Pharmacokinetics and plasma concentrations of acetylsalicylic acid after intravenous, rectal, and intragastric administration to horses

Ted A. Broome, Murray P. Brown, Ronald R. Gronwall, Matthew F. Casey, Kelly A. Meritt

Abstract

Six healthy adult horses (5 mares and 1 stallion) were given a single dose of acetylsalicylic acid (ASA), 20 mg/kg of body weight, by intravenous (IV), rectal, and intragastric (IG) routes. Serial blood samples were collected via jugular venipuncture over a 36-h period, and plasma ASA and salicylic acid (SA) concentrations were determined by high-performance liquid chromatography. After IV administration, the mean elimination rate constant of ASA (± the standard error of the mean) was 1.32 ± 0.09 h⁻¹, the mean elimination half-life was 0.53 ± 0.04 h, the area under the plasma concentration-versus-time curve (AUC) was 2555 ± 98 µg • min/mL, the plasma clearance was 472 ± 18.9 mL/h/kg, and the volume of distribution at steady state was 0.22 ± 0.01 L/kg. After rectal administration, the plasma concentration of ASA peaked at 5.05 ± 0.80 µg/mL at 0.33 h, then decreased to undetectable levels by 4 h; the plasma concentration of SA peaked at 17.39 ± 5.46 µg/mL at 2 h, then decreased to 1.92 ± 0.25 µg/mL by 36 h. After rectal administration, the AUC for ASA was 439.4 ± 94.55 µg • min/mL and the bioavailability was 0.17 ± 0.037. After IG administration, the plasma concentration of ASA peaked at 1.26 ± 0.10 µg/mL at 0.67 h, then declined to 0.37 ± 0.37 µg/mL by 36 h; the plasma concentration of SA peaked at 23.90 ± 4.94 µg/mL at 4 h and decreased to 0.85 ± 0.31 µg/mL by 36 h. After IG administration, the AUC for ASA was 146.70 ± 24.90 µg • min/mL and the bioavailability was 0.059 ± 0.013. Administration of a single rectal dose of ASA of 20 mg/kg to horses results in higher peak plasma ASA concentrations and greater bioavailability than the same dose given IG. Plasma ASA concentrations after rectal administration should be sufficient to inhibit platelet thromboxane production, and doses lower than those suggested for IG administration may be adequate.

Résumé

Six chevaux adultes en santé (5 juments et 1 étalon) ont reçu une dose unique d’acide acétylsalicylique (ASA), 20 mg/kg de poids corporel, par voie intraveineuse (IV), rectale et intra-gastrique (IG). Une série d’échantillons sanguins ont été prélevés sur une période de 36 h par ponction de la veine jugulaire et les concentrations plasmatiques d’ASA et d’acide salicylique (SA) ont été mesurées par HPLC. Après administration IV, la constante moyenne du taux d’élimination d’ASA (± erreur-type) était de 1,32 ± 0,09 h⁻¹, la demi-vie d’élimination moyenne de 0,53 ± 0,04 h, la surface sous la courbe de la relation concentration plasmatique-vers-temps (AUC) de 2555 ± 98 µg • min/mL, la clearance plasmatique de 472 ± 18,9 mL/h/kg et le volume de distribution à l’état stationnaire de 0,22 ± 0,01 L/kg. Après administration rectale, la concentration plasmatique d’ASA a atteint un pic de 5,05 ± 0,80 µg/mL après 0,33 h, puis diminuait à des seuils non-déetectables après 4 h; la concentration plasmatique de SA a atteint un pic de 17,39 ± 5,46 µg/mL après 2 h, puis diminuait à un niveau de 1,92 ± 0,25 µg/mL après 36 h. Après administration rectale, la valeur AUC pour l’ASA était de 439,4 ± 94,55 µg • min/mL et la biodisponibilité de 0,17 ± 0,037. Après administration IG, la concentration plasmatique d’ASA a atteint un pic de 1,26 ± 0,10 µg/mL après 0,67 h, puis diminuait jusqu’à 0,37 ± 0,37 µg/mL après 36 h; la concentration plasmatique de SA a atteint un pic de 23,90 ± 4,94 µg/mL après 4 h et diminuait jusqu’à 0,85 ± 0,31 µg/mL après 36 h. Après administration IG, la valeur AUC pour l’ASA était 146,70 ± 24,90 µg • min/mL et la biodisponibilité de 0,059 ± 0,013. L’administration d’une dose unique de 20 mg/kg d’ASA par voie rectale à des chevaux entraîne un pic plasmatique d’ASA plus élevé et une plus grande biodisponibilité qu’une même dose administrée par voie IG. Les concentrations plasmatiques d’ASA après administration rectale devraient être suffisantes pour inhiber la production de thromboxane par les plaquettes, et des doses inférieures à celles suggérées pour administration IG pourraient être adéquates.

