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CONCLUSIONS
Results of this study suggest that ceftiofur could have an influence on the pharmacokinetics of ketoprofen after IM administration to cattle allowing a complete bioavailability in ketoprofen (99.6%) with the combination C. Indeed, AUC_{last} parameter was significantly increased in the presence of ceftiofur.

2.12.
Influence of the administration of omeprazole on the oral absorption of cephalexin: differences between adults and aged dogs

M. P. LUPI, S. PASSINI, L. MONTOYA & G. ALBARELLOS
Department of Pharmacology, Faculty of Veterinary Science, UBA, Ciudad Autónoma de Buenos Aires, Argentina

INTRODUCTION
Cephalexin, a first generation cephalosporin is frequently used in dogs. Studies in humans have shown that co-administration of oral cephalexin and omeprazole, a proton pump inhibitor, delayed absorption of the antibiotic with negative consequences on antibiotic efficacy (Madaras-Kelly, 2004).

OBJECTIVE
The aim of this study was to evaluate the impact of previously administered omeprazole between adults and aged dogs on cephalexin oral pharmacokinetic.

MATERIALS AND METHODS
Ten dogs, five between 5–6 years old (group A), and five between 10–14 years old (group B) were used. The trial was divided into two stages (I and II). Stage I: A and B received a single dose of cephalexin tablets (25 mg kg^{-1}, oral). Stage II: both groups received omeprazole (1 mg kg^{-1}, oral) for 5 days and a single dose of cephalexin (25 mg kg^{-1}, oral) on day 5. After cephalexin administration, blood samples were taken at predetermined times. Cephalexin plasma concentrations were determined by a microbiological assay. Pharmacokinetic parameters were analysed using a computer program (Phoenix® WinNonlin® 6.3, Certara, LP).

RESULTS
Plasma concentrations were best described by a one-compartmental model. Main pharmacokinetic parameters (mean ± sd) obtained for Group A (stage I/stage II) were: $AUC_{(0-inf)}$ (mg/h*mL) 197.17 ± 48.48/171.14 ± 29.35; C_{max} (mg ml^{-1}) 38.49 ± 7.44/28.56 ± 5.90; $t_{½abs}$ (h) 0.70 ± 0.49/1.21 ± 0.62; $t_{½}$ (h) 2.14 ± 0.72/2.06 ± 0.62; T_{max} (h) 2.31 ± 0.57/2.68 ± 0.75. For Group B the results were: $AUC_{(0-inf)}$ (mg h^{-1}*ml^{-1}) 185.52 ± 37.52/187.65 ± 39.83; C_{max} (mg ml^{-1}) 28.66 ± 5.63/27.07 ± 5.08; $t_{½abs}$ 0.91 ± 0.36/0.84 ± 0.46; $t_{½}$ (h) 2.63 ± 0.76/3.08 ± 1.28; T_{max} (h) 2.37 ± 0.61/2.19 ± 0.58.

CONCLUSIONS
Significant differences in C_{max} of adult animals were found between stage I and II. In humans, significant differences were only observed in T_{max}. This could be explained by the reduced effectiveness of omeprazole in older patients where stomach pH is naturally higher than in younger ones. The T>MIC was not affected between stages or groups; so, the observed differences would not affect clinical efficacy of cephalexin in dogs.

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2.13.
Integrated assessment of ivermectin kinetics, metabolism and tissue residues in laying hens

L. MORENO, P. DOMÍNGUEZ, C. FARIAS, L. CANTÓN, G. VIRKEL, L. MATÉ, L. CEBALLOS, C. LANUSSE & L. ALVAREZ
Laboratorio de Farmacología, Centro de Investigación Veterinaria de Tandil (CIVETAN), CONICET, Facultad de Ciencias Veterinarias, UNCPBA, Tandil, Argentina

INTRODUCTION
Ivermectin (IVM) is reported to be effective against nematode parasites in poultry (Ibarra-Velarde *et al.* 2011), but is not approved for use in avian production. The extralabel use of this drug has been reported (Bennett and Cheng, 2012) mainly to control endo and ectoparasites. The available information on the pharmacokinetic behaviour of IVM in poultry is scarce. The aim of the current work was to investigate the IVM plasma disposition kinetics, liver microsomal metabolism and tissue and egg residues profiles following its administration to laying hens.

MATERIALS AND METHODS
One hundred *Plymouth Rock Barrada* laying hens were used in three experiments. Experiment 1: Eight animals were intravenously treated (0.4 mg kg^{-1}) with IVM. Blood samples were taken at different times. Experiment 2: Eighty-eight hens were treated with IVM administered daily in water (0.4 mg kg^{-1}, for 5 days). Forty hens were kept and their daily produced eggs collected until 20 days post-treatment. Forty-eight hens were sacrificed in groups of eight at different times (1, 3, 5, 7, 10, and 15 days post-treatment) and blood, muscle, liver, kidney, and skin+fat samples taken. Samples were frozen until analysis by HPLC. Experiment 3: The *in vitro* enzymatic biotransformation of IVM was studied in liver microsomes obtained from not treated hens (n = 4).

RESULTS
After its IV administration, IVM plasma concentration decreased from 739.6 to 0.38 ng ml^{-1} (10 days). Pharmacokinetic parameters were: AUC 85.1 ng·day ml^{-1}; Vdss 4.43 L kg^{-1}; Cl 4.8 l day^{-1} kg^{-1}; $T_{½el}$ 1.73 days; MRT 0.95 days. Low IVM tissue residues were quantified after its oral administration in water. The highest IVM concentration was measured in liver tissue, followed by skin+fat, kidney, plasma and muscle. Although IVM residues were not found in egg white, significant residues were quantified in yolk. After 30 min of microsomes incubation, IVM concentrations decreased 27.8 ± 4.4%.

