Pharmacokinetics of meloxicam in rabbits after oral administration of single and multiple doses

Daniel V. Fredholm, MS, DVM; James W. Carpenter, MS, DVM; Butch KuKanich, DVM, PhD; Micah Kohles, DVM, MPA

Objective—To determine the pharmacokinetics of meloxicam (1 mg/kg) in rabbits after oral administration of single and multiple doses.

Animals—6 healthy rabbits.

Procedures—A single dose of meloxicam (1 mg/kg, PO) was administered to the rabbits. After a 10-day washout period, meloxicam (1 mg/kg, PO) was administered to rabbits every 24 hours for 5 days. Blood samples were obtained from rabbits at predetermined intervals during both treatment periods. Plasma meloxicam concentrations were determined, and noncompartmental pharmacokinetic analysis was performed.

Results—The mean peak plasma concentration and area under the plasma concentration-versus-time curve extrapolated to infinity after administration of a single dose of meloxicam were 0.83 µg/mL and 10.37 h•µg/mL, respectively. After administration of meloxicam for 5 days, the mean peak plasma concentration was 1.33 µg/mL, and the area under the plasma concentration-versus-time curve from the time of administration of the last dose to 24 hours after that time was 18.79 h•µg/mL. For single- and multiple-dose meloxicam experiments, the mean time to maximum plasma concentration was 6.5 and 5.8 hours and the mean terminal half-life was 6.1 and 6.7 hours, respectively.

Conclusions and Clinical Relevance—Plasma concentrations of meloxicam for rabbits in the present study were proportionally higher than those previously reported for rabbits receiving 0.2 mg of meloxicam/kg and were similar to those determined for animals of other species that received clinically effective doses. A dose of 1 mg/kg may be necessary to achieve clinically effective circulating concentrations of meloxicam in rabbits, although further studies are needed. (Am J Vet Res 2013;74:636–641)
Effects are dose dependent, and the COX-2 specificity of meloxicam is decreased at high doses. Therefore, veterinarians should have knowledge of the pharmacokinetics of this drug before prescribing it for animals.

Pain management is important for the successful treatment of various conditions in rabbits. Rabbits commonly develop adverse effects caused by pain and distress and can develop secondary conditions (eg, ileus) if pain is not controlled. During recovery from surgery, the potential for development of ileus in rabbits is high and can be potentiated via treatment with opioids. Additionally, rabbits do not always develop obvious signs of pain. Therefore, accurate assessment of discomfort in rabbits can be challenging and it is important to administer effective analgesic drugs to such animals. Although meloxicam is not labeled for use in rabbits by the US FDA, it is commonly used for analgesia in such animals.

Two studies have been conducted to determine the pharmacokinetics of meloxicam in rabbits. Results of those studies indicate that rabbits eliminate meloxicam faster than animals of many other species; the authors of those studies suggested that a high dose of meloxicam might be necessary to provide adequate analgesia for rabbits during a 24-hour period. However, results of those studies were different regarding accumulation of meloxicam after administration of multiple doses, and investigators could not recommend use of a dose exceeding 0.3 mg/kg during a 24-hour period because of the study designs. The objectives of the study reported here were to determine the pharmacokinetics of meloxicam (1 mg/kg) in rabbits after oral administration of a single dose and after administration of multiple doses during a 5-day period and to measure plasma biochemical analysis variables to determine the safety of meloxicam at the evaluated dosages. Our hypotheses were that administration of a high dose of meloxicam would cause high plasma concentrations of the drug and that accumulation of meloxicam in plasma would develop during a 5-day treatment period.

Materials and Methods

Animals—Six clinically normal 8-month-old New Zealand white rabbits (Oryctolagus cuniculus; body weight range, 2.41 to 2.89 kg) were included in this study. The rabbits were obtained from a commercial source and were specific pathogen-free Pasteurella multocida (University College of Veterinary Medicine at a constant temperature (21.1°C) and humidity (60%). Rabbits were housed individually in stainless steel cages at the research facilities of the Kansas State University College of Veterinary Medicine at a constant temperature (21.1°C) and humidity (60%). Rabbits were exposed to cycles of 16 h of light and 8 h of dark/darkness. The rabbits were kept in a room with air conditioning and humidity (60%) and a temperature (21.1°C) and humidity (60%). Rabbits were given access to food and water ad libitum.

