Poultry Science

Pharmacokinetics of meloxicam in pigeons after single intravenous, oral, and intramuscular administration

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ABSTRACT This study aimed to determine the pharmacokinetics of meloxicam in pigeons. Twenty-four 7-wk-old meat pigeons (*Columba livia*) were randomly divided into 3 groups (PO, IM, and IV) and given a single dose of 1 mg/kg body weight of meloxicam. Plasma samples were taken at predetermined times, which were then analyzed using a validated high-performance liquid chromatography (**HPLC**) method and subjected to noncompartmental analysis using Phoenix software. Results indicated that meloxicam was absorbed effectively and quickly after PO and IM dosing. Peak concentrations (0.83 ± 0.21 and 1.59 ± 0.49 μg/mL) were achieved at 2 and 0.26 h, respectively, with mean absorption times of 2.56 ± 1.50 and 1.47 ± 0.89 h. Bioavailability was high at 86.31 ± 43.45% and 81.57 ± 52.58%, respectively, and the area under the concentration-time curve ($\mathbf{AUC_{0-\infty}}$) was 5.33 ± 2.68 and 5.03 ± 3.26 h·μg/mL. After IV administration, the elimination was faster with a total body clearance (**CL**) of 188.75 ± 83.23 mL/h/kg, an elimination half-life ($\boldsymbol{t_{1/2\lambda z}}$) of 1.76 ± 0.56 h, and a volume of distribution at steady-state ($\boldsymbol{V_{SS}}$) of 427.50 ± 188.43 mL/kg. Considering the lack of a precise analgesic threshold of meloxicam in pigeons and the notable differences in its analgesic threshold among various animal species, formulating a dosing regimen in pigeons presented a significant challenge. Based on the previous analgesic threshold (3.5 μg/mL) in parrots, a higher dose (e.g., 2 mg/kg) or shorter dosing interval (e.g., every 6 h) is recommended for treating pain in pigeons. Nonetheless, further pharmacodynamic research is required to verify these recommendations.

Key words: meloxicam, meat pigeons, bioavailability, pharmacokinetics, HPLC

2023 Poultry Science 102:102869
https://doi.org/10.1016/j.psj.2023.102869

INTRODUCTION

China produces 80% of the world's meat pigeons with an annual sale of 680 million birds (Jiang et al., 2019). Pigeon meat is highly praised for its delicious taste, low-fat content, high protein content, and versatility in cooking options. Additionally, it is rich in beneficial substances such as pantothenic acid that can be used in dietary therapy, contributing to its increasing popularity in the catering industry and resulting in significant growth in the pigeon breeding sector (Xie et al., 2020). However, due to intensive breeding and their thin bones and low subcutaneous fat content, pigeons are more susceptible to ailments such as infections, foot dermatitis, and trauma (Sánchez-González et al., 2021). These diseases cause pain, fever, and inflammation, which can seriously compromise the welfare of the pigeons. If these diseases are not promptly and effectively treated, they can significantly diminish pigeon growth rate and quality, and in severe cases, may result in pigeon mortality. Therefore, it is crucial to explore analgesic and anti-inflammatory drugs for pigeons.

Nonsteroidal anti-inflammatory drugs (**NSAIDs**) are commonly used globally (Walters and Woessner, 2016). They are available in various types such as aspirin, acetamido, ibuprofen, and meloxicam, which differ in chemical structure but are effective in relieving pain, reducing inflammation, and inhibiting the synthesis of central prostaglandin. Veterinarians have also adopted NSAIDs in treating a wide range of animals, including mammals (Jacobs et al., 2022), birds (Castineiras et al., 2021), and fish (Stancová et al., 2015), with positive therapeutic outcomes.

Meloxicam is an enolic acid-type NSAID that has preferential selectivity for inhibitory the activity of cyclooxygenase-2 (**COX-2**) and blocks the synthesis of prostaglandins (Shao et al., 2022). Its anti-inflammatory, heat-relief, and analgesic properties are stronger in the inflammatory site than in the gastric mucosa,

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Received May 3, 2023.
Accepted June 8, 2023.

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making it highly effective with lower gastrointestinal irritation and other adverse reactions as compared to other NSAIDs (Gates et al., 2005). In clinical practice, meloxicam is commonly used for treating mastitis, osteoarthritis, and inflammations in animals such as cows and sheep (Depenbrock et al., 2021; Jyothi et al., 2022), as well as for pain relief (Deneuche et al., 2004; Burkemper et al., 2020). Due to its effective therapeutic properties, meloxicam is increasingly popular in poultry for anti-inflammatory, antipyretic, and analgesic purposes.

