

Pharmacokinetics of meloxicam during multiple oral or intramuscular dose administration to African grey parrots (*Psittacus erithacus*)

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OBJECTIVE

To determine the pharmacokinetics of meloxicam in African grey parrots (*Psittacus erithacus*) during administration of multiple doses.

ANIMALS

6 healthy African grey parrots.

PROCEDURES

Meloxicam was administered at each of 3 dosages (1 mg/kg, IM, q 24 h, for 7 days; 1 mg/kg, PO, q 24 h, for 12 days; and 1.6 mg/kg, PO, q 24 h, for 7 days) with an 8-week washout period between treatments. Blood samples were collected 12 and 24 hours after each drug administration (times of presumptive peak and trough drug concentrations) for pharmacokinetic analysis. Birds were visually assessed during all experiments and monitored for changes in selected plasma and urine biochemical variables after administration of the drug at 1.6 mg/kg.

RESULTS

Mean trough plasma concentrations at steady state were 10.7 and 9.16 µg/mL after meloxicam administration at 1 mg/kg, IM, and 1 mg/kg, PO, respectively. Plasma drug accumulation was evident (accumulation ratios of 2.04 ± 0.30 [IM treatment] and 2.45 ± 0.26 [PO treatment]). Plasma and urine *N*-acetyl-β-D-glucosaminidase activities were significantly increased at the end of meloxicam treatment at 1.6 mg/kg.

CONCLUSIONS AND CLINICAL RELEVANCE

Plasma concentrations of meloxicam were maintained at values greater than effective analgesic concentrations described for other avian species. Although administration of meloxicam at a dosage of 1 mg/kg IM and PO daily for 1 week and 12 days, respectively, was not associated with adverse clinical effects in this population, further studies are needed to assess the efficacy and safety of the drug during prolonged treatment and the clinical relevance of its accumulation. (*Am J Vet Res* 2019;80:201–207)

Meloxicam is the most widely used anti-inflammatory medication in exotic animal veterinary medicine, and is the analgesic drug of choice in birds.^{1,2} It is commonly administered to birds because it is readily available in a palatable liquid preparation that is easy to administer. In mammals, meloxicam is a COX-2 selective drug and does not have the gastric irritation properties of other NSAIDs when administered at a therapeutic dose. Although meloxicam is effective and has a wide safety margin in many avian species, it can produce adverse effects in birds, and these effects can vary among avian families.³ At high doses, the COX-2 specificity of meloxicam decreases, and the drug may bind to and obstruct COX-1, resulting in decreased production of physiologic pro-

taglandins. The variability in adverse effects could be related to the large differences observed in drug disposition and the interspecies variation described for the relative expression of COX-1 and COX-2 enzymes.^{4–6}

Meloxicam has a long elimination half-life in dogs (23.7 to 24 hours).⁶ There is variation in its pharmacokinetic behavior in other mammals and avian species that can affect dosing frequency. Meloxicam has been studied with single-dose experiments in domestic broiler chickens (*Gallus gallus*),⁵ mallard ducks (*Anas platyrhynchos*),⁵ various vulture species (*Gyps africanus*, *Gyps coprotheres*, *Torgos tracheliotos*, and *Neophron pernopterus*),⁷ rock pigeons (*Columba livia*),⁵ common ostriches (*Struthio camelus*),⁵ flamingos (*Phoeniconaias minor*),⁸ domestic turkeys (*Meleagris gallopavo*),⁵ Hispaniolan Amazon parrots (*Amazona ventralis*),⁹ African grey parrots (*Psittacus erithacus*),¹⁰ red-tailed hawks (*Buteo jamaicensis*),¹¹ great horned owls (*Bubo virginianus*),¹¹ and Caribbean flamingos (*Phoenicopterus*

ABBREVIATIONS

AUC _{0–last}	Area under the concentration-versus-time curve from time 0 to the last measured concentration
COX	Cyclooxygenase
NAG	<i>N</i> -acetyl-β-D-glucosaminidase

ruber).¹² The half-life of the drug in chickens and pigeons was 3 times as long as in ostriches, ducks, and turkeys.⁵

Pharmacokinetic studies that include multiple doses of orally or parenterally administered drugs are rare in avian medicine. Several studies^{13–15} have evaluated the safety and adverse effects of meloxicam when administered orally every 12 hours for 2 weeks to Hispaniolan Amazon parrots (*A ventralis*), African grey parrots (*P erithacus*), and Japanese quails (*Coturnix japonica*). Results of those studies^{13–15} have established an empirical oral dose range for meloxicam of 0.1 to 2 mg/kg in birds.

