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Effects of Piroxicam on Pharmacokinetics of Sulphadimidine in West African Dwarf Male and Female Goats (*Capra hircus*)

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Abstract

Sulphadimidine is used in the treatment of susceptible enteric bacteria that could cause enteritis and since piroxicam is a potent anti-inflammatory agent, it is co-administered with piroxicam intramuscularly. In view of this, effects of piroxicam on the pharmacokinetics of sulphadimidine were studied in West African Dwarf (WAD) goats. Twenty goats of both sexes, aged 1-year-old and weighing 10.4 ± 1.3 kg were divided into two groups of 10 each (5 males; 5 females) were administered 100 mg/kg body weight of sulphadimidine via right thigh muscle, whereas piroxicam (5 mg/kg) was administered to WAD goats (5 males; 5 females). Blood samples were collected over a range of time (0-192 hrs) and analyzed for presence of sulphadimidine. The results showed significant increase ($p<0.05$) in time maximum (T_{max}=1.90 ± 0.45 hr), elimination half-life ($T_{1/2\beta}$=9.13 ± 1.26 hr) and mean residence time (13.51 ± 1.90 hr) in male goats administered sulphadimidine/piroxicam as compared to T_{max} (1.10 ± 0.29 hr), $T_{1/2\beta}$ (7.24 ± 0.59 hr) and MRT (10.54 ± 0.92 hr) of male goats administered sulphadimidine alone. However, WAD goats showed significant increase ($P<0.05$) in time maximum (T_{max}=1.50 ± 0.22 hr), volume of distribution area (Vdarea=3.94 ± 0.55 L/kg), elimination half-life ($T_{1/2\beta}$=8.72 ± 0.84 hr) and mean residence time (MRT=12.77 ± 1.90 hr) in female goats administered sulphadimidine with piroxicam as compared to T_{max} (0.90 ± 0.18 hr), Vdarea (3.39 ± 0.38 l/kg), $T_{1/2\beta}$ (70.68 ± 0.72 hr) and MRT (11.25 ± 1.11 hr) of female goats administered sulphadimidine alone. Co-administration of piroxicam with sulphadimidine may delay elimination of sulphadimidine, prolong its therapeutic effect and withdrawal period in West African Dwarf goats.

Keywords: Piroxicam; Sulphadimidine; Pharmacokinetics; West African dwarf goats

Introduction

Sulphadimidine has proven to be clinically useful since its introduction in veterinary medicine as therapeutic agent for a wide range of microbial diseases, including chlarmydiosis, actinomycosis, toxoplasmosis and coccidiosis. Sulphadimidine is 79% bound to plasma proteins with a half-life of 3.88 to 15.4 hrs and has particularly large percentage (60-90%) excretion as acetylated derivatives. The disposition kinetics of sulphadimidine has been reported in cows, sheep and goat, hen, guinea fowl, domestic chicken and duck, rabbit, turkey poult, grower turkey, dog, broilers, Calves and Swine [1-19].

Non-steroidal Anti-inflammatory Drugs (NSAIDs) are commonly used in animals to reduce pain, fever and inflammation and in the treatment of different clinical conditions such as rheumatoid disorders, osteoarthritis, foot rot and mastitis [20-23]. Piroxicam, is bound to plasma proteins, and has a half-life of 50 hrs and excreted in urine and faeces [24]. It could antagonize the release of prolactin leading to improved fertility, offers neuroprotection in cerebral ischemia which may be positively correlated with lipid solubility at high doses [25-27]. But sex dependent metabolism of the drug appears to be a major determinant of sex related differences in piroxicam pharmacokinetics [28]. The chronic effect of piroxicam is attributed to its chemical transformation [29]. So the risk of bioequivalence is very low. The pharmacokinetics of piroxicam has been reported in rats [28,30-32].