Introduction

Acetylsalicylic acid (ASA) is a nonsteroidal anti-inflammatory drug (NSAID) that has antipyretic, analgesic, and potent antiplatelet properties. Its pharmacokinetics have been evaluated after intravenous (IV), oral, and rectal administration in humans (1–3), after oral administration in cattle (4), and after oral and IV administration in horses (5,6). Acetylsalicylic acid is poorly absorbed from the gastrointestinal tract of horses after oral administration and disappears rapidly from the plasma (5). The
half-life ($t_{1/2}$) of ASA after IV administration to horses is 0.11 h (6). Acetylsalicylic acid is rapidly converted to salicylic acid (SA) via deacetylation by endogenous esterases and by hepatic mechanisms. Doses of 35 mg/kg administered orally every 2 h are necessary to maintain effective anti-inflammatory plasma concentrations (5). Because of its poor absorption and short half-life, ASA is not used routinely for treatment of inflammatory conditions of horses.

Acetylsalicylic acid is used for the treatment and prevention of arterial thrombotic diseases in humans and has likewise been recommended for the treatment of equine diseases that have arterial thrombosis as part of their pathogenesis; such diseases include laminitis, endotoxemia, disseminated intravascular coagulation, and thromboembolic colic (7–9). Arterial thrombus formation is initiated by damage to vascular endothelium and propagated by interaction of platelets with the damaged vessel wall. Stimulated platelets produce thromboxane, which potentiates platelet aggregation and causes local vasoconstriction. Acetylsalicylic acid irreversibly inhibits platelet cyclooxygenase by covalent acetylation of the enzyme (6,10). Because platelets are non-nucleated cells and are incapable of synthesizing additional cyclooxygenase, platelet thromboxane production will be inhibited for the life of any circulating platelets exposed to ASA (8,10). Administration of a single oral dose of ASA (20 mg/kg) to horses decreases the plasma thromboxane concentration by 68% to 93% for 3 d (7).

Arterial thrombosis may occur concurrently with gastrointestinal diseases, such as postoperative ileus and proximal enteritis, that prevent the use of orally administered drugs. An alternative route of administration is needed in these instances. Administration of rectal suppository forms of ASA is effective in humans when oral administration is impractical (3). Drugs such as metronidazole and indomethacin have been shown to be absorbed after rectal administration in horses (11,12). We hypothesized that the bioavailability of ASA after rectal administration to horses would be comparable or superior to that seen after oral administration. The purposes of the studies reported here were to determine the pharmacokinetics of ASA after a single IV dose of 20 mg/kg and to compare the plasma concentrations of ASA and SA and the bioavailability of ASA after a single intragastric (IG) and a single rectal dose of 20 mg/kg as a test of this hypothesis.