The existing researches in poultry, including chickens and parrots, highlight the application prospect of meloxicam (Cole et al., 2009; Souza et al., 2018, 2021). However, limited research has been conducted on pigeons, despite their notable anti-inflammatory and analgesic effects in birds. Previous studies have only reported the pharmacokinetic of meloxicam in pigeons for an intravenous administration route at 0.5 mg/kg body weight (**BW**) (Baert and De Backer, 2003). The rate and extent of absorption are unknown by other extravascular dosing routes, leaving significant gaps in understanding the pharmacokinetics of meloxicam in pigeons. Therefore, this study aimed to investigate the pharmacokinetics of meloxicam in pigeons by 3 routes of administration: intravenous (**IV**), oral (**PO**), and intramuscular (**IM**), all at 1 mg/kg BW.

MATERIALS AND METHODS

Drugs and Reagents

The reference substance of meloxicam (Lot No. G1025591; purity of 99.66%) was obtained from LGC Labor Gmbh (Luckenwalde, UK). Meloxicam oral suspension (Lot No. 903104003; 32 mL:48 mg) and injection (Lot No. 907011004; 20 mL:40 mg) were purchased from Qilu Animal Health Products Co., Ltd. (Jinan, Shandong, China). Other reagents, including phosphoric acid ($\mathbf{H_3PO_4}$), triethylamine, methanol (chromatographic grade), acetonitrile (chromatographic grade), and potassium dihydrogen phosphate ($\mathbf{KH_2PO_4}$), were obtained from Tianjin Kemiou Chemical Reagent Co., Ltd. (Tianjin, China).

Experimental Animals

We acquired 24 healthy meat pigeons (*Columba livia*) (12 males and 12 females), aged 7 wk, from a commercial farm in Luoyang City. These birds were kept in 3 wire cages measuring 80 × 80 × 80 cm. There were 8 pigeons in each cage, with 4 males and 4 females. Before any procedures, the pigeons were acclimatized for a week and fed antibacterial-free food and water ad libitum. The breeding environment was properly ventilated, amply illuminated, and kept at a constant temperature of about 25°C ± 1°C. The study protocol was approved by the Institutional Animal Care and Use Committee (**IACUC**) at Henan University of Science and Technology, with the approval number DK20220303.

Experimental Design and Sample Collection

Using the Excel software, these pigeons were randomly divided into 3 groups (PO, IM, and IV) with BWs of 0.27 to 0.39 kg, 0.23 to 0.35 kg, and 0.28 to 0.35 kg, respectively. The PO group received meloxicam oral suspension at a dosage of 1 mg/kg (0 h) via gavage, and blood samples were drawn via the wing vein at 15, 45 min, 1, 1.5, 2, 3, 4, 6, 12, and 24 h. The IM group was administered meloxicam injection intramuscularly in the right pectoral muscle at 1 mg/kg (0 h), and blood samples were taken via the wing vein at 15, 45 min, 1, 1.5, 2, 3, 4, 6, 12, and 24 h. Similarly, the IV group received the same 1 mg/kg dose of meloxicam injected intravenously into the left-wing inferior vein, and blood samples were collected at 5, 15, 30 min, 1, 1.5, 2, 4, 6, 12, and 24 h. At each time point, approximately 0.5 mL of blood was collected via the wing vein in a 1.5-mL centrifuge tube and then centrifuged at 4,000 × *g* for 10 min to obtain plasma. All plasma samples are stored at −20° C until detection.

Determination of Meloxicam Concentrations in Plasma

The extraction of meloxicam from plasma and further chromatographic analysis was based on one previous report (Shao et al., 2022) with minor modifications. Plasma (0.1 mL) was mixed with acetonitrile (0.3 mL) and vortically agitated for 3 min. The mixture was then centrifuged at 15,000 × *g* for 10 min, and 20 μL of the supernatant was injected into the high-performance liquid chromatography (**HPLC**) system for detection. The concentration of meloxicam was determined using the Waters e2695 HPLC system, which was connected to a 2489 ultraviolet detector and a computer with Empower software (Waters Corporation, Milford, MA). Separation was performed using a Hypersil BDS C18 column (4.6 × 250 mm, 5 μm, Elite Analytical Instruments Co., Ltd., Dalian, China) kept at 30°C. The mobile phase consisted of a mixture of 0.05 mol/L phosphate amine buffer (adjusted to pH 2.6 with phosphoric acid) and acetonitrile (v:v = 60:40), delivered at a flow rate of 1 mL/min for 12 min. Detection was achieved at a wavelength of 365 nm.

