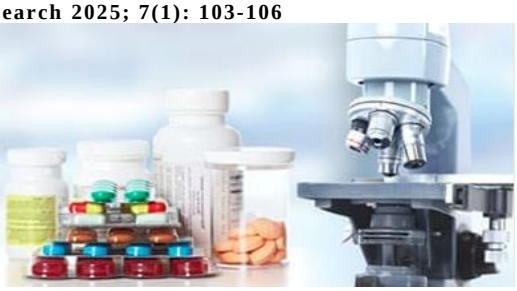
International Journal of Pharmacology and Clinical Research



ISSN Print: 2664-7613
ISSN Online: 2664-7621
Impact Factor: RJIF 8
IJPCR 2025; 7(1): 103-106
www.pharmacologyjournal.in
Received: 23-01-2025
Accepted: 28-02-2025

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Effect of Meloxicam on the Kinetic Profile of Sulphadimidine in West African Dwarf (WAD) Goats

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DOI: https://www.doi.org/10.33545/26647613.2025.v7.i1b.59

Abstract
The use of antibiotics and non-steroidal anti-inflammatory drugs in the management of disease conditions in animals is widespread. This study aims to determine the effect of meloxicam at a single dose of 0.5 mg/kg body weight on the kinetic profile of sulphadimidine administered at a single dose of 100 mg/kg body weight in West African Dwarf (WAD) goats.
Four healthy West African Dwarf (WAD) goats, aged 6 to 7 months and weighing between 7 and 9 kg, were utilized in a two-phase crossover study with a one-month washout period. In phase one, the goats received sulphadimidine (100 mg/kg) administered into the left gluteus muscle. In phase two, the goats were given sulphadimidine at the same dosage concurrently with meloxicam (0.5 mg/kg) administered into the right gluteus muscle. Two milliliters of blood were collected from all the goats in an ethylenediaminetetraacetic acid (EDTA) bottle before drug administration (0 hours) and subsequently at intervals up to 48 hours. The concentrations of sulphadimidine in plasma were measured using a UV-visible spectrophotometer. Concentration-time curves were fitted, and pharmacokinetic parameters were estimated for each administration group.
The area under the curve (AUC) for the group receiving only sulphadimidine was notably lower (1350.05±113.39 µg/ml.hr, $p< 0.05$) when compared to the group that was administered both sulphadimidine and meloxicam together (22901.07±1222.36 µg/ml.hr). This suggests that systemic exposure to sulphadimidine is enhanced when meloxicam is used in combination.
The concurrent use of sulphadimidine and meloxicam did not show any significant changes to the pharmacokinetic profile of sulphadimidine, aside from the area under the curve. Thus, these two medications can be utilized together for treating bacterial infections in goats that need an antipyretic, anti-inflammatory, or analgesic treatment.

Keywords: Sulphadimidine, Meloxicam, Pharmacokinetics, Goats

Introduction
Sulphadimidine is widely used in the treatment of animal diseases. It has a broad spectrum of activity against both gram-positive and gram-negative bacteria, as well as some protozoa (Such as Coccidia, Neospora, and Toxoplasma), fungi (Including Actinomyces and Nocardia), and Chlamydia [1]. Sulphonamides are effective only in cells that must synthesize their folic acid; mammalian cells and bacteria that utilize preformed folic acid are not affected by these compounds.
Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) belonging to the oxicam class, which primarily inhibits the cyclooxygenase-2 isoform (COX-2) [2-3]. It has been widely utilized in both human and veterinary medicine due to its anti-inflammatory, analgesic, and antipyretic properties. In veterinary practice, meloxicam is effective in treating conditions such as osteoarthritis, musculoskeletal disorders, acute respiratory infections, puerperal septicemia, mastitis, and mastitis-metritis-agalactia syndrome. Additionally, its use is recommended for managing pain and inflammation associated with procedures like castration or dehorning in various animal species [4-7].
The pharmacokinetics of sulphadimidine and meloxicam have been extensively studied in various animal species, including dogs, goats, sheep, cattle, pigs, chickens, and other species of veterinary interest. To the best of my knowledge, there is currently no information available regarding the effect of meloxicam on the pharmacokinetics of sulphadimidine in WAD goats. Because the majority of diseases in animals are linked to bacterial infections, pain, inflammation, and fever, this research was conducted to evaluate how meloxicam influences the pharmacokinetics of sulphadimidine in WAD goats.