Materials and methods

Animals

We used 6 healthy adult horses (5 mares and 1 stallion), of various breeds, with weights ranging from 463 to 586 kg, for all experiments. The horses were determined to be clinically normal before each experiment by physical examination and a complete blood count. Serum biochemical testing was not performed. The horses were housed in box stalls for 24 h before and during the first 12 h of each experiment. They were fasted for 24 h before and during the first 12 h of experiment 2 (rectal administration), to mimic the clinical situation that occurs in horses with gastrointestinal disease that prevents oral intake, but were allowed free choice of coastal bermudagrass hay at all times during experiments 1 (IV administration) and 3 (IG administration). Each horse participated in all 3 experiments. There was at least a 10-d interval between experiments. The use of the horses in this study was approved by the Institutional Animal Care and Use Committee of the University of Florida.

Drug administration

In each experiment, the horses received a single ASA dose of 20 mg/kg of body weight by IV, rectal, or IG administration.

For the IV experiment, an indwelling catheter (Abbocath; Abbott Hospitals, North Chicago, Illinois, USA) was placed into a jugular vein after aseptic preparation of the catheter site. The calculated dose of reference standard ASA (Sigma Chemical Company, St. Louis, Missouri, USA) was dissolved in 120 mL of warm ethanol (absolute ethyl alcohol; Florida Distillers Company, Lake Alfred, Florida, USA) immediately before injection. The ethanol/ASA solution was injected through the jugular catheter over a 4-min period.

In the rectal-administration experiment, contents were manually removed from the distal 65 cm of the rectum immediately before the ASA was administered. Boluses of ASA, 15.6 g (The Butler Company, Columbus, Ohio, USA), were crushed and suspended in 40 mL of tap water. A 30 french Foley catheter was inserted 40 cm into the rectum, and the ASA suspension was injected through the catheter with a 60-mL catheter-tip syringe. The syringe was rinsed with an additional 30 mL of water, which was then injected through the catheter. The horses were monitored for defecation throughout the first 12 h of sampling, and the time to 1st defecation was recorded.

In the IG-administration experiment, ASA boluses were crushed and suspended in approximately 120 mL of tap water and administered by nasogastric tube. The tube was flushed with an additional 120 mL of water.

Collection and handling of samples

Blood was collected from the jugular vein into chilled 14-mL evacuated glass tubes containing 14.0 mg of potassium oxalate and 17.5 mg of sodium fluoride (Vacutainer; Becton Dickinson, Rutherford, New Jersey, USA). Samples were taken immediately before and at 0.08, 0.17, 0.25, 0.33, 0.50, 0.67, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, and 36 h after ASA administration in all the experiments. Additional samples were collected at 0.03 and 0.12 h after IV administration. Time 0 was recorded as the time when half the dose had been administered. Samples were collected from either jugular vein after rectal or IG administration. After IV administration, all samples were collected from the jugular vein opposite to that used for injection. The blood samples were immediately placed on ice slush. All samples were centrifuged within 30 min of collection, at 3000 × g for 20 min at 4°C, and the plasma was harvested and frozen in polypropylene tubes (Sarstedt, Princeton, New Jersey, USA) at −70°C. Plasma ASA and SA concentrations were determined within 72 h of sample collection by means of high-performance liquid chromatography (HPLC).

Determination of plasma ASA and SA concentrations

Plasma ASA and SA concentrations were determined by HPLC according to a modification of the method of Mason and Gillilan (13). Samples were kept chilled at all times during the assay procedure to prevent hydrolysis of ASA to SA. Acetylsalicylic acid and SA were...
extracted from 0.5 mL of plasma by the addition of 0.2 mL of 50% v/v phosphoric acid containing 0.25 g/mL of ammonium sulfate and 8.0 mL of 50% v/v ethyl acetate in butyl chloride. Samples were agitated on a horizontal shaker for 2 min, then centrifuged at 4°C for 10 min at 3000 × g. The organic supernatant was removed and transferred to 13 × 100-mm glass tubes. The tubes were placed on ice slush in an evaporation rack (Evap-O-Rac; Cole-Parmer, Niles, Illinois, USA), and the organic layer was evaporated to near dryness under air stream. The remaining organic layers were individually evaporated to dryness to prevent sublimation of the ASA. Immediately thereafter, the samples were resuspended in 2 mL of the mobile phase for HPLC or stored dry at −70°C and analyzed by HPLC within 24 h of extraction.