The stock solution of meloxicam (1 mg/mL) was prepared in dimethyl sulfoxide and stored at 4°C away from light. Gradient dilutions of the stock solution were created into working solutions using the mobile phase. The working solutions were then used to draw the standard curve by testing a range of concentrations (0.1−10 μg/mL). Three replicates at 3 different concentrations (0.1, 1, and 10 μg/mL) were tested for 3 d to evaluate the coefficients of variation and recoveries, respectively. Furthermore, the limits of detection (**LOD**) and

quantification (**LOQ**) were determined by examining the signal-to-noise ratio (**S/N**) with a minimum of ≥3 and ≥10, respectively.

Pharmacokinetics Analysis

The concentration-time data of meloxicam in each pigeon were analyzed using a noncompartmental method in Phoenix WinNonLin software (Version 8.1; Pharsight, Cary, NC), and the resulting pharmacokinetic parameters were obtained. To calculate the first-order rate constant associated with the terminal phase (λz), linear regression was used, and from this, the terminal half-life ($t_{1/2\lambda z}$) was determined as $\ln 2/\lambda z$. The area under the concentration-time curve (**AUC**) and the first moment curve (**AUMC**) were both calculated using the linear trapezoidal rule with extrapolation to time infinity (Chen et al., 2023). The mean residence time (**MRT**) was obtained by dividing $AUMC_{0-\infty}$ by $AUC_{0-\infty}$. The initial concentration (C_0) after IV administration was estimated using the back extrapolation method. Total body clearance (**Cl**) was calculated as the ratio of intravenous dose to AUC (Yang et al., 2019), while the volume of distribution (V_Z) was determined as $V_Z = \text{Dose}/\text{AUC}/\lambda z$, where Dose represented the intravenous dose. The volume of distribution at steady-state (V_{SS}) was calculated as $V_{SS} = \text{MRT}_{IV} \times \text{Cl}$. After administration via PO and IM routes, the peak concentration (C_{max}) and time to reach it (T_{max}) were observed. While the mean absorption time (**MAT**) was determined as $\text{MRT}_{PO/IM}$ minus MRT_{IV} (Bello et al., 2022). Bioavailability (**F**) was calculated as the ratio of extravascular AUC to the IV AUC.

Statistical Analysis

The mean ± SD of pharmacokinetic parameters was presented, with statistical analysis of 3 dosing routes conducted using SPSS 22.0 software. Shapiro-Wilk test was used to assess normality, indicating that λz, AUMC, AUC, and T_{max} did not follow a normal distribution. Subsequently, one factor ANOVA was employed for their analysis, while an independent sample t test was used for the remaining parameters. A P value below 0.05 indicates significant differences.

RESULTS

Validation of Analytical Methods

The extraction method used in this study demonstrates strong reproducibility and a linear relationship in the concentration range of 0.1 to 10 μg/mL meloxicam, with an R^2 value of 0.9998. The retention time for meloxicam is 9 min, and the calibration curve regression equation is $C = 4E - 05 \times S + 0.0239$ (where C is the calculated concentration and S is the peak area of meloxicam in the chromatogram). The mean recovery rate of meloxicam was 98.91% in spiked samples. Additionally, the intraday coefficient variation of meloxicam ranged from 0.35 to 9.27%, and the intraday coefficient of variation ranged from 6.14 to 6.77%. The LOD and LOQ for the method were determined to be 0.05 and 0.1 μg/mL, respectively.

Pharmacokinetics

The 24 pigeons in our experiment exhibited stable vital signs with no observed adverse reactions postadministration. In Figure 1, we present the concentration-time curve of meloxicam after 3 administration routes, along with corresponding pharmacokinetic parameters detailed in Table 1. The $t_{1/2\lambda z}$ values were 2.59 ± 1.09, 2.53 ± 0.85, and 1.76 ± 0.56 h for PO, IM, and IV routes, respectively, showing no significant difference ($P > 0.05$). However, we observed significant differences ($P < 0.05$) in MRT between PO and the other 2 administration routes: 4.91 ± 1.50 h for PO, 3.41 ± 1.06 h for IM, and 2.35 ± 0.71 h for IV. Additionally, the peak concentration of meloxicam differed significantly ($P < 0.05$) between the PO group (0.83 ± 0.21 μg/mL at 2 ± 0.72 h) and IM group (1.59 ± 0.49 μg/mL at 0.26 ± 0.02 h).

