
F %	Bioavailability.
Fu	Free drug in serum
LOD	Limits of detection
LOQ	Limit of quantification

7. SUMMARY

In the present work, the pharmacokinetic parameters of marbofloxacin (2mg/kg b.wt.) after intravenous and intramuscular administration either alone or in combination with tolfenamic acid (2mg/kg b.wt.) in adult male goats were studied. This experiment was studied in twenty four clinically normal adult male goats. Goats were divided into 4 groups. The first and second group consisted of six goats each allocated for the pharmacokinetic study of marbofloxacin after intravenous administration either alone or in combination with tolfenamic acid. The third and fourth group consisted of six goats each allocated for the pharmacokinetic study of marbofloxacin after intramuscular administration either alone or in combination with tolfenamic acid. Also *in-vitro* antibacterial activity of marbofloxacin against *E.coli, Salmonella typhimurium* and *staphylococcus aureas* was studied by the agar well diffusion method.

Following a single intravenous injection of marbofloxacin 2mg/kg b.wt.in adult male goats, marbofloxacin could be detected till 24hours post intravenous injection with mean values 0.12±.0.013 μg/ml. The plasma concentration-time data of marbofloxacin following intravenous injection showed that the drug was best fitted to a two compartments open model.

Marbofloaxcin after intravenous injection in adult male goats revealed a distribution phase (α=3.98±0.82 μg/ml) with a distribution half-life ($t_{1/2\alpha}$) of 0.79±0.18h. The volume of distribution to central compartment (V_1) was 0.59±0.03 (mg)/(μg/ml), whereas the volume of distribution to peripheral compartment (V_2) was 0.65±0.14 (mg)/(μg/ml). At steady state (Vdss), it was 1.25±0.16 (mg)/(μg/ml). Marbofloxacin was transferred from central to peripheral compartment (K_{12}) at 0.39±0.08 μg/ml and transferred from peripheral to central compartment (K_{21}) 0.38±0.16 μg/ml. Marbofloxacin was eliminated after intravenous injection with a half-life ($t_{1/2\beta}$) value of 7.01±1.55h

and cleared by all clearance processes in the body at a rate of 0.15±0.01 (mg)/(µg/ml)/h.

After single intravenous injection of marbofloxacin in combination with tolfenamic acid in adult male goats marbofloxacin could be detected till 24hours post injection with mean values 0.15± 0.009µg/ml. It revealed a distribution phase (α=9.22±0.994 µg/ml) with a distribution half-life ($t_{1/2\alpha}$) of 0.074±0.008h. The volume of distribution to central compartment (V_1) was 0.440±0.021 (mg)/(µg/ml) , whereas the volume of distribution to peripheral compartment (V_2) was 0.243±0.021 (mg)/(µg/ml). At steady state (Vdss), it was 0.683 ±0.003 (mg)/(µg/ml). Marbofloxacin was transferred from central to peripheral compartment (K_{12}) at 3.275±0.652 µg/ml and transferred from peripheral to central compartment (K_{21}) 5.859±0.352 µg/ml. Marbofloxacin was eliminated after intravenous injection with a half-life ($t_{1/2\beta}$) value of 4.517±0.091h and cleared by all clearance processes in the body at a rate of 0.106±0.002 (mg)/(µg/ml)/h.

Following a single intramuscular administration of marbofloxacin at a dose of 2mg/kg b.wt. in adult male goats, the drug reached its maximum plasma concentrations after 1.290 hours of administration with value equal to 1.162±0.071µg/ml. Marbofloxacin could be detected in plasma till 24 hours post intramuscular dose with value equal to 0.25±0.018µg/ml. The pharmacokinetic parameters revealed that the absorption half-life ($t_{1/2ab}$) was 0.629±0.067 hours, the elimination half-life $t_{1/2\beta}$ was 7.141±0.808h and marbofloxacin was cleared by all clearance processes (Cl) with rate equal to 0.054±0.004 (mg)/(µg/ml)/h.

Following a single intramuscular administration of marbofloxacin at a dose of 2mg/kg b.wt. in adult male goats, the drug reached its maximum plasma concentrations after 1.378hours of administration with value equal to 1.703±0.034µg/ml. Marbofloxacin could be detected in plasma till 24 hours post intramuscular dose with value equal to 0.151± 0.008 µg/ml. The pharmacokinetic

parameters revealed that the absorption half-life ($t_{1/2ab}$) was 0.629±0.038 hours, the elimination half-life t1/2β was 6.523±0.27h and marbofloxacin was cleared by all clearance processes (Cl) with rate equal to 0.131±0.002 (mg)/(µg/ml)/h.

Regarding our result tolfenamic acid may be successfully co-administrated with marbofloxacin for combating sensitive bacterial infections with inflammatory conditions. Tolfenamic acid may be administered with marbofloxacin by i.m and i.v routes. It is reasoned that administration of Tolfenamic with marbofloxacin in goats would improve its kinetic profiles. Further studies are however required to buttress these findings and establish the mechanism of interaction.