For HPLC, we used a dual-piston reciprocating pump (LKB 2150 HPLC Pump; LKB Instruments, Gaithersburg, Maryland, USA), a variable wavelength detector (Spectro Flow 757; Kratos Analytical Instruments, Ramsey, New Jersey, USA) operated at 237 nm, and a stainless steel column (25 cm × 4.6 mm) packed with reverse-phase chromatographic medium (5-μm particles) (Microsorb C18; Rainin Instrument Company, Woburn, Massachusetts, USA). The mobile phase consisted of a mixture of HPLC water (71% v/v), acetonitrile (28% v/v), and acetic acid (1% v/v). The mobile-phase flow rate was 1 mL/min. Under these conditions, retention times were about 6.7 min for ASA and 8.6 min for SA.

Standards were prepared by adding ASA or SA stock solutions (1 mg ASA or SA/mL distilled water) to normal equine plasma. Standards were extracted and analyzed exactly as test samples. A standard curve was constructed by linear regression analysis, and ASA and SA concentrations in test samples were determined from the standard curve. The lowest limits of detection for the assay were 0.5 μg/mL for ASA and 0.125 μg/mL for SA.

**Pharmacokinetic analysis**

The following equations were fit to the ASA concentration-versus-time data for each experiment for each horse. For calculations of pharmacokinetic parameters, measured plasma concentrations that were below detectable limits were considered to be zero. A weighted, nonlinear fit of the mathematical model to the data was done with the use of a computer algorithm that minimized the sum of the squared deviations (14). Thus,

\[ C_p = C_1 \cdot e^{-\lambda_1 \cdot t} + C_2 \cdot e^{-\lambda_2 \cdot t} \]

where \( C_p \) is the plasma ASA concentration, \( e \) is the base of the Napierian logarithms, \( C_1 \) and \( C_2 \) are the 0 time intercepts of the 2 exponential components, \( \lambda_1 \) is the distribution rate constant, \( \lambda_2 \) is the overall elimination rate constant (\( K_{\text{el}} \)), and \( t \) is the time in hours after dose administration. The pharmacokinetic parameters were calculated on the basis of noncompartmental kinetics (15). The area under the plasma concentration-versus-time curve (AUC) for IV administration was calculated as follows.

\[ \text{AUC}_{IV} = C_1/\lambda_1 + C_2/\lambda_2 \]

Plasma clearance was calculated as the dose divided by the AUC. The area under the moment curve (AUMC) for IV administration was calculated as follows.

\[ \text{AUMC}_{IV} = C_1/\lambda_1^2 + C_2/\lambda_2^2 \]

The volume of distribution at steady state \( [V_{d(ss)}] \) was calculated as the dose multiplied by the AUMC divided by the square of the AUC, as follows.

\[ V_{d(ss)} = \text{dose} \cdot \text{AUMC}/\text{AUC}^2 \]

The plasma ASA concentration-versus-time data after rectal or IG administration of ASA were estimated as follows.

\[ C_p = C_1 \cdot (e^{-\lambda_1 \cdot t} - e^{-\lambda_2 \cdot t}) \]

The AUC for rectal or IG administration was calculated as follows.

\[ \text{AUC}_{\text{rectal or IG}} = C_1/\lambda_1 - C_1/\lambda_2 \]

The bioavailability (F) of ASA after rectal or IG administration was calculated as follows.

\[ F_{\text{rectal or IG}} = \frac{\text{AUC}_{\text{rectal or IG}}}{\text{AUC}_{IV}} \]

A paired Student’s t-test was used to determine significant differences between rectal and IG pharmacokinetic values and peak plasma concentrations of ASA. Probabilities of less than 5% (\( P < 0.05 \)) were considered significant.