DISCUSSION

To our knowledge, this paper reported the first-ever findings on the pharmacokinetics of meloxicam in pigeons administered by intramuscular injection and oral administration. After oral administration, pigeons attained a peak concentration of 0.83 ± 0.21 μg/mL at 2 ± 0.72 h. Notably, the peak time was shorter than that in other birds such as laying hens (3.04 h; Shao et al., 2022), Hispaniolan Amazon parrots (5 h; Molter et al., 2013), African penguins (12 h; Morrison et al., 2018), and African gray parrots (13.2 h; Montesinos et al., 2017). At the same oral dose, the current peaking concentration in pigeons (0.83 ± 0.21 μg/mL) was lower

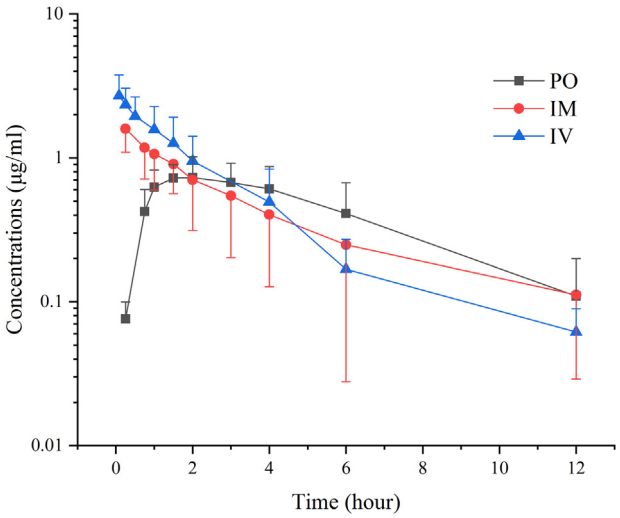

Figure 1. Mean ± SD plasma concentrations (mg/mL) of meloxicam in pigeons following oral (PO; $n = 8$), intramuscular (IM; $n = 8$), and intravenous (IV; $n = 8$) administration at a single dose of 1 mg/kg BW.

Table 1. Pharmacokinetics parameters (mean ± SD) of meloxicam in pigeons after oral (PO; $n = 8$), intramuscular (IM; $n = 8$), and intravenous (IV; $n = 8$) administration at a single dose of 1 mg/kg BW.

Parameters	Unit	PO	IM	IV
λz	1/h	0.33 ± 0.18^{a}	0.31 ± 0.11^{a}	0.43 ± 0.16^{a}
$t_{1/2\lambda z}$	h	2.59 ± 1.09^{a}	2.53 ± 0.85^{a}	1.76 ± 0.56^{a}
T_{max}	h	2 ± 0.72^{a}	0.26 ± 0.02^{b}	NA
C_{max}	μg/mL	0.83 ± 0.21^{a}	1.59 ± 0.49^{b}	NA
C_0	μg/mL	NA	NA	3.15 ± 1.28
$AUC_{0-\infty}$	h·μg/mL	5.33 ± 2.68^{a}	5.03 ± 3.26^{a}	6.17 ± 2.60^{a}
$AUC_{\%}$	%	5.72 ± 4.93^{ab}	8.49 ± 4.36^{b}	4.19 ± 4.21^{a}
$AUMC_{0-\infty}$	h^2·μg/mL	29.08 ± 20.81^{a}	19.82 ± 19.10^{a}	14.95 ± 8.21^{a}
MRT	h	4.91 ± 1.50^{a}	3.41 ± 1.06^{b}	2.35 ± 0.71^{b}
Cl	mL/h/kg	NA	NA	188.75 ± 83.23
V_Z	mL/kg	NA	NA	458.75 ± 201.45
V_{SS}	mL/kg	NA	NA	427.50 ± 188.43
MAT	h	2.56 ± 1.50^{a}	1.47 ± 0.89^{b}	NA
F	%	86.31 ± 43.45^{a}	81.57 ± 52.58^{a}	NA

Within a row, values not sharing a common superscript letter are significantly different ($P < 0.05$).