Water was available ad libitum. Rabbits were acclimatized to the facility for 5 days after their arrival and were habituated to handling prior to initiation of the study. Immediately prior to the start of the study, each rabbit underwent a physical examination, evaluation of a fecal sample, and collection of a blood sample (0.5 mL) from a posterior saphenous or cephalic vein or an auricular artery for determination of Hct and plasma total protein concentration and biochemical analysis variables. All rabbits were determined to be healthy and behaviorally normal.

Experimental design and sample collection—Immediately prior to meloxicam administration, 0.5 mL of blood was collected from each rabbit for determination of baseline values of plasma biochemical analysis variables. Meloxicam (1 mg/kg) was orally administered to each rabbit; a 3-mL syringe containing the dose of meloxicam was inserted into the diastema, and the drug was slowly administered so that none of the medication escaped the oral cavity. Blood samples (0.5 mL) were collected from a lateral saphenous or cephalic vein or an auricular artery of each rabbit by use of 23-gauge needles and syringes containing heparin. Blood was collected immediately before (0 hours) and 0.25, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, and 36 hours after meloxicam administration. This was followed by a 10-day washout period. After the washout period, each rabbit received meloxicam (1 mg/kg, PO) every 24 hours for 5 days. During this time, blood samples (0.5 mL) were collected from each rabbit immediately before and 4 hours after meloxicam administration on each of the first 4 days. On the fifth day, blood samples were collected immediately before and 0.25, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, and 36 hours after meloxicam administration. Meloxicam was administered at 24-hour intervals in the present study on the basis of results of other studies in which the pharmacokinetics of meloxicam in rabbits was determined. Also, the use of this meloxicam administration interval enabled assessment of meloxicam accumulation in the plasma of rabbits. Therefore, 32 blood samples were collected from each rabbit during the study period for determination of meloxicam concentrations. At the final blood collection time, an additional blood sample (0.5 mL) was collected for performance of plasma biochemical analyses. Within 20 minutes after each collection time, blood samples were centrifuged (10 minutes at approx 2,000 x g) and the plasma supernatant was harvested and stored at −70°C until analysis.

Plasma sample analysis—Plasma concentrations of meloxicam were determined via high-pressure liquid chromatography and triple quadrupole mass spectrometry. Plasma samples or rabbit plasma standards (50 µL) were added to 200 µL of internal standard (piroxicam [0.5 µg/mL] in methanol with 0.1% formic acid) to precipitate proteins, vortexed for 5 seconds, then centrifuged for 10 minutes (10,000 x g). Supernatant (200 µL) was transferred to injection vials (injection volume setting, 10 µL). The high-pressure liquid chromatography mobile phase consisted of acetoniitrile and formic acid (0.1%) at a flow rate of 0.4 mL/min (85% formic acid [0.1%] from 0 to 0.5 minutes, then a linear gradient to 30% formic acid [0.1%] at 2.5 minutes that was maintained until 3 minutes, followed by a linear gradient to 85% formic acid [0.1%] at 4 minutes; total mobile phase time, 5 minutes). Separation was achieved by use of a C8 column at 40°C. The qualifying and quantifying ions for meloxicam were an m/z of 352.09 and 114.90, respectively. The qualifying and quantifying ions for the internal standard (piroxicam) were an m/z of 340.08 and 117.90, respectively. The m/z values were determined via high-pressure liquid chromatography and triple quadrupole mass spectrometry.
were \( m/z \) 332.12 and 95.10, respectively. The ion source voltage was 5,000 \( \text{V} \), and the source temperature was maintained at 400\( ^\circ \text{C} \). The standard curve was linear from 0.01 to 10 \( \mu \text{g/mL} \) and was accepted if the correlation coefficient was > 0.99 and predicted values were within the range of values 15% higher or lower than the actual values. The accuracy of the assay at 0.01, 0.1, 0.5, 1, and 5 \( \mu \text{g/mL} \) was 100.7%, 99.6%, 97.5%, 98.0%, and 102.2% of the expected value, respectively. The coefficient of variation at 0.01, 0.1, 0.5, 1, and 5 \( \mu \text{g/mL} \) was 2%, 4%, 10%, 14%, and 7%, respectively.