### Results

One horse had an increase in respiratory rate and signs of mild abdominal pain after IV injection of the ethanol/ASA solution. These signs were transient and resolved without treatment within 45 min.

The pharmacokinetic values for ASA and the plasma concentrations of ASA and SA after IV administration of ASA were calculated from data obtained from 5 horses; the IV data from the 6th horse were discarded owing to perivascular injection of a portion of the ASA solution. After IV administration, the mean plasma concentration (± standard error of the mean) of ASA peaked at 207.76 ± 30.70 μg/mL at 0.03 h and decreased to undetectable levels by 6 h (Figure 1). The plasma clearance was 472 ± 18.9 mL/h/kg and the \( t_{\text{1/2}} \) 0.53 ± 0.04 h (Table I). The mean plasma SA concentration was 26.52 ± 5.81 μg/mL at 0.03 h, reached a maximum of 124.18 ± 23.62 μg/mL at 1 h, and then decreased to 0.57 ± 0.29 μg/mL by 36 h (Table II).

After rectal administration of ASA, the plasma concentration of ASA was 0.87 ± 0.46 μg/mL and that of SA 0.32 ± 0.08 μg/mL at 0.08 h. The ASA concentration peaked at 5.05 ± 0.80 μg/mL at 0.33 h and decreased to undetectable levels by 4 h. The SA concentration peaked at 17.39 ± 5.46 μg/mL at 2 h and decreased to 1.92 ± 0.25 μg/mL by 36 h. The AUC for ASA was 439.4 ± 94.55 μg · min/mL, and the bioavailability was 0.17 ± 0.037. The greatest individual peak concentration (665.16 μg/mL) and bioavailability (0.24) for ASA were in the male horse. In the female horses, the peak concentrations ranged from 181.24 to 586.95 μg/mL and the bioavailability from 0.07 to 0.23.

The time to defecation after rectal administration of ASA had no apparent effect on the peak plasma ASA concentration. One horse passed feces containing crushed ASA approximately 3 min after rectal administration; the peak plasma ASA concentration in this horse was 3.79 μg/mL. In 2 horses with a time to defecation of 47 min in 1 horse and 3 h in the other, the peak plasma ASA concentrations were 8.74 and 4.68 μg/mL, respectively. In the remaining 3 horses, the time to defecation was greater than 12 h, and...
The curve represents the fit of the mathematical model to the mean concentration at each time.

Figure 1. Mean plasma concentration of acetylsalicylic acid (ASA) in 5 horses given a single intravenous dose (20 mg/kg) of ASA (experiment 1). The curve represents the fit of the mathematical model to the mean concentration at each time.

the peak plasma ASA concentrations were 3.06, 5.76, and 7.40 µg/mL, respectively.

After IG administration, ASA and SA were first detectable in plasma at 0.08 h, at mean concentrations of 0.12 ± 0.12 and 0.39 ± 0.25 µg/mL, respectively. The mean ASA concentration reached a maximum of 1.26 ± 0.10 at 0.67 h and declined to 0.37 ± 0.37 µg/mL by 36 h. The mean SA concentration reached a maximum of 23.90 ± 4.94 µg/mL at 4 h and decreased to 0.85 ± 0.31 µg/mL by 36 h. The AUC of ASA was 146.7 ± 24.90 µg • min/mL and the bioavailability 0.059 ± 0.013 after IG administration.

Discussion

This study demonstrated that the bioavailability of ASA was approximately 3 times greater (0.17 ± 0.037 versus 0.059 ± 0.013; \( P = 0.02 \)) after rectal administration to fasted horses than after IG administration to nonfasted horses, and the peak plasma ASA concentration was approximately 4 times greater (5.05 ± 0.80 µg/mL versus 1.26 ± 0.10 µg/mL; \( P = 0.007 \)). The ASA was eliminated rapidly after IV administration. The \( t_{1/2} \) value of 0.53 ± 0.04 h was higher than the \( t_{1/2} \) of 0.11 ± 0.02 h reported by Lees and colleagues (6) after IV administration of 19 mg/kg of lysine acetylsalicylate to horses. The difference may be due to the different formulations of ASA used in the 2 studies.