Attending to interspecific kinetics and safety variations, it is wise to note that assumptions regarding the clinical efficacy of meloxicam in avian species should not be made on the basis of results of studies including animals of other species and that extrapolation of study results to animals of other species should be performed cautiously.¹⁶ Thus, research on the pharmacokinetics and pharmacodynamics of meloxicam administered via different routes in a species of interest is necessary to determine the appropriate dosage for analgesia. The objective of the study reported here was to determine the pharmacokinetics of meloxicam in healthy African grey parrots after multiple IM (1 mg/kg, q 24 h, for 7 days) and PO (1 and 1.6 mg/kg, q 24 h, for 12 and 7 days, respectively) administrations. An additional goal was to perform plasma and urine biochemical analyses to determine whether changes attributable to administration of the drug at the 1.6 mg/kg dose developed.

Materials and Methods

Animals

Six healthy adult African grey parrots were used in the study. The population included 3 males and 3 females. The mean $\pm$ SD age of birds was 12 ± 1.5 years (range, 8 to 22 years), and mean $\pm$ SD weight was 0.48 ± 0.02 kg (range, 0.43 to 0.52 kg). The parrots were individually housed in stainless steel indoor cages (60 X 60 X 90 cm) with 2 perches and 1 hanging toy in each cage. The parrots had access to commercially available parrot food^a and water ad libitum except for the 2-hour urine collection period as described. Prior to the start of the study, all birds were determined to be healthy and free of disease by thorough physical examination, CBC, plasma biochemical analysis, urine analysis, and testing for *Chlamydia psittaci* and avian circovirus and bornavirus by PCR assay.

All parrots were observed 4 times/d during the experimental phase of the study and for 6 hours immediately after treatment for any change in behavior (mentation, attitude, and activity level), food and water consumption, and fecal production. Parrots did not receive any other medication during or for ≥ 2 months prior to the beginning of the study. The study protocol strictly followed European (directive 2010/63/EU) and Spanish laws (RD 53/2013) regarding animal experimentation. The study was

performed under the guidance of the deontologist committee of the Madrid Local Government and was approved by the Grupo de Rehabilitación de la Fauna Autóctona y su Hábitat Ethics and Animal Welfare Committee (reference No. 15/001).

Experimental design and sample collection

Parrots were randomly allocated into 3 experimental groups (2/group) by drawing numbers from a hat. A 3-way complete crossover study design was used. Each parrot received injectable meloxicam solution^b (1 mg/kg, IM, q 24 h, for 7 days) as well as meloxicam oral suspension^c at 2 dosages (1 mg/kg, PO, q 24 h, for 12 days and 1.6 mg/kg, PO, q 24 h, for 7 days) with two 8-week washout periods between any 2 consecutive experimental phases. The first day of each treatment was considered day 0. Treatment and sample collection subsequent to day 7 was performed to monitor changes and potential adverse effects for extended treatment at the clinically recommended dose only; concentration data subsequent to day 7 were not included in the study. For IM treatment, the drug was injected into the left pectoral muscle by use of a 1.0-mL syringe and 30-gauge needle. For PO administration, an 18-gauge metal ball-tipped gavage tube was placed into the crop for drug delivery (volumes ranged from 0.29 to 0.35 mL for the 1-mg/kg dose and from 0.46 to 0.56 mL for the 1.6-mg/kg dose). The tube was then flushed with water to ensure the entire measured drug dose was delivered. The oral formulation of meloxicam used contained xylitol, but the sweetener has no known toxic effects in parrots.