Values of plasma biochemical analysis analytes were determined for baseline (before meloxicam administration) and posttreatment (after administration of the last dose of meloxicam) times. These analytes included plasma glucose, BUN, total protein, albumin, globulin (calculated), total calcium, phosphorus, sodium, potassium, chloride, bicarbonate, and total bilirubin concentrations and creatine kinase alanine aminotransferase and alkaline phosphatase activities.

Pharmacokinetic analysis—Values of pharmacokinetic parameters were determined for each rabbit by use of noncompartmental analysis performed with commercially available software.\(^{14,15,16}\) The following parameters were determined: AUC\(_{\text{inf}}\), AUC\(_{0-24}\), area under the first moment curve extrapolated to infinity, \( \lambda_z \), terminal half-life, \( C_{\text{max}} \), mean residence time extrapolated to infinity, and \( T_{\text{max}} \) (a parameter derived from precisely timed blood sampling related to the time the peak plasma concentration occurred). The percentage AUC extrapolated to infinity was also determined by dividing the AUC including all time points > 0.01 \( \mu \text{g/mL} \) by AUC\(_{\text{inf}}\). The AUC\(_{\text{inf}}\) was determined by adding the AUC including all time points > 0.01 \( \mu \text{g/mL} \) and the last measured plasma concentration/\( \lambda_z \). The ratio of the AUC\(_{0-\infty} \) (for the last dose of the multiple meloxicam dose experiment) to the AUC\(_{\text{inf}}\) (for the single meloxicam dose experiment) was determined to assess plasma accumulation of meloxicam; for this evaluation, it was assumed that steady-state meloxicam concentrations in rabbits were achieved by the time the last dose of meloxicam was administered during the multiple-dose experiment.

Statistical analysis—Values of plasma biochemical analysis variables for baseline and posttreatment blood samples were compared with a paired \( t \) test. Values of \( P < 0.05 \) were considered significant.

Results

Meloxicam was easily administered to each rabbit, and none of the animals seemed to develop an aversion to the treatment during the study. All of the rabbits seemed to remain healthy during the study, and none had changes in behavior, attitude, mentation, amount of activity, amount of food or water consumed, or fecal production that could be attributed to an adverse drug reaction. Significant differences were detected between baseline and posttreatment plasma BUN concentrations (mean ± SD, 11.0 ± 1.9 mg/dL and 13.7 ± 3.1 mg/dL, respectively) and alkaline phosphatase activities (mean ± SD, 109.3 ± 29.6 U/L and 143.5 ± 32.5 U/L, respectively). However, the mean baseline and posttreatment BUN concentrations were considered normal when compared with published reference ranges (13 to 29 mg/dL\(^{16}\); 15 to 50 mg/dL\(^{17}\)). No significant differences were detected between baseline and posttreatment values of any other plasma biochemical analysis variables (Table 1).

![Figure 1](image) **Figure 1**—Mean ± SD plasma concentrations of meloxicam in 6 rabbits following oral administration of 1 dose (1 mg/kg). Notice that the y-axis is not linear.

Table 1—Comparison of results of plasma biochemical analyses of samples collected from 6 rabbits before (baseline) and after (posttreatment) administration of meloxicam (1 mg/kg, PO) once per day for 5 days.

<table>
<thead>
<tr>
<th>Analyte Baseline</th>
<th>Posttreatment</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>117 ± 21</td>
<td>117 ± 3.5</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>11.0 ± 1.9</td>
<td>13.7 ± 3.1</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.9 ± 0.23</td>
<td>0.9 ± 0.12</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>5.2 ± 0.67</td>
<td>5.3 ± 0.28</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.8 ± 0.86</td>
<td>5.1 ± 0.39</td>
</tr>
<tr>
<td>Globulin (g/dL)</td>
<td>0.35 ± 0.27</td>
<td>0.27 ± 0.24</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>12.6 ± 1.7</td>
<td>13.7 ± 0.77</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>4.9 ± 0.27</td>
<td>4.9 ± 0.45</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>149.1 ± 1.9</td>
<td>149.1 ± 1.9</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.2 ± 0.64</td>
<td>4.7 ± 0.23</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>108 ± 3.9</td>
<td>108 ± 3.1</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>19.8 ± 2.8</td>
<td>19.7 ± 2.4</td>
</tr>
<tr>
<td>Alkaline aminotransferase (U/L)</td>
<td>40 ± 15</td>
<td>41 ± 15</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>109.3 ± 29.6</td>
<td>143.5 ± 32.5</td>
</tr>
<tr>
<td>Creatine kinase (U/L)</td>
<td>526 ± 204</td>
<td>908 ± 496</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>0.15 ± 0.37</td>
<td>0.03 ± 0.05</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>63 ± 25</td>
<td>48 ± 12</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