West African Dwarf (WAD) goats (*Capra hircus*) are believed to be the wild Bezoar goat. It is endowed with capacity to resist trypanosome, gastrointestinal nematode, produce wool, milk, improved carcass yield leading to more than 90% of the overall household keeping goats in Nigeria [33-35]. The meat of WAD goats is preferred to other animal meats most especially in the North-Central and South-Eastern Nigeria, because of its flavour, tenderness and palatability [36,37]. It commands higher market price than beef on marriage, religious rites and are insurance against crop failure, a good medium for friendship and peace [38-40].

Piroxicam has higher binding capacity to albumin (91%) and could interfere with the pharmacokinetics of sulphadimidine with albumin binding capacity (79%). In view of the above, effects of piroxicam on the pharmacokinetics of sulphadimidine were studied in male and female West African Dwarf goats.

Materials and Methods

Drugs

Sulphadimidine sodium (33.3 mg/ml) produced by kepro, Holland was used for the study at a single dose of 100 mg/kg body weight and Piroxicam (0.5%) produced by Hanbet, Shandong China was used for the study at a single dose of 5 mg/kg body weight.

Experimental animals and design

This study was conducted in the Department of Veterinary Physiology, Pharmacology and Biochemistry laboratory, College of

Veterinary Medicine, University of Agriculture Makurdi. Twenty healthy goats of both sexes, aged 1-year-old, weighing 10.4 ± 1.3 kg were randomly selected and assigned into two groups of ten each. The goats were fed corn offal and fresh grass; clean water was provided ad libitum. All the animals were handled according to international guiding principle for biomedical research involving animals (CIOMS and ICLAS, 2012) and approved by the appropriate animal care review committee of the University of Agriculture, Makurdi, Nigeria.

Drug administration and sampling

Twenty goats were divided into two groups of 10 each (5 males; 5 females) were used. The first group was administered sulphadimidine im (100 mg/kg body weight) alone, and the second group was administered 100 mg/kg of sulphadimidine and 5 mg/kg of piroxicam via right and left thigh muscle respectively.

Pre-treatment blood samples were collected from the jugular vein into EDTA bottles using 23G needle and 5 ml syringe which served as control, 10 min before drug administration and thereafter at 0.08, 0.16, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 24, 48, 72, 96, 120, 144, 168, and 192 hrs for sulphadimidine assay. The blood samples collected were centrifuged at 5000 rpm and the plasma obtained using a micropipette into cryogenic vials and stored at -20°C for analysis.

Assay of plasma sulphadimidine

Free sulphadimidine in plasma was determined according to the method of Bratton and Marshall and modified by Salinas et al. [41,42]. For the analysis of plasma sulphadimidine, 3.8 ml of distilled water was mixed with 0.2 ml of plasma and treated with 1 ml of 20% trichloroacetic acid. After thorough mixing, the samples were allowed to stand for 10 min. They were centrifuged at 3000 rpm for 10 min. To 2 ml of clear supernatant, 0.1 ml of 0.1% sodium nitrate was added and mixed. The mixtures were allowed to stand for 3 min followed by addition of 0.2 ml 0.5% ammonium sulphamate and mixed. The samples were allowed to stand for 2 min before adding 0.2 ml 0.5% N-(1-naphthyl) ethylene diammine dihydrochloride. The samples were mixed and the optical density of the resulting color determined at 540 nm wavelength using a spectrophotometer. The minimum detection limit of the assay was 0.05 µg/ml. The linear calibration curve of sulphadimidine in plasma within the range of 1-10 µg/ml was obtained by plotting percentage absorbance against drug concentration. The correlation coefficient (R2) was greater than 0.93. The concentration of sulphadimidine in plasma was calculated using the formula below:

Concentration of the drug (D)=Concentration of Standard × Optical Density of Drug/Optical Density of Standard

Calculation of pharmacokinetic parameters

The pharmacokinetic parameters for individual animals were calculated using established pharmacokinetic equations [43-47].