Abbreviations: λz, the first-order rate constant associated with the terminal phase; $AUC_{0-\infty}$, the area under the concentration-time curve from the time of dosing to infinity; $AUC_{\%}$, the percentage from the last data point to the concentration-time curve infinity; $AUMC_{0-\infty}$, the area under the moment curve from the time of dosing to infinity; C_0, initial concentration; Cl, total body clearance; C_{max}, observed peak concentration; F, absolute bioavailability after oral administration; MAT, mean absorption time; MRT, mean residence time extrapolated to infinity; $t_{1/2\lambda z}$, apparent elimination half-life; T_{max}, time to reach peak concentration; V_Z, the volume of distribution; V_{SS}, the volume of distribution at steady-state.

than that in these animals, except for American flamingos, where the concentrations were comparable (1.00 ± 0.88 μg/mL; Boonstra et al., 2017). These differences in pharmacokinetics suggest the possibility of varied plasma protein binding rates, biotransformation pathways, and species-specific distinctions.

After a single intramuscular injection of meloxicam in pigeons, the drug was rapidly absorbed into the bloodstream. The first blood collection showed a peak concentration of 1.59 ± 0.49 μg/mL at 0.26 ± 0.02 h. Early peak times were also observed in other birds, such as flamingos (0.28 h; Boonstra et al., 2017), zebra finches (0.5 h; Miller et al., 2019), African gray parrots (0.5 h; Montesinos et al., 2017), vultures (0.6 h; Naidoo et al., 2008), and laying hens (0.8 h; Shao et al., 2022). Although the dosage (0.4−2.2 mg/kg) and species vary significantly, the peak time after intramuscular injection is short.

Meloxicam was efficiently absorbed with 86.31 and 81.57% bioavailability for PO and IM administration, respectively, with no significant difference between them. These findings contradict popular beliefs that IM dosing is more effective. Interestingly, similar results were observed in lesser flamingos (Zordan et al., 2016). The current oral bioavailability meloxicam in pigeons was higher than those in red-tailedhawks (74%; Lacasse et al., 2013), laying hens (70.13%; Shao et al., 2022), geese (64.2%; Sartini et al., 2020), and great horned owls (62%; Lacasse et al., 2013). Conversely, when administered intramuscularly, its bioavailability was lower than that in laying hens (125.5%; Shao et al., 2022), and Hispaniolan Amazon parrots (100%; Molter et al., 2013); however, higher than that in African gray parrots (78.4%; Montesinos et al., 2017). These differences could be attributed to variations in breed and weight.

In this study, we found that there was little difference in the elimination half-life ($t_{1/2\lambda z}$) between PO administration and IM injection, with values of 2.59 ± 1.09 h and 2.53 ± 0.85 h, respectively. However, IV injection resulted in a slightly shorter $t_{1/2\lambda z}$ of 1.76 ± 0.56 h (Table 1). The $t_{1/2\lambda z}$ values in laying hens ranged from 5.45 to 5.79 h for the same 3 dosing routes (Shao et al., 2022), which were all longer than our results. But what is consistent with our results is that there is no statistical difference in $t_{1/2\lambda z}$ between these 3 different dosing methods. Although dosage varied between studies, a subcutaneous administration of meloxicam in American flamingos resulted in shorter $t_{1/2\lambda z}$ values (1.10−1.76 h; Sim and Cox, 2018). Additionally, a longer $t_{1/2\lambda z}$ (2.4 h) was observed in another intravenous study conducted in pigeons at a different dosage of 0.5 mg/kg (Baert and De Backer, 2003). This suggests that dosage and species may affect the elimination half-life of meloxicam.

After injecting 1 mg/kg of meloxicam intravenously, pigeons had an $AUC_{0-\infty}$ of 6.17 ± 2.60 h·μg/mL. This value is lower than those recorded in laying hens (38.63 h·μg/mL; Shao et al., 2022) and African gray parrots (23.6 h·μg/mL; Montesinos et al., 2017) under the same dosage. After injecting 0.5 mg/kg of meloxicam intravenously, pigeons had an $AUC_{0-\infty}$ of 18.35 h·μg/mL (Baert and De Backer, 2003), which is higher than our results. These differences could be due to regional and variety discrepancies. Similar dissimilarities have been noted in African gray parrots (23.6 h·μg/mL; Montesinos et al., 2017) and Hispaniolan Amazon parrots (169 h·μg/mL; Molter et al., 2013).