Table 2—Pharmacokinetic parameters of meloxicam in 6 rabbits that received 1 dose (1 mg/kg, PO) of the drug.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Median</th>
<th>Maximum</th>
<th>Mean*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUCAextrap (%)</td>
<td>1.3</td>
<td>2.6</td>
<td>4.9</td>
<td>2.6</td>
</tr>
<tr>
<td>AUCAinf (h•µg/mL)</td>
<td>8.44</td>
<td>10.72</td>
<td>12.45</td>
<td>10.37</td>
</tr>
<tr>
<td>AUUMC (h•µg/mL)</td>
<td>96.37</td>
<td>121.93</td>
<td>169.16</td>
<td>126.75</td>
</tr>
<tr>
<td>Cmax (µg/mL)</td>
<td>0.65</td>
<td>0.85</td>
<td>1.02</td>
<td>0.83</td>
</tr>
<tr>
<td>Terminal half-life (h)</td>
<td>4.9</td>
<td>6.1</td>
<td>7.1</td>
<td>6.1</td>
</tr>
<tr>
<td>2x (1/h)</td>
<td>0.097</td>
<td>0.113</td>
<td>0.141</td>
<td>0.113</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>10.6</td>
<td>11.8</td>
<td>14.7</td>
<td>12.2</td>
</tr>
<tr>
<td>T_max (h)</td>
<td>4.0</td>
<td>7.0</td>
<td>8.0</td>
<td>6.5</td>
</tr>
</tbody>
</table>

*All mean values are geometric mean except terminal half-life, which is harmonic mean.

AUCAextrap = Percentage of the AUC extrapolated to infinity.

AUMC = Area under the first moment curve extrapolated to infinity.

MRT = Mean residence time extrapolated to infinity.
The mean Cmax of meloxicam (0.83 µg/mL) was achieved 6.5 hours after oral administration of a single dose (1 mg/kg) of meloxicam (Figure 1). The harmonic mean of the terminal half-life was 6.1 hours, and the AUCinf was 10.37 h•µg/mL after administration of a single dose of meloxicam (Table 2).

The mean ± SD plasma concentrations of meloxicam in plasma samples collected 4 hours after administration on days 1 through 5 of the multiple-dose experiment were 0.55 ± 0.16 µg/mL, 0.59 ± 0.20 µg/mL, 0.64 ± 0.21 µg/mL, 0.51 ± 0.11 µg/mL, and 1.05 ± 0.67 µg/mL, respectively. The mean ± SD plasma concentrations of meloxicam in plasma samples collected 24 hours after administration on days 1 through 5 of the multiple-dose experiment were 0.13 ± 0.03 µg/mL, 0.17 ± 0.06 µg/mL, 0.17 ± 0.04 µg/mL, 0.22 ± 0.13 µg/mL, and 0.32 ± 0.03 µg/mL, respectively (Figure 2).

After administration of the last dose during the multiple-dose experiment, the mean Cmax of meloxicam was 1.33 µg/mL, the mean AUC0–24 was 16.08 h•µg/mL, the mean Tmax was 5.8 hours, and the harmonic mean of the terminal half-life was 6.7 hours. The mean ratio of the AUC0–24 (for the multiple dose experiment) to the AUCinf (for the single dose experiment) was 1.55; this value indicated meloxicam accumulated in plasma of the rabbits (Table 3).