Statistical analysis

The data on plasma kinetics and pharmacokinetic parameters of sulphadimidine administered and co-administered with piroxicam were presented in graphical and tabular form respectively. Plasma concentrations and pharmacokinetic parameters were presented as mean ± Standard Error of Mean (SEM). Test for significance between the parameters in respect of male and female WAD goats administered sulphadimidine at 100 mg/kg body weight and sulphadimidine (100 mg/kg) co-administered with piroxicam (5 mg/kg) were performed using paired samples Student's t test at 5% level of significance [48].

Results

The result showed male goats to have increased time maximum (T_{max}=1.90 ± 0.45 hr), absorbtion rate constant (α=0.72 ± 0.08 hr), elimination half-life ($t_{1/2\beta}$=9.13 ± 1.26 hr), mean residence time (MRT=13.51 ± 1.90 hr), mean absorption time (MAT=2.93 ± 0.40 hr), area under moment curve (AUMC=67.12 ± 16.60 mg.hr 2/l) and volume of distribution to central compartment (Vc=7.73 ± 3.51 l/kg) in goats administered sulphadimidine/piroxicam as compared to (T_{max}=1.10 ± 0.29 hr), (α=0.58 ± 0.02 hr), ($t_{1/2\beta}$=7.24 ± 0.59 hr), (MRT=10.54 ± 0.92 hr), (MAT=1.72 ± 0.058 hr), (AUMC =37.37 ± 10.58 mg.hr 2/l) and (Vc =6.32 ± 2.70 l/kg) of goats administered sulphadimidine respectively. However elimination intercept (B=1.36 ± 0.83 µg/ml), concentration maximum (C_{max}=244.08 ± 10.11 µg/ml), volume of distribution area (Vdarea=2.88 ± 0.20 l/kg), absorbtion half-life ($t_{1/2\alpha}$=1.03 ± 0.17 hr), body clearance (Clb=0.23 ± 0.03 l/kg/hr) and elimination rate constant from central compartment to peripheral compartment (K12=0.37 ± 0.085 hr^{-1}) were significantly lower (P<0.05) in goats administered sulphadimidine/piroxicam, in comparison with B (13.91 ± 4.30 µg/ml), C_{max} (262.42 ± 29.13 µg/ml), Vdarea (3.91 ± 0.76 l/kg), $t_{1/2\alpha}$ (1.90 ± 0.007 hr), Clb (0.39 ± 0.094 l/kg/hr) and K12 (0.52 ± 0.09 hr^{-1}) of male goats administered sulphadimidine. Other parameters such as absorption intercept (A), elimination rate constant (β), area under curve from zero to 192 hrs (AUCo-92 hr), area under curve from zero to infinity ($AUC_{o-\infty}$), volume of distribution in peripheral compartment (Vext), elimination rate constant from central compartment to outside (K10) and elimination rate constant from peripheral to central compartment (K21) did not increase significantly (P>0.05) between the groups administered sulphadimidine and sulphadimidine/piroxicam (Table 1). The pharmacokinetic evaluation of sulphadimidine in male goats indicated that the data fit a two compartment open model.

Female goats showed significant increase (P<0.05) in elimination intercept (B=25.68 ± 17.32 µg/ml), time maximum (T_{max}=1.50 ± 0.22 hr), volume of distribution area (Vdarea=3.94 ± 0.55 l/kg), elimination half-life ($T_{1/2\beta}$=8.72 ± 0.84 hr), mean residence time (MRT=12.77 ± 1.90 hr), and volume of distribution steady state (Vss=41.99 ± 3.00 mg/l) in female goats administered sulphadimidine with piroxicam as compared with B (11.74 ± 9.73 µg/ml), T_{max} (0.90 ± 0.18 hr), Vdarea (3.39 ± 0.38 l/kg), $t_{1/2\beta}$ (70.68 ± 0.72 hr), MRT (11.25 ± 1.11 hr) and Vss (14.98 ± 5.24 mg/l) of the female West African dwarf goats administered sulphadimidine alone. However, concentration maximum (C_{max}=236.32 ± 16.80 µg/ml) decreased significantly (P<0.05) in the goats administered sulphadimidine/piroxicam as compared to the goats administered sulphadimidine (C_{max}=243.02 ± 16.45 µg/ml) respectively. Other pharmacokinetic parameters investigated did not increase significantly (p>0.05) between goats administered sulphadimidine and sulphadimidine/piroxicam (Table 2). The pharmacokinetic evaluation of the sulphadimidine in female goats indicated that the data fit a two compartment open model.