Following a single IV injection, meloxicam was found to be widely distributed in meat pigeons, with a V_Z of 458.75 ± 201.45 mL/kg. This is significantly higher than in Hispaniolan Amazon parrots (104 mL/kg; Molter et al., 2013), but lower than in red-tailed hawks (832 mL/kg; Lacasse et al., 2013). The study showed that meloxicam was rapidly cleared, with a Cl of 188.75 ± 83.23 mL/h/kg, which is higher than in laying hens (26.48 mL/h/kg; Shao et al., 2022), broilers (25 mL/h/kg; Baert and De Backer, 2002), and African gray parrots (21.8 mL/h/kg; Montesinos et al., 2017). Interestingly, the clearance of meloxicam was found to be affected by age in Dromaius novaehollandiae

(Castineiras et al., 2021). The pigeons we selected for this study were 7-wk old, while laying hens were 14-wk old, and the African gray parrot was 7.25-yr old, as mentioned earlier. These differences in age and body metabolism may have contributed to the observed variations in meloxicam clearance.

According to our findings, the mean residence time (**MRT**) of meloxicam was the longest when administered orally, compared to intramuscular and intravenous injections. The MRTs for PO, IM, and IV administration were 4.91 ± 1.5, 3.41 ± 1.06, and 2.35 ± 0.71 h, respectively (Table 1). Similar results were observed in laying hens, with corresponding MRTs of 8.46, 6.13, and 5.63 h, respectively (Shao et al., 2022). In American flamingos, longer MRT (4.80 h) was also found after oral administration compared with intramuscular injection (1.77 h) (Boonstra et al., 2017). These findings suggest that meloxicam needs more absorption time after PO administration compared with IM injection.

A previous study treated pigeons with femoral fractures using meloxicam at a dosage of 2 mg/kg orally, every 12 h, for 10 consecutive days, and 3 methods were employed to evaluate the extent of postoperative pain, namely an electronic perch for measuring the differential load on the pelvic limbs, 4 pain scales, and an analysis of partial ethograms captured on video to monitor bird activity and posture (Desmarchelier et al., 2012). The results showed that this treatment effectively relieved the pain without causing any adverse effects on the blood, kidney, or gastrointestinal tract (Desmarchelier et al., 2012). However, previous studies have found that the analgesic threshold of meloxicam varies across different bird species. For instance, parrots require a blood concentration of 3.5 μg/mL for analgesia (Molter et al., 2013), while horses may need 0.130 to 0.195 μg/mL (Toutain and Cester, 2004). Considering the lack of a precise analgesic threshold of meloxicam in pigeons and the notable differences in its analgesic threshold among various animal species, formulating a dosing regimen in pigeons presented a significant challenge. In the present study, meloxicam exhibited good bioavailability when administered orally (86.31%) or intramuscularly (81.57%) in pigeons. Nonetheless, its quick elimination led to low blood drug concentrations at 12 h (roughly 0.05−0.1 μg/mL). Therefore, assuming that the pigeons have the same analgesic threshold with parrots, a higher dose (e.g., 2 mg/kg) or shorter dosing interval (e.g., every 6 h) is recommended for treating pain in pigeons. However, given the significant differences in the pharmacological and pharmacokinetic parameters of meloxicam across bird species, further pharmacodynamic studies are necessary to validate these recommendations.

ACKNOWLEDGMENTS

This study was supported by the Natural Science Foundation of Henan Province (Grant No. 212300410037) and the Foundation for the University Young Key Teacher Program of Henan Province (Grant No. 2021GGJS044).

Ethical Approval: All applicable international, national, and institutional guidelines for the care and use of animals were followed.

DISCLOSURES

All authors declare that they have no conflicts of interest.

REFERENCES

Baert, K., and P. De Backer. 2002. Disposition of sodium salicylate, flunixin and meloxicam after intravenous administration in broiler chickens. J. Vet. Pharmacol. Ther. 25:449–453.

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

Bello, A., B. Poźniak, A. Smutkiewicz, and M. Świtała. 2022. The influence of the site of drug administration on florfenicol pharmacokinetics in turkeys. Poult. Sci. 101:101536.