CONCLUSIONS

IVM pharmacokinetic behaviour in laying hens is characterized by larger apparent volume of distribution and higher plasma clearance compared to mammalian species. IVM half-life was shorter and plasma exposure lower than in other species, probably associated to a higher excretion/metabolism. IVM tissue residues were below the MRLs established for mammalian species. Residues quantified in eggs were greater than some MRLs values, suggesting that a withdrawal period would be necessary for eggs after IVM oral administration in laying hens.

KEY-WORDS

ivermectin, pharmacokinetics, *in vitro* metabolism, residues, laying hens

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2.14.

Pharmacokinetic and optimal dosage of marbofloxacin in Hanwoo, Korean native cattle

S.-C. PARK, J.-Y. PARK & S.-J. LEE

College of Veterinary Medicine, Kyungpook National University, Daegu, South Korea

INTRODUCTION/OBJECTIVE

Marbofloxacin (MRFX) is a fluoroquinolone that exhibits concentration-dependent bactericidal activity against gram-positive and gram-negative bacteria (Aliabadi *et al*, 2002). Owing to this broad spectrum of bactericidal activity, MRFX has been indicated in the treatment of bacterial infections in animals (Thomas *et al*, 2001). The pharmacokinetics of MRFX has been investigated in different animal species. However, there are no reports that describe pharmacokinetics of MRFX in Hanwoo, Korean native cattle. Hence, investigating MRFX pharmacokinetics in Hanwoo is important to establish optimal dosage for treatment of bacterial infection. Therefore, the study aimed to characterize the pharmacokinetics of MRFX and to determine the optimal dosage on the basis of PK/PD parameters against susceptible and intermediate pathogenic bacteria.

MATERIALS AND METHODS

Six male Hanwoo weighing 300 ± 10 kg were carried out in a two-period crossover manner with animals randomly divided into two groups of three Hanwoo. In two phases, 2 mg kg^{-1} body weight intravenous and intramuscular dose (2 mg kg^{-1}) of marbofloxacin was interchangeably administered for each animal. Blood samples were collected before and at 0.25, 0.5, 0.75, 1, 2, 4, 6, 8, 12 and 24 h after i.v. and i.m. administration and then centrifuged at 2000 × g for 15 min. Serum concentrations of MRFX were assayed using Agilent *1100* series HPLC *system* comprising 4.6 × 250 mm, 5 μm column. The limit of detection and quantification were 0.012 and 0.062 μg ml^{-1}, respectively. Pharmacokinetics analysis was performed using Phoenix WinNonlin 6.0 (Pharsight Corp., St. Louis, MO.) software program.

RESULTS

After i.v. administration, the AUC, $t_{1/2}$ and CL were 6.87 h μg ml^{-1}, 2.44 h and 0.29 L kg^{-1} h^{-1}. After i.m. administration, the AUC, $t_{1/2}$ and CL were 5.07 h μg ml^{-1}, 2.44 h and 0.39 L kg^{-1} h^{-1}. The optimum dosage for i.v. and i.m. administration required to achieve target $AUC_{0-24\ h}$/MIC ratio of 125 h against susceptible (MIC ≤ 1 μg ml^{-1}) and intermediate (MIC ≤ 2 μg ml^{-1}) pathogenic bacteria in the present study indicates that the administered dose (2 mg kg^{-1} day^{-1}) is inadequate to achieve target end point associated with efficacy of fluoroquinolones. Due to this, 2.9 and 5.8 mg kg^{-1} day^{-1} (i.v.) and 3.9 and 7.8 mg kg^{-1} day^{-1} (i.m) doses are suggested to achieve target PK/PD indices ($AUC_{0-24\ h}$/MIC = 125 h) against susceptible (MIC ≤ 1 μg ml^{-1}) and intermediate (MIC ≤ 2 μg ml^{-1}) pathogenic bacteria, respectively.

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2.15.

Pharmacokinetic parameters of amoxicillin against Streptococcus spp. in olive flounder (*Paralichthys olivaceus*)

J. PARK, S.-J. LEE & S.-C. PARK

College of Veterinary Medicine, Kyungpook National University, Daegu, South Korea

INTRODUCTION

The olive flounder (*Paralichthys olivaceus)* is the most common flatfish species raised in aquaculture in East Asia, including Korea, Japan and China. Amoxicillin (AMX) is a beta-lactam antibiotics largely used in veterinary medicine for its broad spectrum, and has been reported to provide good results in the specific field of fish antimicrobial therapy. *Streptococcus iniae (S. iniae)* and *Streptococcus parauberis (S. parauberis) h*ave been reported as major causes of economic damages on the fish farming. There is rarely reported pharmacokinetics (PK) of amoxicillin after intramuscular (IM) administration in olive flounder. Therefore, the present study was carried out to obtain amoxicillin PK parameters and minimal inhibitory concentration (MIC) values against *S. iniae and S. parauberis* in olive flounder and then recommended optimal dosage of AMX.

MATERIALS AND METHODS

AMX was injected to flounder with the accurate dose of 12.5 mg kg^{-1} and 125 mg kg^{-1} via IM administration in order to calculate PK parameters in healthy olive flounder. The bodyweight of the fish and water temperature were 150 ± 10.4 g (100 ± 10d) and 23 ± 1°C. The blood samples