Kinetic parameters	Sulphadimidine alone	Sulphadimidine/piroxicam	P-value
A (µg/ml)	98.14 ± 36.02	72.29 ± 18.42	P>0.05
B (µg/ml)	13.91 ± 4.30	1.36 ± 0.83	P<0.05
C_{max} (µg/ml)	262.42 ± 29.13	244.08 ± 10.11	P<0.05
T_{max} (hr)	1.10 ± 0.29	1.90 ± 0.45	P<0.05
Vd (area) (L/kg)	3.91 ± 0.76	2.88 ± 0.20	P<0.05
α (1/h)	0.58 ± 0.02	0.72 ± 0.08	P<0.05
β (1/h)	0.098 ± 0.007	0.084 ± 0.014	P>0.05
$T_{1/2\alpha}$ (hr)	1.90 ± 0.088	1.03 ± 0.17	P<0.05
$T_{1/2\beta}$ (hr)	7.24 ± 0.59	9.13 ± 1.26	P<0.05
CLb (L/kg/hr)	0.39 ± 0.094	0.23 ± 0.031	P<0.05
MRT (hr)	10.54 ± 0.92	13.51 ± 1.90	P<0.05
MAT (hr)	1.72 ± 0.058	2.93 ± 0.40	P<0.05
AUC_{0-96} (mg/l/hr)	3.33 ± 0.68	4.62 ± 0.65	P>0.05
$AUC_{0-\infty}$ (mg/l/hr)	3.34 ± 0.69	4.65 ± 0.65	P>0.05
AUMC (mg.hr 2/l)	37.37 ± 10.58	67.12 ± 16.60	P<0.05
Vss (mg/l)	13.79 ± 3.68	26.31 ± 9.30	P<0.05
Vc (L/kg)	6.32 ± 2.70	7.73 ± 3.51	P>0.05
K10	0.0014 ± 0.0006	0.00061 ± 0.00022	P>0.05
K12	0.52 ± 0.09	0.37 ± 0.085	P<0.05

A: Absorption phase; B: Elimination phase; C_{max}: Peak concentration; T_{max}: Peak time; Vd(area): Volume of distribution area; α: Absorption rate constant; β: Elimination rate constant; $t_{1/2\alpha}$: Absorption half-life; $t_{1/2\beta}$: Elimination half-life; Clb: Clearance; MRT: Mean residence time; MAT: Mean absorption time; AUC0-96: Area under the curve zero to 96 h; AUC0-∞: Area under the curve zero to infinity; AUMC: Area under the moment curve; Vss: Volume of distribution steady state; Vc: Volume of distribution central compartment; K10: Elimination rate constant from central compartment to outside; K12: Elimination rate constant from central compartment to peripheral compartment

Table 1: Pharmacokinetic parameters of sulphadimidine in male WAD goats following intramuscular treatment with sulphadimidine alone (100 mg/kg) body weight and sulphadimidine (100 mg/kg) co-administered with piroxicam (5 mg/kg).