### Discussion

Results of this study indicated that oral administration of meloxicam at a dose of 1 mg/kg to rabbits caused plasma meloxicam concentrations that were proportionally higher than those attained after administration of the currently recommended dose (0.2 to 0.3 mg/kg). Moreover, the plasma concentrations of meloxicam measured in the study reported here were similar to those measured for animals of species that receive clinically effective doses.18–20 The clinical efficacy of meloxicam in rabbits was not determined in the present study. Further studies may be warranted in which the efficacy of orally administered meloxicam at a dose of 1 mg/kg in rabbits is assessed. Results of this study indicated that meloxicam accumulated in plasma of rabbits after 5 days of oral administration at a dose of 1 mg/kg. Further studies may be warranted to confirm results of the present study and to determine the pharmacokinetics of meloxicam for administration periods longer than 5 days.

Results of another study13 in which the pharmacokinetics of a single dose of meloxicam (0.2 mg/kg, PO) in rabbits was determined indicated a mean ± SD Cmax of 0.17 ± 0.06 µg/mL and a mean ± SD AUC of 1.8 ± 0.5 h•µg/mL. Results of the present study indicated that administration of 1 dose of meloxicam that was 5-fold as high as the dose administered to rabbits in that other study caused a proportionally (ie, approx 5-fold) higher mean Cmax (0.83 µg/mL) and AUCinf (10.37 h•µg/mL). These findings indicated that an increase in an orally administered dose of meloxicam from 0.2 to 1 mg/kg caused a proportional increase in circulating concentrations of the drug.

The high mean Cmax value of meloxicam determined for rabbits in this study (0.83 µg/mL) was especially notable because of the similarity of that value to the Cmax values for clinically effective doses of meloxicam in other species. For example, the Cmax of meloxicam is 0.82 µg/mL for dogs that receive a clinically effective meloxicam dose of 0.2 mg/kg.19 Additionally, investigators of a pharmacokinetic and pharmacodynamic study19 of meloxicam in cats estimated that plasma concentrations of 0.87 ± 0.3 µg/mL may inhibit ≥ 50% of the COX enzymes that are upregulated because of pain. Results of a study20 in which blood samples collected from adult humans that received clinically effective doses of meloxicam were analyzed indicated a Cmax of 0.88 to 1.92 µg/mL. Although plasma concentrations of meloxicam seemed to be similar in rabbits of the present study and animals of other species after administration of clinically effective doses in other studies, the effective meloxicam doses for animals of other species are lower than the dose administered to rabbits in this study. For example, clinically effective doses of meloxicam for 50- to 70-kg humans range from 0.1 to 0.3 mg/
kg,21 and dogs are commonly treated with 0.1 to 0.2 mg of meloxicam/kg.2 Extrapolation of data for animals of other species should be performed cautiously, and assumptions regarding the clinical efficacy of meloxicam in rabbits should not be made on the basis of results of studies including animals of other species. Therefore, results of the present study should be used to design further studies to determine the efficacy of meloxicam (1 mg/kg, PO) in rabbits.

Results of the present study indicated that the AUC and Cmax were higher after administration of multiple doses of meloxicam than they were after administration of 1 dose of that drug. These findings suggested that meloxicam accumulated in plasma of rabbits after administration of multiple doses, which was consistent with results of one study13 but was not consistent with results of another study.12 These differences in results among studies may be attributable to ages of rabbits used in the studies. The rabbits used in the present study and the other study13 in which meloxicam accumulation in plasma was found were 8 months old, whereas rabbits used in the study13 with conflicting results were 3 months old. Further studies may be warranted in which the effects of age on the pharmacokinetics of meloxicam in rabbits are determined because female rabbits attain sexual maturity when they are 5 months old.22 Additionally, the mean and SD of the plasma concentration of meloxicam in plasma samples collected 4 hours after administration of the fifth dose of meloxicam in the multiple-dose experiment of the present study seemed to be higher than they were for plasma samples obtained at earlier times during that experiment. The reasons for this finding could not be determined. That finding may have been attributable to accumulation of meloxicam in rabbits, but the magnitude of the differences in values suggested that experimental factors may have also contributed. Factors such as alterations in feeding time, amount of stress, hydration status, or quantity of food ingested within a short period before or after drug administration may have contributed to that finding, although rabbits had no variations in husbandry or experimental procedures during the study to which that finding could be attributed, to the authors’ knowledge.