Boonstra, J. L., S. K. Cox, and T. Martin-Jimenez. 2017. Pharmacokinetics of meloxicam after intramuscular and oral administration of a single dose to American flamingos (*Phoenicopertus ruber*). Am. J. Vet. Res. 78:267–273.

Burkemper, M. C., M. D. Pairis-Garcia, L. E. Moraes, R. M. Park, and S. J. Moeller. 2020. Effects of oral meloxicam and topical lidocaine on pain associated behaviors of piglets undergoing surgical castration. J. Appl. Anim. Welf. Sci. 23:209–218.

Castineiras, D., L. Armitage, L. P. Lamas, S. De Baere, S. Croubels, and L. Pelligand. 2021. Perioperative pharmacokinetics and pharmacodynamics of meloxicam in emus (*Dromaius novaehollandiae*) of different age groups using nonlinear mixed effect modelling. J. Vet. Pharmacol. Ther. 44:603–618.

Chen, J. C., J. J. Kang, M. Zhang, H. T. Shao, Z. W. Song, K. L. Ma, F. Yang, and F. Yang. 2023. Pharmacokinetics of danofloxacin after single oral and intravenous administration in non-laying hens. J. Vet. Pharmacol. Ther. 46:119–124.

Cole, G. A., J. Paul-Murphy, L. Krugner-Higby, J. M. Klauer, S. E. Medlin, N. S. Keuler, and K. K. Sladky. 2009. Analgesic effects of intramuscular administration of meloxicam in Hispaniolan parrots (*Amazona ventralis*) with experimentally induced arthritis. Am. J. Vet. Res. 70:1471–1476.

Deneuche, A. J., C. Dufayet, L. Goby, P. Fayolle, and C. Desbois. 2004. Analgesic comparison of meloxicam or ketoprofen for orthopedic surgery in dogs. Vet. Surg. 33:650–660.

Depenbrock, S., T. Urbano, J. Ziegler, S. Wetzlich, M. O. Clapham, and L. A. Tell. 2021. Pharmacokinetic parameters and tissue withdrawal intervals for sheep administered multiple oral doses of meloxicam. Animals 11:2797.

Desmarchelier, M., E. Troncy, G. Fitzgerald, and S. Lair. 2012. Analgesic effects of meloxicam administration on postoperative orthopedic pain in domestic pigeons (*Columba livia*). Am. J. Vet. Res. 73:361–367.

Gates, B. J., T. T. Nguyen, S. M. Setter, and N. M. Davies. 2005. Meloxicam: a reappraisal of pharmacokinetics, efficacy and safety. Expert Opin. Pharmacother. 6:2117–2140.

Jacobs, C. C., L. V. Schnabel, C. W. McIlwraith, and A. T. Blikslager. 2022. Non-steroidal anti-inflammatory drugs in equine orthopaedics. Equine Vet. J. 54:636–648.

Jiang, S., N. Pan, M. Chen, X. Wang, H. Yan, and C. Gao. 2019. Effects of dietary supplementation with dl-methionine and dl-methionyl-dl-methionine in breeding pigeons on the carcass characteristics, meat quality and antioxidant activity of squabs. Antioxidants 8:435.

Jyothi, V., C. K. Babu, R. Kumar, P. K. Singh, D. K. Khatri, S. B. Singh, and J. Madan. 2022. Meloxicam in combating clinical mastitis: nanotechnology-driven hope and opportunities. J. Pharm. Bioallied Sci. 14:121–125.

Lacasse, C., K. C. Gamble, and D. M. Boothe. 2013. Pharmacokinetics of a single dose of intravenous and oral meloxicam in red-tailed hawks (*Buteo jamaicensis*) and great horned owls (*Bubo virginianus*). J. Avian Med. Surg. 27:204–210.

Miller, K. A., N. J. Hill, S. E. Carrasco, and M. M. Patterson. 2019. Pharmacokinetics and safety of intramuscular meloxicam in zebra finches (*Taeniopygia guttata*). J. Am. Assoc. Lab. Anim. 58:589–593.

Molter, C. M., M. H. Court, G. A. Cole, D. J. Gagnon, S. Hazarika, and J. R. Paul-Murphy. 2013. Pharmacokinetics of meloxicam after intravenous, intramuscular, and oral administration of a single dose to Hispaniolan Amazon parrots (Amazona ventralis). Am. J. Vet. Res. 74:375–380.