Materials and Methods

Drugs

Sulphadimidine and Meloxicam (Ashish Life Science Pvt Ltd., Maharashtra, India)

Experimental design and drug administration

Four healthy WAD goats aged 6 to 7 months and weighing between 7 and 9 kg, were procured from breeders within the Makurdi metropolis. The animals were examined for any apparent clinical signs prior to the commencement of the study. They were fed a diet of pasture and concentrate, with water provided *ad libitum*. All animals were vaccinated, dewormed, and acclimatized to their new environment. The handling of the animals adhered to the international guiding principles for biomedical research involving animals, as outlined by the International Council for Laboratory Animal Science (ICLAS) and the Council for International Organizations of Medical Sciences (CIOMS) [8].

A two-phase crossover study with a one-month washout period was conducted. In phase one, the goats received sulphadimine alone (100 mg/kg) administered to the left gluteus muscle. In phase two, the goats received sulphadimidine at the same dose as phase one on the left gluteus muscle concurrently with meloxicam (0.5 mg/kg) administered to the right gluteus muscle.

Blood samples (2 ml) was collected from each goat prior to medication, with additional samples taken at fixed intervals: 15, 30, and 45 minutes, as well as 1, 2, 4, 6, 8, 10, 12, 24, and 48 hours after the administration of the drug preparation. Blood samples were centrifuged at 1500 g for 10 minutes, after which the resulting plasma was collected and stored at -20 °C until analysis.

The plasma levels of sulphadimidine were assessed using a modified technique [9]. A UV-visible spectrophotometer (752N, 200-1000 nm) was employed for the analysis.

Pharmacokinetic analysis

The analysis of plasma concentrations from a pharmacokinetic perspective was performed utilizing the pharmacokinetic software 'PC Modfit V7.8'.

Statistical Analysis

The plasma concentrations and kinetic parameters were expressed as the Mean± Standard Error of the Mean (SEM) and examined with a paired Student's t-test using GraphPad Prism 5.03 for Windows at a significance level of 5%.

Results

The mean plasma concentration of sulphadimidine alone and its combination with meloxicam in WAD goats is presented in Table 1. The mean plasma concentration of sulphadimidine alone was 70 µg/ml, while that of sulphadimidine in combination with meloxicam was 51.68 µg/ml at 0.25 hours. These plasma concentrations increased until reaching peak values of 79.27 µg/ml for the sulphadimidine alone group and 72.27 µg/ml for the combination with meloxicam at 1 hour, respectively. Following this peak, the plasma concentrations gradually decreased, and at 48 hours post-drug administration, the concentrations were 2.44 µg/ml for the sulphadimidine alone group and 3.28 µg/ml for the combination with meloxicam.

Plasma concentrations were significantly lower ($P< 0.05$) ($p<0.05$) in the group receiving group receiving sulphadimidine alone compared to the group administered both sulphadimidine and meloxicam concurrently, from 6 to 12 hours post-drug administration.

The plasma concentration of sulphadimidine, plotted semi-logarithmically against time following intramuscular administration in both groups, is illustrated in Figure 1. The figure represents a two-compartment open model.