The range of values of the meloxicam terminal half-life determined for rabbits during single- (4.9 to 7.1 hours) and multiple-dose (5.6 to 7.8 hours) experiments in the present study was within the range of values determined for rabbits in another study,13 although the range of values in that other study was larger (4.5 to 42 hours). The time to peak plasma meloxicam concentration was slightly longer for rabbits of the present study (approx 6 hours) than it was for rabbits in that other study13 (4 hours). Because the meloxicam Tmax for rabbits was approximately 6 hours in the study reported here, the meloxicam Cmax was not determined for days 1 to 4 of the multiple-dose experiment because blood samples were obtained 4 hours after drug administration during those days.

Results of plasma biochemical analyses in the present study indicated BUN concentrations and alkaline phosphatase activities for rabbits were significantly higher in posttreatment plasma samples than they were in baseline plasma samples. These findings may have been attributable to physiologically normal variations in values or to experimental factors (housing, collection of multiple blood samples, handling, or stress of rabbits associated with experimental procedures) rather than the effects of meloxicam. A control (untreated) group of rabbits was not included in this study; therefore, the effects of those experimental factors could not be determined. However, plasma BUN concentrations were lower than the upper limit of the reference range for rabbits,16,17 and both baseline and posttreatment plasma alkaline phosphatase activities were higher than the reference range for rabbits.16,17 Suggesting that increases in values of these analytes were not attributable to experimental procedures. Potential causes for high circulating alkaline phosphatase activities include hepatic induction, hepatobiliary disease, bone formation, or physiologically normal variation among animals. Because plasma values of other biochemical analysis hepatic analytes (eg, alanine aminotransferase activity and total bilirubin and albumin concentrations) were within the reference ranges for rabbits of the present study, it was unlikely that increases in plasma alkaline phosphatase activities were attributable to meloxicam-induced liver damage.23,24 In addition, the range of values included in the SDs of the posttreatment plasma sample BUN concentrations and alkaline phosphatase activities included the baseline plasma sample values, and the statistically significant increases in the values of these variables may not have indicated clinically relevant changes. In addition, the rabbits of this study did not develop clinical signs attributable to adverse effects of meloxicam. Rabbits undergoing surgery, geriatric rabbits, or rabbits with preexisting diseases may be at a greater risk for adverse effects of meloxicam versus rabbits without those factors; therefore, further studies may be warranted to determine the clinical safety of meloxicam for rabbits.

In the multiple-dose experiment of the present study, the value for meloxicam accumulation was expected to be approximately 1.33 as determined on the basis of the expected ratio of the terminal half-life and the dosing interval. Accumulation of meloxicam was determined via calculation of the ratio of AUC_{0–24} to AUC_{inf}. The reason the AUC_{0–24} (for the multiple-dose experiment) was used for determination of meloxicam accumulation was to account for residual amounts of meloxicam in plasma from previously administered doses. If steady-state concentration had been achieved, the AUC_{0–24} would have been equivalent to the AUC_{inf} at 24 hours after administration of 1 dose. The observed accumulation value was larger than expected (mean, 1.55; range, 1.27 to 2.08) on the basis of the AUCs. This finding suggested that accumulation of meloxicam varied among rabbits of this study. Long-term administration of meloxicam to rabbits was not evaluated in this study, but the potential for drug accumulation in rabbits may warrant reduction of the dose if meloxicam is administered for > 5 days. Further studies are warranted to determine the safety of meloxicam (1 mg/kg, PO) for various treatment durations.

Nonsteroidal anti-inflammatory drugs (eg, meloxicam, carprofen, and ketoprofen) are commonly pre-
scribed for short- and long-term pain control in animals. Meloxicam is commonly administered to rabbits because it is readily available in a palatable liquid preparation that is easy to administer. The peak plasma concentration of meloxicam after oral administration to rabbits of this study was similar to the peak plasma concentration in animals of other species after administration of a clinically effective dose. Oral administration of 1 mg of meloxicam/kg was well tolerated by rabbits of this study. Findings of the study suggested that oral administration of 1 mg of meloxicam/kg may be necessary to attain clinically effective circulating concentrations in rabbits. However, that meloxicam dose should be evaluated in further studies to determine safety and clinical efficacy for rabbits.

References