Discussion

The lower elimination intercept (B), Volume of distribution (Vd), Concentration maximum (Cmax), time of maximum drug concentration (Tmax), absorbtion half-life (t1/2α, elimination half-life (t1/2β), body clearance (Clb) and distribution from central compartment to peripheral compartment (K12) in WAD goats administered sulphadimidine/piroxicam in comparison with the goats administered sulphadimidine, show that piroxicam and sulphadimidine compete for same binding site, albumin [49]. However, the increased Tmax, α, t1/2β, MAT, AUMC and Vss of goats administered sulphadimidine/piroxicam in comparison with sulphadimidine show that piroxicam can increase bioavailability of sulphadimidine in goats. The Cmax of sulphadimidine was higher in the goats administered sulphadimidine alone (Cmax=262.42 ± 29.13 µg/ml) than in the goats administered sulphadimidine/piroxicam (Cmax=244.08 ± 0.11 µg/ml) but lower in the non-starved guinea fowl (52.5 ± 2.62 µg/ml) administered intramuscular sulphadimidine [50].

But the elimination half-life ($T_{1/2\beta}$=9.13 ± 1.26 hr) of goats administered sulphadimidine/piroxicam is higher than that of non-starved guinea fowl (7.2 ± 2.6 hr) administered intramuscular sulphadimidine at the same dose rate. However the elimination half-life of sulphadimidine in the two groups of goats (t1/2β=7.24 ± 0.59;9.13 ± 1.26 hr) is lower than that of dog, 16.80 ± 3.9 hr, 16.00 ± 0.00 hr, camel (13.20 ± 0.00 hr), horse, 13.00 ± 0.00 hr, 9.80 ± 0.00 hr, 11.40 ± 2.26 hr, cattle, 11.2 ± 0.43 hr, pigs, 11.9 ± 0.7 hr, 11.05 ± 2.76 hr,13.00 ± 0.00 hr, but similar to that of buffalo 7.69 ± 2.39 hr, 9.38 ± 0.00 hr) and higher than that of sheep (2.9 ± 0.7 hr, 4.75 ± 0.00 hr, 4.00 ± 0.00 hr), rabbit (3.00 ± 0.00 hr) and chickens, 3.00 ± 0.00 hr and male turkeys, 7.62 ± 0.51. Interspecies comparisons of sulphadimidine disposition have been considered in connection with the influence of variations in metabolic rate in relation to body weight and glomerular filtration rate [7,8,15,18,50-59].

Kinetic parameter	Sulphadimidine alone	Sulphadimidine/piroxicam	P-value
A (µg/ml)	106.86 ± 20.54	109.34 ± 20.04	P>0.05
B (µg/ml)	11.74 ± 9.73	25.68 ±17.32	P<0.05
C_{max} (µg/ml)	243.02 ± 16.45	236.32 ± 16.80	P<0.05
T_{max} (hr)	0.90 ± 0.18	1.50 ± 0.22	P<0.05
Vd (area) (L/kg)	3.39 ± 0.38	3.94 ± 0.55	P<0.05
α (1/h)	0.54 ± 0.10	0.46 ± 0.04	P>0.05
β (1/h)	0.09 ± 0.008	0.082 ± 0.08	P>0.05
$T_{1/2\alpha}$ (hr)	1.58 ± 0.37	1.53 ± 0.14	P>0.05
$T_{1/2\beta}$ (hr)	7.68 ± 0.72	8.72 ± 0.84	P<0.05
CLb (L/kg/hr)	0.29 ± 0.032	0.30 ± 0.019	P>0.05
MRT (hr)	11.25 ± 1.11	12.77 ± 1.19	P>0.05
MAT (hr)	2.28 ± 0.51	2.09 ± 0.28	P>0.05
AUC0-192 (mg/L/hr)	3.45 ± 0.53	3.36 ± 0.31	P>0.05
AUC0-∞ (mg/L/hr)	3.46 ± 0.53	3.38 ± 0.31	P>0.05
AUMC (mg.hr 2/l)	39.27 ± 6.86	40.09 ± 4.94	P>0.05
Vss (mg/l)	14.98 ± 5.24	41.99 ± 3.00	P>0.05
Vc (L/kg)	2.77 ± 0.60	3.15 ± 0.69	P>0.05
K10	0.00050 ± 0.00011	0.00052 ± 0.00017	P>0.05
K12	0.53 ± 0.09	0.51 ± 0.06	P>0.05