In humans, absorption of drugs, including ASA, is usually poorer after rectal administration than after oral administration (3,16). In horses, peak serum concentrations of metronidazole are lower when the drug is given rectally than when an equivalent dose is given by the IG or oral route (12). There may be several reasons for the enhanced absorption and higher bioavailability of ASA after rectal administration in this study. Gastrointestinal absorption of ASA is determined by the rate of dissolution, the luminal pH, and the rate of gastric emptying (17). The solubility of ASA is limited in the normal acid environment of the equine stomach and proximal small intestine (18,19). In the less acidic environment of the rectum (pH 6.0 to 6.5) (18), ASA solubility is increased, which should result in greater absorption (20). In human subjects with oral administration, plasma ASA concentrations peaked sooner, at levels approximately 48% higher, when sodium bicarbonate was administered with ASA than when ASA was administered alone (21).

Drugs that are administered in the distal rectum in humans may be subject to reduced first-pass hepatic metabolism (22). The rectum of the horse is approximately 20 to 30 cm long. Venous drainage of the orad half occurs via the caudal mesenteric vessels, which empty into the portal circulation. Venous outflow from the distal portion of the rectum, however, drains into the caudal vena cava via the internal iliac or pudendal veins, thus bypassing the portal circulation (23). It is unlikely that a reduction in first-pass hepatic metabolism after rectal administration contributed significantly to the higher plasma concentrations of ASA in this study, because the ASA suspension was deposited approximately 10 cm orad to the rectum (in the terminal small colon). A portion of drug, however, could have spread to and been absorbed from the caudal rectum (22), avoiding first-pass hepatic metabolism.

The low absorption of ASA after IG administration may be due to the feeding of hay to the horses before and during the IG-administration experiments. The presence of food in the stomach can lead to slower gastric emptying and increased drug binding by organic matter (24–26). In humans, ASA absorption is delayed and plasma ASA concentrations are lower when the drug is administered after a meal (24). Absorption of orally administered phenylbutazone was reduced by approximately 50% in horses fed hay before and after the drug’s administration (25). The absorption of rectally administered drugs can also be lowered by binding of the drug to organic matter in the gastrointestinal tract (16). The influence of such drug binding was reduced in this study because feces were removed from the rectum before drug administration; this may have contributed to the increased bioavailability of ASA administered rectally compared with that after oral administration. Similarly, fecal material would be decreased in the rectum of horses with gastrointestinal diseases in which food intake is reduced or absent. Although we realize that the study design (the horses being nonfasted for IG administration) created a condition that would lower the absorption of intragastrically administered ASA, the IG administration of ASA to nonfasted horses would likely mimic the clinical situation in which horses are not routinely fasted before oral administration of NSAIDs.

The peak plasma SA concentrations after IG administration were higher than those after rectal administration of ASA. The presence of food in the stomach of the nonfasted horses would delay gastric emptying and may have resulted in increased gastric retention of ASA. ASA is rapidly hydrolyzed to SA within the gastrointestinal tract (26). Consequently, larger intestinal concentrations of SA would have been available for absorption, resulting in higher plasma concentration.

Oral administration of NSAIDs, including ASA, can result in gastric irritation and ulceration (27,28). Damage to the gastric mucosa may result more from the physical interaction of the drug with the
mucosa than from the inhibition of local prostaglandin synthesis. In rats, 100 mg of ASA/kg in a single dose caused significant gastric mucosal irritation when administered orally but no gastric damage when administered rectally (28). Thus, rectal administration of ASA may prevent the gastric mucosal damage that can occur after oral administration. We did not examine the rectal mucosa of our horses after rectal administration of ASA. Long-term rectal administration of ASA, however, has been shown to cause anorectal ulceration and stricture in humans (29,30).