Montesinos, A., M. Ardiaca, J. A. Gilabert, C. Bonvehí, J. Oros, and T. Encinas. 2017. Pharmacokinetics of meloxicam after intravenous, intramuscular and oral administration of a single dose to African grey parrots (Psittacus erithacus). J. Vet. Pharmacol. Ther. 40:279–284.

Morrison, J., C. B. Greenacre, R. George, S. Cox, and T. Martín-Jiménez. 2018. Pharmacokinetics of a single dose of oral and intramuscular meloxicam in African penguins (*Spheniscus demersus*). J. Avian. Med. Surg. 32:102–108.

Naidoo, V., K. Wolter, A. D. Cromarty, P. Bartels, L. Bekker, L. Mcgaw, M. A. Taggart, R. Cuthbert, and G. E. Swan. 2008. The pharmacokinetics of meloxicam in vultures. J. Vet. Pharmacol. Ther. 31:128–134.

Sánchez-González, R., A. Ramis, M. Nofrarías, N. Wali, R. Valle, M. Pérez, A. Perlas, and N. Majó. 2021. Infectivity and pathobiology of H7N1 and H5N8 high pathogenicity avian influenza viruses for pigeons (*Columba livi*a var. domestica). Avian Pathol. 50:98–106.

Sartini, I., B. Lebkowska-Wieruszewska, A. Lisowski, A. Poapolathep, H. Owen, and M. Giorgi. 2020. Pharmacokinetic profiles of meloxicam after single IV and PO administration in Bilgorajska geese. J. Vet. Pharmacol. Ther. 43:26–32.

Shao, H. T., F. Yang, J. C. Chen, M. Zhang, Z. W. Song, and F. Yang. 2022. Pharmacokinetics of meloxicam in laying hens after single intravenous, oral, and intramuscular administration. J. Vet. Pharmacol. Ther. 45:488–494.

Sim, R. R., and S. K. Cox. 2018. Pharmacokinetics of a sustained-release formulation of meloxicam after subcutaneous administration to American flamingos (*Phoenicopterus ruber*). J. Zoo Wildl. Med. 49:839–843.

Souza, M. J., J. Bailey, M. White, K. Gordon, L. Gerhardt, and S. K. Cox. 2018. Pharmacokinetics and egg residues of meloxicam after multiple day oral dosing in domestic chickens. J. Avian Med. Surg. 32:8–12.

Souza, M. J., L. E. Gerhardt, L. Shannon, C. Fortner, R. Davis, M. Condon, J. B. Bergman, and S. K. Cox. 2021. Breed differences in the pharmacokinetics of orally administered meloxicam in domestic chickens (*Gallus domesticus*). J. Am. Vet. Med. Assoc. 259:84–87.

Stancová, V., A. Ziková, Z. Svobodová, and W. Kloas. 2015. Effects of the non-steroidal anti-inflammatory drug (NSAID) naproxen on gene expression of antioxidant enzymes in zebrafish (*Danio rerio*). Environ. Toxicol. Pharm. 40:343–348.

Toutain, P. L., and C. C. Cester. 2004. Pharmacokinetic-pharmacodynamic relationships and dose response to meloxicam in horses with induced arthritis in the right carpal joint. Am. J. Vet. Res. 65:1533–1541.

Walters, K. M., and K. M. Woessner. 2016. An overview of nonsteroidal antiinflammatory drug reactions. Immunol. Allergy Clin. 36:625–641.

Xie, P., X. P. Wan, C. X. Yang, J. G. Zhu, Y. G. Xu, and D. Q. Gong. 2020. Effects of incubation and chick rearing on intestinal morphology, digestive enzyme activities, and mRNA expression of nutrient transporter genes in the pigeon (*Columba livia*) under artificial farming conditions. Poult. Sci. 99:2785–2797.

Yang, F., F. Yang, G. Y. Wang, T. Kong, and B. B. Liu. 2019. Pharmacokinetics of florfenicol and its metabolite florfenicol amine in crucian carp (*Carassius auratus*) at three temperatures after single oral administration. Aquaculture 503:446–451.

Zordan, M. A., M. G. Papich, A. A. Pich, K. M. Unger, and C. R. Sanchez. 2016. Population pharmacokinetics of a single dose of meloxicam after oral and intramuscular administration to captive lesser flamingos (*Phoeniconaias minor*). Am. J. Vet. Res. 77:1311–1317.