A: Absorption phase; B: Elimination phase; C_{max}: Peak concentration; T_{max}: Peak time; Vd(area): Volume of distribution area; α: Absorption rate constant; β: Elimination rate constant; $t_{1/2\alpha}$: Absorption half-life; $t_{1/2\beta}$: Elimination half-life; Clb: Clearance; MRT: Mean residence time; MAT: Mean absorption time; AUC0-96: Area under the curve zero to 96 h; AUC0-∞: Area under the curve zero to infinity; AUMC: Area under the moment curve; Vss: Volume of distribution steady state; Vc: Volume of distribution central compartment; K10: Elimination rate constant from central compartment to outside; K12: Elimination rate constant from central compartment to peripheral compartment.

Table 2: Pharmacokinetic parameters of sulphadimidine in female WAD goats following intramuscular treatment with sulphadimidine alone at 100 mg/kg body weight and sulphadimidine (100 mg/kg) co-administered with piroxicam (5 mg/kg).

The lower elimination half-life in group administered sulphadimidine is suggestive of higher level of distribution in various body fluids and tissues. But the value of elimination rate constant (0.098 ± 0.07 hr^{-1}) in the WAD goats administered sulphadimidine in this study is comparable with that of non-starved guinea fowls (0.096 ± 0.02 hr^{-1}) administered intramuscular sulphadimidine [50] suggesting that two different species of animals may have similar way of eliminating sulphadimidine from their bodies. Sulphadimidine has been documented to be more rapidly eliminated after injection faster than oral sulphadimidine mixed with feed or drinking water [60]. The renal clearance of metabolites of sulphadimidine was reported to be 10 times greater than that of sulphadimidine as a parent drug indicating that its metabolites are excreted faster than the parent drug [9].

Once pseudo-distribution equilibrium has been established; the rate of decline in plasma concentration is reduced and determined mainly by the elimination of the drug from the central compartment [46].

The half-lives of the majority of drugs including sulphadimidine which are used as the therapeutic agents in humans and domestic animals are independent of dose administered, since their overall elimination obeys first order kinetics (i.e. exponential) which implies that a constant fraction of the drug present in the body is eliminated per unit of time. However, the higher the absorption rate constant (0.72 ± 0.08 hr) observed in WAD goats administered sulphadimidine/piroxicam in comparison with β (0.58 ± 0.02 hr) of goats administered sulphadimidine, may suggest that piroxicam can delay the absorption of intramuscular sulphadimidine. But an estimate of the absorption rate of a drug from a particular dosage form is given by the time at which the peak is reached on the plasma concentration versus time curve, plotted in arithmetic coordinates. Absorption continues after the peak plasma concentration has been reached [46]. However, the decrease in elimination intercept (B), C_{max}, Vd, $t_{1/2\beta}$, Clb, and K12 show that the rate of absorption of sulphadimidine and its concentration in the central compartment and peripheral compartment can be affected by co-administration of piroxicam. This may be as a result of depletion of body protein which is the biological fuel of last result [60,61].