Parrots were gently manually restrained for drug administration and venipuncture. Serial blood samples (< 0.7 mL) were collected from the right jugular vein into lithium heparin tubes 12 and 24 hours after each drug administration for determination of the presumptive peak and trough concentrations of meloxicam, respectively, according to previously published data from single-dose experiments.¹⁰ The 24-hour samples were obtained immediately prior to administration of the next scheduled drug dose. A 1.0-mL syringe and 30-gauge needle were used for venipuncture. The sampling schedule was repeated for all 3 experiments. The total blood volume extracted was ≤ 1.4 mL/d (ie, 2.5% to 3.5% of total blood volume). Blood samples were centrifuged at $2,400 \times g$ and 25°C for 10 minutes, and plasma was transferred to microtubes and stored at -20°C until analysis (≤ 15 days). Blood samples (1.0 mL) collected before (day -1) and after (day 8 or day 13) each of the 3 experimental phases of the study were used for routine hematologic and biochemical analysis; these analyses were performed immediately after sample collection.

Each day between 7 AM and 9 AM (before room lights were turned on for the day), water bowls were removed from each parrot cage, and urine samples were collected with disposable Pasteur pipettes from

wax paper placed beneath the cages. Urine samples were stored at room temperature (approx 25°C) and transferred to the laboratory of Centro Veterinario Los Sauces, where they were processed ≤ 30 minutes after collection. Urine samples were centrifuged at 500 X g and 25°C for 15 minutes to obtain the supernatant.

Hematologic, plasma, and urine analyses

Hematologic variables were determined by manual counts as described previously, and biochemical analysis of plasma samples was performed with commercial colorimetric kits^d and an automated spectrophotometric wet chemistry analyzer.^{17,18,e} Furthermore, plasma and urine NAG activities (an indicator of cellular necrosis and acute renal injury in some species¹⁹) were measured at the beginning and end of the experiments in which birds were given 1.6 mg of meloxicam/kg PO; NAG activities were determined by use of a spectrophotometer^f at 505 nm and 37°C with 2-methoxy-4-(2-nitrovinyl)-phenyl 2-acetamido-2-deoxy- β -D-glucopyranoside^g as the substrate. Assessment of NAG activities in urine and plasma of 44 healthy African grey parrots (samples previously obtained in the authors' laboratory) yielded mean $\pm$ SEM values of 2.43 ± 1.14 U/L (median, 2.45 U/L; range, 0.4 to 4.3 U/L) and 0.03 ± 0.141 U/L (median, 0.0 U/L; range, 0.0 to 0.6 U/L). Owing to the absence of established reference ranges for these values in African grey parrots, these data were used as working reference values for study purposes.

Determination of meloxicam concentrations

Plasma concentrations of meloxicam were determined with a previously described reverse-phase high-performance liquid chromatography assay with minor modifications.²⁰ Briefly, the system^h was equipped with a 150 X 4.6-mm (5- μ m particle size) C18 column.ⁱ The isocratic mobile phase consisted of 20mM potassium phosphate buffer (pH, 3.5) and acetonitrile (50:50 [vol:vol]) that was delivered at 1.2 mL/min. The UV detector was set to 355 nm. The retention time for meloxicam was approximately 5.64 minutes, and drug quantification was calculated by peak integration. The calibration standards of blank plasma spiked with meloxicam^j were linear between 0.06 and 2.5 μ g/mL ($R^2 > 0.98$); the limit of quantification was 28 ng/mL, and the interassay and intra-assay coefficients were 7.3% and 5.1%, respectively.

For analysis of plasma samples, 0.5 mL of plasma was mixed with 100 μ L of hydrochloric acid solution (5M) and vortexed for 1 minute. Next, 5 mL of diethyl ether was added, and the solution was vortexed for 5 minutes and centrifuged at 3,500 X g and 5°C for 10 minutes. The organic layer was transferred to another test tube, evaporated to dryness (at 42°C, under a vacuum stream), and reconstituted in 0.25 mL of methanol for injection into the chromatography system in

duplicate. The mean $\pm$ SD meloxicam recovery in African grey parrot plasma samples was $90.9 \pm 2.0\%$.