Table 1: Plasma concentration of sulphadimidine alone and its combination with meloxicam (n=4), Mean±SEM

Time (h)	Sulphadimidine alone	Sulphadimidine and Meloxicam	P- value
0.250	70.444±14.05	51.678±4.67	p>0.05
0.500	76.054±16.35	62.700±1.26	p>0.05
0.750	77.616±17.19	70.620±7.90	p>0.05
1.000	79.266±16.64	72.270±7.45	p>0.05
2.000	78.276±17.53	66.220±1.66	p>0.05
4.000	58.762±11.91	65.890±10.37	p>0.05
6.000	49.412±8.39	62.920±12.22	*p*<0.05
8.000	39.930±8.91	65.780±8.86	*p*<0.05
10.000	33.726±9.14	53.240±0.76	*p*<0.05
12.000	27.720±9.10	53.746±1.59	*p*<0.05
24.000	16.368±7.64	29.700±1.77	*p*<0.05
48.000	2.442±2.03	3.278±1.87	p>0.05

Table 2: Kinetic profile of sulphadimidine and its combination with meloxicam (n=4), Mean±SEM

Profile	Sulphadimidine alone	Sulphadimidine and meloxicam	P-value
Tmax (h)	1.50±0.20	2.13±0.66	p>0.05
Cmax (h)	97.72±18.66	80.52±7.66	p>0.05
α (h^{-1})	0.50±0.12	0.41±0.26	p>0.05
T1/2α (h)	1.70±0.41	1.49±0.51	p>0.05
MAT (h)	2.45±0.60	5.69±2.10	p>0.05
AUC_{0-t} (µg/ml/.h)	1282.16±81.87	1630.01±87.49	*P*<0.05
$AUC_{0-\infty}$ (µg/ml/.h)	1350.51±113.39	1684.09±104.71	*P*<0.05
AUMC (µg/ml/.h^2)	15869.58±3743.06	22901.07±1222.36	*P*<0.05
β (h^{-1})	0.12±0.05	0.10±0.02	p>0.05
$T_{½\beta}$ (h)	9.12±2.96	8.23±1.89	p>0.05
CL (L/kg/h)	0.74±0.20	0.41±0.05	p>0.05
MRT (h)	14.38±3.47	15.59±1.28	p>0.05
Vd (L/kg)	7.99±2.45	5.05±1.41	p>0.05

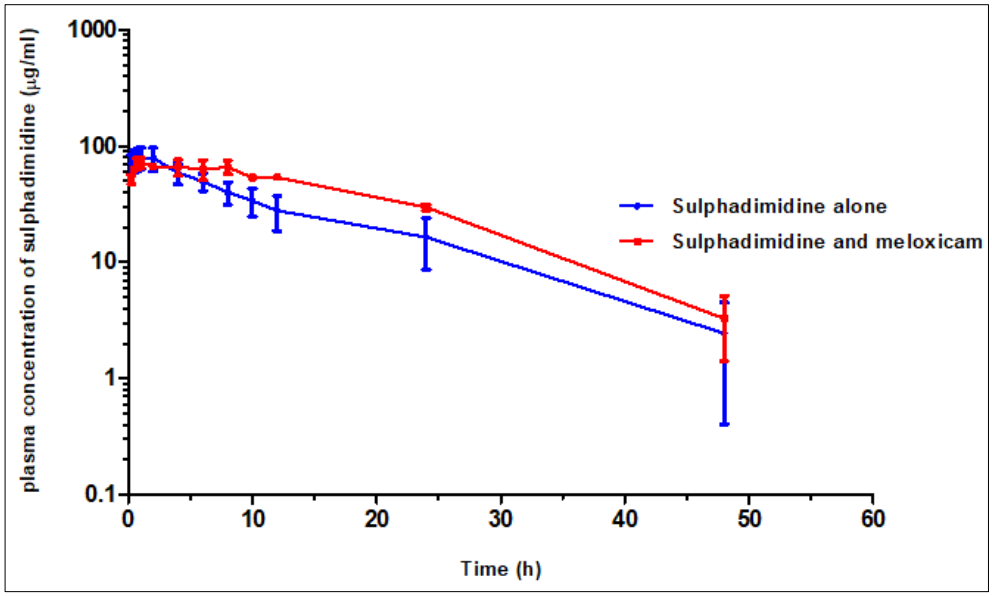

Fig 1: Mean semi-log plasma a concentration-time of suplhadimidine alone and its combination with meloxicam