The pharmacokinetic behavior of sulphadimidine in the West African dwarf goats under the present study is best described by two compartment open model. This is at variance with findings in turkey poults [12], guinea fowl, domestic chicken and duck [10], sheep, goat and buffaloes [51] where the drug was eliminated by one compartment model. This may be due to variation in the species and co-administration of two drugs and route of administration. However, our findings are in agreement with the findings in dogs, broiler chicken, Cows and buffaloes indicating that the kinetic profile of a drug may differ from one animal to another or even among the same species of animals [7,15,16,51,56,62]. The higher increased intercept (B), T_{max}, Vd, $t_{1/2\beta}$ and Vss of the goats administered sulphadimidine/piroxicam in comparison with the values of goats administered sulphadimidine show that piroxicam can decrease time maximum, volume of distribution, half-life and volume of distribution, steady state of sulphadimidine in goats. However, the increased T_{max} and decreased C_{max} of sulphadimidine in the goats administered sulphadimidine/piroxicam show that the lower the concentration, the higher the time maximum. However, the volume of distribution (Vd=3.94 ± 0.55 L/kg) is higher in the goats administered sulphadimidine/piroxicam as compared with the goats administered sulphadimidine (3.39 ± 0.38 L/kg). However, Vd values are lower in guinea-fowl (1.29 ± 0.47 L/kg), chicken 1.08 ± 0.06 L/kg, dog 0.68 ± 0.12 L/kg and sheep 0.6 ± 0.11 L/kg [10,15,54,63]. The more extensive distribution of sulphadimidine in West African dwarf goats may be suggestive of slower elimination of the drug in the animals as shown by low rate of elimination from central compartment to outside. The greater the volume of distribution, the longer the half-life and the slower the drug eliminated from the body [16]. The elimination half-life of the WAD goats administered sulphadimidine ($t_{1/2\beta}$=7.68 ± 0.72 hr) and sulphadimidine/piroxicam ($t_{1/2\beta}$=8.72 ± 0.84 hr) are lower than the elimination half-life of starved broiler chicken ($t_{1/2\beta}$=11.60 ± 0.72 hr), ducks ($t_{1/2\beta}$=9.0 ± 0.9 hr) sheep, 3.93 ± 0.61 hr, 4.50 ± 0.3 hr, 4.5 hr, 4.0 hr,3.28 hr (54,18,64,8,65), but higher than that of guinea fowl ($t_{1/2\beta}$=6.0 ± 0.9 hr), domestic chicken, $t_{1/2\beta}$=6.2 ± 0.8 hr, cow, 11.30 hr, 11.08 ± 2.68 hr, 14.5 hr, 10.53 hr administered intravenous sulphadimidine. However, Silvestri et al. reported elimination half-life (8 hr) of sulphadimidine in cow [7,10,54,64-67].

There are considerable within-species and inter-species variations in half-life which are likely to be due in part, to the method applied in the corresponding investigations [54]. However, interspecies variations in half-life not related to size could be introduced by other factors. It could be assumed that these differences also illustrate the need for analyses of correlation between the half-life and body weight of sulphadimidine, before a decision is made as to the extent the available pharmacokinetic data are of relevance in the prediction of an appropriate dosage regimen [54]. Lack of significant difference in body clearance, mean resident time, area under the curve zero to 96 hr, area under the curve zero to infinity, area under the moment curve and volume of distribution of central compartment of goats administered sulphadimidine/piroxicam in comparison with sulphadimidine may connote that piroxicam can not affect these parameters in female West African Dwarf goats. The observation may not affect extent of metabolism, rate of renal clearance of the drug and the acetylation-deacetylation equilibrium which govern the elimination half-life of sulphadimidine and its persistence in the body, hence sulphadimidine is eliminated by an extensive biotransformation and by renal excretion of metabolites and parent substance [17,18]. The ultimate objective of a satisfactory dosage regimen is to maintain the plasma drug level above minimum inhibitory concentration (MIC) during treatment period. For sulphonamides the MIC was reported to be 50 µg/ml [1,4]. Concentration of sulphadimidine in the goats administered Sulphadimidine and sulphadimidine/piroxicam under the present study appeared above 50 µg/ml of MIC, 7 and 9 hr respectively.

Conclusion

Co-administration of piroxicam with sulphadimidine delay elimination of sulphadimidine invariably prolonging its therapeutic effect but may prolong withdrawal period of sulphadimidine in West African Dwarf goats. Hence the tissues may pose threat of Stevens-Johnsons syndrome to susceptible humans.

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