Pharmacokinetics and statistical analysis

Pharmacokinetic parameters were determined individually and expressed as the arithmetic mean $\pm$ SEM. Presumptive peak and trough plasma concentrations of meloxicam were directly obtained from the raw data of concentrations measured 12 and 24 hours after each drug administration, respectively. The AUC_{0-last} was calculated independently via log-trapezoidal integration for the peak and trough meloxicam values with commercially available software.^{21,k} The differences in AUC_{0-last} for peak and trough drug concentrations were also calculated for each experiment.

The time to attainment of steady state was assessed by visual inspection and statistical comparison of the trough concentrations within each treatment. To estimate the extent of drug accumulation after multiple-dose administration, the peak concentration accumulation ratio was calculated as the mean of peak concentrations during steady state divided by the peak concentration after the first meloxicam administration.²²

The pharmacokinetic parameters and plasma biochemical variables were analyzed with a statistical software package.^l Considering the small size of the study groups, and in agreement with Powers recommendations,²³ a nonparametric Wilcoxon rank sum test for paired samples was used to compare data between different administration routes (PO vs IM) and between the 2 PO drug doses (1 vs 1.6 mg/kg). An independent-groups Student *t* test was used to compare the previously obtained NAG activity data from healthy parrots and data obtained from study parrots prior to meloxicam treatment; a paired Student *t* test was used to compare NAG activity data before and after meloxicam administration at 1.6 mg/kg. Values of $P < 0.05$ were considered significant.

Results

Mean presumptive peak and trough concentrations of meloxicam (ie, data for samples collected 12 hours after each drug administration and immediately prior to the next scheduled treatment, respectively) were plotted for days 0 through 6 for all treatments (**Figure 1**). During repeated administration of meloxicam at 1 mg/kg, IM, every 24 hours, mean trough plasma drug concentrations after the fourth, fifth, and sixth doses were similar ($P = 0.87$), suggesting that a steady state of plasma meloxicam concentration was achieved around the start of the fifth day of the multiple-dose treatments. Findings during repeated administration of the drug at 1 mg/kg, PO, every 24 hours were similar, with the time to reach steady state estimated as day 5. Nevertheless, a steady-state concentration could not be verified within the 7-day experiment when the drug was given at 1.6 mg/kg, PO, every 24 hours. Mean peak plasma drug

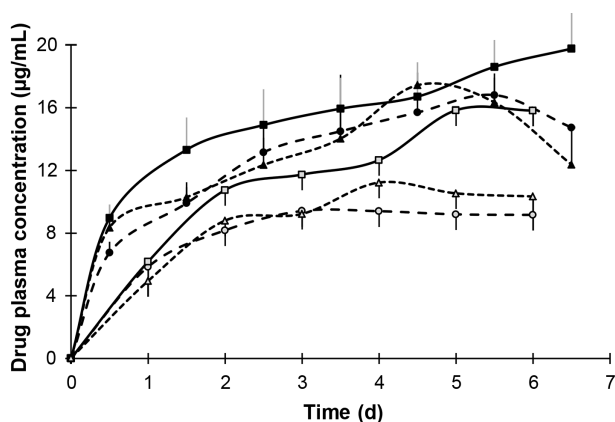


Figure 1—Mean (+ SEM) peak and mean (– SEM) trough plasma concentrations of meloxicam in 6 African grey parrots that received meloxicam at each of 3 dosages (1 mg/kg, IM, q 24 h, for 7 days [triangles]; 1 mg/kg, PO, q 24 h, for 12 days [circles]; and 1.6 mg/kg, PO, q 24 h, for 7 days [squares]) with an 8-week washout period between treatments. Presumptive peak and trough concentrations were determined from raw concentration data for samples collected 12 and 24 hours after each drug administration, respectively, according to previously published data from single-dose experiments.¹⁰ Data are shown for days 0 (day of first drug administration) through 6. Black and white symbols represent peak and trough values, respectively.

concentrations at steady state were 15.38 ± 1.49 µg/mL and 14.93 ± 1.88 µg/mL for IM and PO administration at 1 mg/kg, respectively ($P = 0.54$). Mean trough plasma drug concentrations at steady state were 10.70 ± 0.97 µg/mL and 9.16 ± 0.58 µg/mL for IM and PO administration at 1 mg/kg, respectively ($P = 0.24$).