Orally administered ASA significantly inhibits plasma thromboxane production and prolongs bleeding time in horses (6–9,31). Oral administration of ASA is not always feasible in horses with gastrointestinal disease. Currently in the United States, there is no commercially available preparation of ASA that can be given intravenously. Although an IV formulation of SA is available, SA does not inhibit platelets (10). To our knowledge, plasma or tissue concentrations of ASA necessary to inhibit thromboxane production in horses have not been determined. Baxter (7) showed that a single IG dose of ASA of 5 to 20 mg/kg administered to fasted horses significantly inhibited thromboxane production for 3 to 5 d, in a dose-dependent manner. Although we compared the bioavailability of ASA after rectal administration to fasted horses with that after IG administration to nonfasted horses, Kopp and associates (9) demonstrated that 17 mg/kg of ASA given orally once daily to nonfasted horses significantly reduced serum thromboxane B₂ concentrations, to barely detectable levels, during the administration period.

<table>
<thead>
<tr>
<th>Route of administration; mean ± standard error of the mean (sₓ)</th>
<th>Intravenous (IV) (n = 5)</th>
<th>Rectal (n = 6)</th>
<th>Intra gastric (IG) (n = 6)</th>
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<tr>
<td>Pharmacokinetic value</td>
<td></td>
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<tr>
<td>Elimination rate constant (h⁻¹)</td>
<td>1.32 ± 0.09</td>
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<td>ND</td>
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<tr>
<td>Elimination half-life (h)</td>
<td>0.53 ± 0.04</td>
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<td>ND</td>
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<tr>
<td>Area under plasma-versus-concentration time (AUC) (µg • min/mL)</td>
<td>2555 ± 98</td>
<td>439.4 ± 94.55ᵃ</td>
<td>146.7 ± 24.90</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
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<td>Estimated from AUC</td>
<td>0.36 ± 0.02</td>
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<td>ND</td>
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<tr>
<td>At steady state</td>
<td>0.22 ± 0.01</td>
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<tr>
<td>Plasma clearance (mL/h/kg)</td>
<td>472 ± 18.9</td>
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<td>ND</td>
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<tr>
<td>Bioavailability</td>
<td>N/A</td>
<td>0.17 ± 0.037ᵃ</td>
<td>0.059 ± 0.013</td>
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ND — not determined; N/A — not applicable
ᵃ Significantly different (P < 0.05) from IG values

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<th>Time after administration (h)</th>
<th>Route of administration; concentration, mean ± sₓ (µg/mL)</th>
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<td>0.03</td>
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<td>36</td>
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NS — no sample; ND — not detectable; sₓ — standard error of the mean

Table I. Pharmacokinetic mean values for acetylsalicylic acid (ASA) after a single dose (20 mg/kg) administered intravenously, rectally, or intragastrically to healthy adult horses

Table II. Mean plasma acetylsalicylic acid (ASA) and salicylic acid (SA) concentrations in the horses after the single dose of ASA
We have shown that a single rectal dose of ASA of 20 mg/kg in fasted horses results in higher peak plasma ASA concentrations and greater bioavailability than the same dose given IG to nonfasted horses. Our findings, when combined with those of Kopp and associates (9), suggest that rectal administration of ASA should result in adequate inhibition of serum thromboxane production when oral administration is contraindicated. Therefore, under these experimental conditions, our hypothesis that the bioavailability of ASA after rectal administration would be comparable or superior to that after oral administration is supported. Additionally, lower doses than those suggested for IG administration may be sufficient.

References

20. Feldman M, Cryer B. Aspirin absorption rates and platelet inhibition times with 325-mg buffered aspirin tablets (chewed or swallowed intact) and with buffered aspirin solution. Am J Cardiol 1999;84:404–409.