Materials and Methods cont.

HPLC Assay

Plasma samples were analyzed by high performance liquid chromatography using a published method (Hardie & Lai, 1982) with modifications (Navarre et. al., 2001). The HPLC system consisted of a Waters pump and auto-injector and a variable wavelength Jasco UV/VIS detector interfaced with an integrator. The mobile phase consists of acetone, methanol and 1 M acetic acid solution (40:30:30) and the injection was done on a C-18 column at a wavelength of 313 nm, and a flow rate of 1.3 ml/min. The amount of flunixin in each sample was quantified based on a peak area ratio method with respect to the internal standard, naproxen.

The standard curve was prepared for flunixin plasma concentrations of 0.01 to 100 ug/mL. The intra- and inter-day variation was < 8%. The extraction efficiency for flunixin and the internal standard were 97% and 95%, respectively.

Extraction procedure:

To 0.5 ml of plasma 1.5 ml of acetone containing (1 mg/mL) naproxen was added in order to precipitate the proteins. The samples were then vortexed for 30 seconds and then centrifuged at 2500 rpm for 15 minutes. The supernatant was transferred to a fresh tube. To the remaining pellet, 1 ml of acetone was added followed by vortexing for 15 seconds and centrifuging at 2500 rpm for 5 minutes. Both the supernatants were pooled together and evaporated to dryness, at 35°C, under a gentle stream of nitrogen. The residue remaining after evaporation was reconstituted in 0.5 ml of mobile phase and a 50 μL aliquot of the same was injected into the HPLC system.

Pharmacokinetic Analysis:

Pharmacokinetic parameters for flunixin following single IV and oral administration were determined by non-compartmental analysis with the assistance of the program Phoenix WinNonlin v6. The terminal decline in the LN plasma concentrations was used to identify the elimination rate constant (t1/2) based on 1/2 weighting. The linear/log transform of the AUC vs. time curve was then plotted. The AUC and its corresponding SD were obtained from individual values of AUC, AUMC, and t1/2. An estimate of the extent of oral absorption was made based on the ratio of AUCs for oral to IV. No compartmental analysis was performed since some IV and oral plasma concentration profiles showed secondary peaks suggesting drug redistribution or recycling.

Results

Following a single 2.2 mg/kg intravenous dose of flunixin, the maximum plasma concentration obtained was 30.2+/- 2.5 ug/mL with a mean half-life of 9.65 hours. A range of 3.4-3.8 hours. The clearance(Cl) was 30.2+/- 2.5 ug/mL IV with a mean half-life of 9.65 hours. A range of 3.4-3.8 hours. The clearance(Cl) was

Discussion

The intravenous half-life of flunixin in alpacas (8-11.5 hours) was much longer than llamas, (1.47 +/- 0.61 hr), sheep (3.4-5.8 hr) and cattle (3.1 and 8.1 hr) and horses (3.1 and 6.3 hr). There was greater assay sensitivity to the terminal phase which may account for a difference in half-lives, but there is a distinct difference between llamas and alpacas which may be due to a difference in pharmacokinetic modeling. Clearance is the same order of magnitude as llamas.

The bioavailability was erratic and ranged from 12.27% to 96.94%. A large and standard deviation of 37.2% was seen with other drugs administered orally to alpacas. Oral absorption is not a reliable route of administration to destruction of the drug through enzymatic pathways and there is evidence of hepatic or intestinal recycling leading to secondary peaks and longer half lives.

Materials and Methods

Six adult alpacas ranging in weight (51-94 kg) were administered a single dose of 2.2 mg/kg flunixin (a non-steroidal anti-inflammatory drug) intravenously (IV), then orally. These animals were randomly assigned to two treatment groups, using an open, single-dose, four-week, randomized cross-over design. Blood samples were taken over a 72-hour period of time from a separate catheter, processed and frozen at -80 degrees C until analysed by a high performance liquid chromatography.

Abstract

Six adult alpacas were administered a single dose of 2.2 mg/kg flunixin (a non-steroidal anti-inflammatory drug) intravenously (IV), then orally. These animals were randomly assigned to two treatment groups, using an open, single-dose, four-week, randomized cross-over design. Blood samples were taken over a 72 hour period of time from a separate catheter, processed and frozen at -80 degrees C until analysed by a high performance liquid chromatography. Pharmacokinetic parameters for flunixin IV and oral administration were determined by a non-compartmental analysis with the assistance of the program Phoenix WinNonlin v6.

The maximum plasma concentration obtained was 30.2+/- 2.5 ug/mL with a mean half-life of 9.65 hours with a range of 8-11.5 hours. The clearance(Cl) was 30.2+/- 2.5 ug/mL IV with a mean half-life of 9.65 hours. A range of 3.4-3.8 hours. The clearance(Cl) was

Introduction

Non-steroidal anti-inflammatory drugs are commonly used in veterinary medicine as an analgesic, anti-inflammatory and antipyretic therapy. These drugs are currently being administered to small animals, horses, cattle and even llamas with a species specific drug study. Alpacas have shown evidence of gastrointestinal ulcers. The use of flunixin meglumine in alpacas is made based on the ratio of AUCs for oral to IV. No compartmental analysis was performed since some IV and oral plasma concentration profiles showed secondary peaks suggesting drug redistribution or recycling.

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Six adult alpacas ranging in weight (51-94 kg) were administered a single dose of 2.2 mg/kg flunixin (a non-steroidal anti-inflammatory drug) intravenously (IV), then orally. These animals were randomly assigned to two treatment groups, using an open, single-dose, four-week, randomized cross-over design. Blood samples were taken over a 72 hour period of time from a separate catheter, processed and frozen at -80 degrees C until analysed by a high performance liquid chromatography.

Pharmacokinetic Parameters and Toxicity

Pharmacokinetic parameters for flunixin following single IV and oral administration were determined by non-compartmental analysis with the assistance of the program Phoenix WinNonlin v6. The terminal decline in the LN plasma concentrations was used to identify the elimination rate constant (t1/2) based on 1/2 weighting. The linear/log transform of the AUC vs. time curve was then plotted. The AUC and its corresponding SD were obtained from individual values of AUC, AUMC, and t1/2. An estimate of the extent of oral absorption was made based on the ratio of AUCs for oral to IV. No compartmental analysis was performed since some IV and oral plasma concentration profiles showed secondary peaks suggesting drug redistribution or recycling.

Pharmacokinetics of Intravenous and Oral Flunixin in Alpacas

Materials and Methods

Six adult alpacas ranging in weight (51-94 kg) were administered a single dose of 2.2 mg/kg flunixin (a non-steroidal anti-inflammatory drug) intravenously (IV), then orally. These animals were randomly assigned to two treatment groups, using an open, single-dose, four-week, randomized cross-over design. Blood samples were taken over a 72 hour period of time from a separate catheter, processed and frozen at -80 degrees C until analysed by a high performance liquid chromatography.

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