The $AUC_{0-\text{last}}$ for peak plasma drug concentrations during IM (84.32 ± 6.93 µg•d/mL) and PO (81.51 ± 9.77 µg•d/mL) administration at 1 mg/kg did not differ significantly ($P = 0.85$). The $AUC_{0-\text{last}}$ for trough plasma drug concentrations during IM (49.94 ± 2.30 µg•d/mL) and PO (47.37 ± 4.63 µg•d/mL) administration at this dose also did not differ significantly ($P = 0.74$). However, $AUC_{0-\text{last}}$ values for peak (113.29 ± 13.42 µg•d/mL) and trough (81.20 ± 10.38 µg•d/mL) plasma drug concentrations during administration at 1.6 mg/kg, PO, were significantly ($P < 0.01$ for both comparisons) greater than those at 1 mg/kg PO. The differences between $AUC_{0-\text{last}}$ for peak and trough drug concentrations within experiments were similar for IM (34.38 ± 6.02) and PO (33.99 ± 5.26) administration at 1 mg/kg ($P = 0.56$); the result for PO administration at 1.6 mg/kg (32.09 ± 3.04) was also similar to that for PO administration at 1 mg/kg ($P = 0.73$). The peak concentration accumulation ratios estimated for the 3 experiments (2.04 ± 0.30 , 2.45 ± 0.26 , and 2.11 ± 0.08) were similar and indicated that meloxicam accumulated in plasma of the parrots after both IM and oral administration. Because a steady state was not attained for the 1.6-mg/kg dose, this ratio was calculated as the peak concentration after the last dose divided by the peak concentration after the first dose.

All doses appeared to be well tolerated. No adverse effects were observed when parrots received

Table 1—Comparison of mean $\pm$ SEM hematologic (CBC and plasma biochemical analysis) and urine variables for 6 African grey parrots before (day –1) and after (day 8) administration of meloxicam at a dosage of 1.6 mg/kg, PO, every 24 hours for 7 days as part of a 3-way crossover-design study.

Variable	Day –1	Day 8	P value
Hematologic samples			
Hct (%)	46.9 ± 0.4	46.0 ± 0.3	0.35
Hb (g/dL)	16.10 ± 0.17	16.09 ± 0.11	1.00
RBCs ($\times 10^6/L$)	3.14 ± 0.04	3.13 ± 0.04	0.85
WBCs ($\times 10^3/L$)	6.86 ± 0.32	6.76 ± 0.38	0.89
Protein (g/L)	4.10 ± 0.10	4.44 ± 0.23	0.36
Glucose (mmol/L)	298.9 ± 3.7	295.6 ± 4.6	0.70
ALP (U/L)	118.2 ± 5.4	131.1 ± 8.1	0.34
Amylase (U/L)	460 ± 20	456 ± 36	0.83
GGT (U/L)	3.56 ± 0.31	3.75 ± 0.21	0.50
NAG (U/L)	0.01 ± 0.00	5.59 ± 1.47	0.01
Urine samples			
Uric acid (mmol/L)	3.49 ± 0.23	3.54 ± 0.28	0.73
GGT (U/L)	38.0 ± 5.7	40.4 ± 9.9	0.81
NAG (U/L)	1.96 ± 0.37	5.86 ± 0.94	0.04

Values of $P < 0.05$ were considered significant.