The pharmacokinetic parameters of sulphadimidine in both groups are presented in Table 2. The kinetic profile in the sulphadimidine-only group, includingarea under the curve from zero to 48 hours (AUC0-48) (1282.16±81.87 µg/ml·h), the± (1282.16±81.87 µg/ml·h), the area under the curve from zero to infinity (AUC0-∞) (1350.51±113.39 µg/ml·h), ±(1350.51±113.39 µg/ml·h), and the the area under the moment curve from zero to 48 hours (AUMC0-48) (15869.58±374.60 µg/ml·h²), was±(15869.58±374.60 µg/ml·h²), was significantly lower (p< 0.05) compared to the the AUC0-48 (1630.01±87.49 µg/ml.h), (AUC0-∞) (1684.09±104.71 µg/ml.h) and AUMC0-48 (22901.07±222.36 µg/ml·h²) of the group that received sulphadimidine and meloxicam concurrently. The time to maximum drug concentration (Tmax), maximum drug concentration (Cmax), elimination rate constant (β), elimination half-life (T1/2β), clearance (Cl), mean residence time (MRT), volume of distribution (Vd), absorption rate constant (α), absorption half-life (T1/2α), and mean absorption time (MAT) in both groups did not differ (p > 0.05).

Discussion

The effect of meloxicam on the plasma concentration of sulphadimidine was evaluated in West African Dwarf (WAD) goats. A single dose of both drugs was administered concurrently via the intramuscular route. Measurable blood levels were obtained for 48 hours, and the elimination of sulphadimidine followed a biphasic process. This finding is consistent with previous reports [10-11].

Tmax and Cmax, which represent the time of maximum drug concentration and the highest plasma concentration, respectively, did not differ significantly (p> 0.05) between the group administered sulphadimidine alone and the group administered sulphadimidine and meloxicam concurrently. The values of Cmax and Tmax in this study are consistent with previous research on sulphadimidine; 99.08±6.40 hours and 1.50±0.2 hours were reported for Cmax and Tmax, respectively [10].

The time required for fifty percent of a drug administered to be absorbed into the bloodstream is referred to as the absorption half-life. In contrast, the mean absorption time (MAT) represents the average duration a drug remains at the site of administration before absorption occurs. In this study, the value of Tmax and MAT did not differ significantly (p > 0.05) between the group receiving group receiving sulphadimidine alone and the group administered sulphadimidine concurrently with meloxicam.

The area under the curve (AUC) represents the total exposure to a drug following its administration. It is influenced by the rate of elimination, the administered dose, and is inversely proportional to the drug's clearance [12]. In the group that received sulphadimidine alone, the AUC was significantly lower (1350.05±113.39 µg/ml·hr; p< 0.05) compared to the group that received sulphadimidine in combination with meloxicam (22901.07±1222.36 µg/ml·hr). This indicates a greater systemic exposure to sulphadimidine when administered alongside meloxicam.

The pharmacokinetic parameters of sulphadimidine did not differ significantly (p> 0.05) between the two groups. This may be attributed to the rapid absorption and elimination of meloxicam in the goats.

The half-life of sulphadimidine's elimination observed in this study was similar to the values documented in cattle (9.46±0.93 hours) [13] and sheep (9.51 hours) [14].

Conclusion

The pairing of sulphadimidine with meloxicam did not cause a notable change in the pharmacokinetic characteristics of sulphadimidine, with the exception of the area under the curve. These two drugs can be used together in the treatment of bacterial infections in goats that require an antipyretic, anti-inflammatory, or analgesic agent.

Acknowledgement

We acknowledge the support of Dr. Mrs Miriam O Oladipo of Del Scan Services for analyzing the samples in her laboratory.

Funding

This research was funded by the authors.

Conflict of Interest

The authors declare that there are no conflicts of interests.

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