ALP = Alkaline phosphatase. GGT = γ -Glutamyltransferase. Hb = Hemoglobin.

the 1-mg/kg dose of meloxicam by either route. All parrots remained in good general health with no changes in mentation, attitude, activity level, and food or water consumption observed throughout the study. There were also no changes in fecal or urine production that could have been attributable to adverse effects of drug administration or repeated blood collection. Mean $\pm$ SEM NAG activities in plasma (0.01 ± 0.00 U/L) and urine (1.96 ± 0.37 U/L) of study birds just prior to administration of the 1.6-mg/kg dose of meloxicam did not differ significantly ($P = 0.593$ and $P = 0.257$, respectively) from those in plasma (0.03 ± 0.141 U/L) and urine (2.43 ± 1.14 U/L) in the described cohort of 44 healthy African grey parrots. However, there were significant ($P < 0.05$ for both comparisons) differences in NAG activities in urine and plasma after administration of the 1.6-mg/kg PO dose, compared with the respective pretreatment values (**Table 1**). No significant differences were detected between the pretreatment and posttreatment values for any other hematologic, plasma, or urine variables for any treatment.

Discussion

To the best of our knowledge, the present study was the first to investigate the pharmacokinetics of meloxicam in African grey parrots during multiple IM and PO administrations. The results suggested that meloxicam accumulated in the plasma of parrots during the 7 days of administration at 1 mg/kg, IM, every 24 hours; 1 mg/kg, PO, every 24 hours; or 1.6 mg/kg, PO, every 24 hours. However, further studies are needed to confirm these results and to determine the pharmacokinetics of meloxicam in African grey parrots receiving the drug for > 7 days, particularly at the higher dose.

The dose of meloxicam used for 2 of the 3 experiments in the present study (1 mg/kg) was selected on the basis of results published for African grey and Hispaniolan Amazon parrots treated with a single dose of meloxicam.^{9,10} Analgesic effects have been detected in Hispaniolan Amazon parrots with plasma meloxicam concentrations of 3.45 µg/mL.²⁴ In the present study, we evaluated presumptive peak and trough concentrations of meloxicam by collection of blood samples 12 and 24 hours, respectively, after each drug administration.¹⁰ The mean trough plasma concentrations of meloxicam at steady state after administration of 1 mg/kg, IM, and 1 mg/kg, PO, were 10.70 and 9.16 µg/mL, respectively, and the mean trough concentration on day 6 after treatment with 1.6 mg/kg, PO, was 16.18 µg/mL. These results suggested that drug concentrations were maintained above the presumed therapeutic level at all 3 dosages tested. Plasma meloxicam concentrations of 0.57 to 0.93 µg/mL in people, 0.13 to 0.195 µg/mL in horses, and 0.82 µg/mL in dogs are associated with anti-inflammatory effects.²⁴⁻²⁷ When studying the efficacy of a drug in any species, it is important to determine its pharmacokinetic and pharmacodynamic properties in that species. The pharmacokinetic property data for analgesics are often insufficient to aid determination of appropriate doses and dosing frequencies because plasma drug concentrations do not always correspond to analgesic effects. Plasma drug concentrations can provide guidance for dosing frequencies, but the duration of analgesia conferred by NSAIDs may be longer than what would be expected from plasma concentrations.²⁸ In our study, the clinical efficacy of meloxicam was not determined, and it is unknown whether the doses tested confer analgesic or anti-inflammatory effects in African grey parrots. However, our results can be used as a basis for further studies in which efficacy of the drug is assessed.

The mean peak plasma meloxicam concentrations during steady state after drug administration (1 mg/kg, IM or PO) in this study were proportionally higher than those obtained after the first of the daily treatments or those reported after administration of a single 1-mg/kg dose in another study.¹⁰ Thus, the peak concentration accumulation ratios for the 1-mg/kg dosages in the present study suggested that meloxicam accumulated in the plasma of African grey parrots after the administration of multiple doses. The accumulation of meloxicam in plasma after multiple doses in rabbits has been previously described.²⁹ Although long-term administration of meloxicam to parrots was not evaluated in the present study, the potential for drug accumulation may warrant a reduced dose if meloxicam is administered for periods ≥ 7 days.

All birds were clinically normal at the end of the study, which was consistent with results of a prior investigation that revealed no adverse effects in African grey parrots that received 0.5 mg of meloxicam/kg, IM, every 12 hours for 14 days.¹⁴ Historically, impaired renal blood flow, gastrointestinal ulceration,

and inhibition of platelet aggregation are the most common adverse effects associated with meloxicam treatment, but very few articles in the literature suggest a risk from meloxicam when administered at a therapeutic dose.³⁰

No evidence of toxicosis was observed in the present study except for increased plasma and urine NAG activities in birds that received 1.6 mg of meloxicam/kg for 7 days. A lysosomal enzyme that is released into the blood and urine when cell necrosis occurs, NAG is an indicator of acute renal damage in mammalian and avian species.^{19,31,32} The diagnostic value of NAG activity has been previously examined in hens, pigeons, and Hispaniolan Amazon parrots treated with various nephrotoxic drugs.^{13,19,32} When renal failure was induced in pigeons by administration of high doses of gentamicin, increased NAG activities in serum (6-fold change) and urine (50-fold change) were detected.¹⁹ Urine and plasma NAG values were also increased in Hispaniolan Amazon parrots after 15 days of meloxicam administration (1.6 mg/kg, PO, q 12 h), but the urine NAG activity increase was greater than that in plasma, and the increase was observed in both treatment and control groups.¹³ The clinical relevance of increased NAG activities after meloxicam administration is still not well defined. Meloxicam administration could be responsible for some part of the changes in activities, but in the aforementioned study of Hispaniolan Amazon parrots,¹³ stress attributable to handling and diminished water intake just prior to sample collection were thought to cause the changes observed in plasma NAG activities in both groups. In the present study, only a 3-fold increase in urine NAG activity was detected, but plasma NAG activity was increased by a substantially greater amount. The NAG activities were not investigated in the present study for birds that received 1 mg/kg, IM or PO, and it was unknown whether changes could have occurred with drug accumulation at the lower doses.

Meloxicam, like other NSAIDs, can adversely affect glomerular filtration rate and renal hemodynamics through inhibition of prostaglandin synthesis. The increased urinary and plasma NAG activities detected in our study could have reflected an adverse effect of meloxicam, although posttreatment plasma uric acid concentrations did not differ from the pretreatment values. Serum and urine biochemical variables (ie, creatinine, uric acid, and BUN concentrations) do not offer a complete picture of nephrotoxic effects. In a study³³ that included budgerigars (*Melopsittacus undulatus*) treated with meloxicam for 7 days (0.1 mg/kg, IM, q 24 h), glomerular congestion or tubular necrosis was observed on necropsy of 1 of 8 meloxicam-treated birds, but plasma uric acid concentrations for this group did not differ significantly from those for control birds that received distilled water as a sham treatment.

Although adverse clinical effects were not identified in this study with healthy parrots, they might occur when meloxicam is used in ill birds. Further studies are still needed to assess the adverse effects of this

treatment in a larger cohort of birds, in ill birds, or in birds treated for longer periods. Although meloxicam is known to have poor bioavailability in African grey parrots after oral administration,¹⁰ the plasma concentrations of this drug obtained after multiple 1-mg/kg doses administered orally were considered clinically equivalent to those observed after IM administration, possibly owing to the similar half-life values estimated after both administration routes for this drug.

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Footnotes

- a. Harrison's Bird Foods, Brentwood, Tenn.
- b. Metacam, 5-mg/mL injectable solution, Boehringer-Ingelheim España SA, Barcelona, Spain.
- c. Metacam, 1.5-mg/mL oral suspension, Boehringer-Ingelheim España SA, Barcelona, Spain.
- d. Biolabo SA, Maizy, France.
- e. Spectrometer BS 120, Mindray Inc, Beijing, China.
- f. Diazyme Laboratories, Poway, Calif.
- g. Thermo Separation Products, San Jose, Calif.
- h. Teknokroma, Barcelona, Spain.
- i. Mediterranean Sea C-18 column, Sigma-Aldrich Química SA, Madrid, Spain.
- j. Pharmaceutical Secondary Standard, Sigma-Aldrich Química SA, Tres Cantos, Madrid, Spain.
- k. PK Solutions, version 2.0, Summit Research Services, Montrose, Colo.
- l. SPSS, version 20.0, IBM Corp, Armonk, NY.

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