POSTER SESSION 2
Tuesday 09-07: 9.00 – 18.00

Section 2.2. Antiparasitic Agents

2.2.37
Doramectin percutaneous absorption in dogs: *in vivo* and *in vitro* characterization

P. NEJAMKIN, G. A. ALBARELLOS, J. M. SALLOVITZ & C. E. LANUSSE
Laboratorio de Farmacología-UNCPBA, Tandil, Argentina

INTRODUCTION

Endectocides (avermectins and milbemycins) are important antiparasitic drugs owing to their wide spectrum of activity, high potency, safety margin and unique mode of action. They are mainly licensed for use in large animals and only few formulations have been approved to control endoparasites in companion animals. Due to its ease and practical administration, topical formulations have received great acceptance by pet owners. However, limited information is available on dermal absorption and disposition of endectocides, particularly doramectin (DRM), in dogs. Time saving *in vitro* methods that allow characterising topical drug absorption and influence of different excipients are also lacking. The objectives of the present work were to characterize doramectin percutaneous permeation both *in vivo* and *in vitro* and to correlate *in vivo* absorption with *in vitro* permeation parameters.

MATERIALS AND METHODS

In vivo experiments: Six Beagles dogs were used in a cross-over design. In the first phase, three animals were treated intravenously (100 μg kg^{-1}) and three topically (1000 μg kg^{-1}), after a 3-month washout period, in the second phase, animals were reversed. Blood samples were collected for up to 35 days post-administration in both experimental phases. *In vitro* experiments: Upper epidermis (500 μm thickness) slices of canine skin were prepared by using a dermatome and mounted on Franz-type diffusion cells (n = 6). Doramectin was applied to the upper side of skin samples (2.8 mg cm^{-2}) and, thereafter, receptor media were sampled up to 72 h. Doramectin concentrations were determined by HPLC.

RESULTS

After its topical administration to dogs, DRM presented a C_{max} of 4.31 ± 2.14 ng ml^{-1} and T_{max} of 5.25 ± 3.18 days. Absolute bioavailability (F) was 2.34 ± 086%, the mean absorption time (MAT) 7.06 ± 2.08 days and the mean elimination half-life 4.73 ± 0.94 days. *In vitro*, the steady-state portion was observed between 14.7 ± 7.4 and 60.0 ± 17.2 h post-administration. A 10.6 ± 6.2 h lag time (Tlag) was observed. Flux was 1.5 ± 1.2 ng h^{-1} cm^{-2} and permeability and diffusion coefficients (mean ± SEM) were $3.1 \times 10^{-7} \pm 2.6 \times 10^{-7}$ and $6.1 \times 10^{-5} \pm 4.9 \times 10^{-5}$, respectively. The correlation coefficients between *in vivo* absorption (partial AUC and percentage absorbed) and *in vitro* permeation (percent permeated) up to 72 h were 0.9833 and 0.9205 (Pearson r), respectively.

CONCLUSIONS

This work described for the first time the percutaneous absorption of topical DRM both *in vivo* and *in vitro*. Topical DRM was absorbed through canine skin; however, due to its high lipophilicity, a skin depot of the drug was observed. This is evidenced by the long absorption times (Tlag and MAT) and the low F obtained. These results will contribute to a better understanding of the dermal absorption process in dogs as well as to developing new topical formulations. Given the low bioavailability achieved in the present work, DRM percutaneous administration of this formulation cannot be suggested for treating endoparasitosis in dogs.

2.2.38
Testing high oxfendazole doses to treat cysticercosis in pigs: a safety assessment

L. I. ALVAREZ[1], G. DOMINGUE[2], L. MORENO[1], L. CEBALLOS[1], M. BISTOLETTI[1], M. DONADEU[2] & C. E. LANUSSE[1]
[1]*Laboratorio de Farmacología, FCV, UNCPBA, Tandil, Argentina;* [2]*Global Alliance for Livestock Veterinary Medicines (GALVmed), Edinburgh, UK*

INTRODUCTION

In addition to its well established nematodicidal activity, oxfendazole (OFZ) has shown good efficacy against the *Taenia solium* cysticercus in pigs following its oral administration at 30 mg kg^{-1} (1). However, the use of this anthelmintic at such a high dose requires safety studies in target animals (pigs) before going ahead with the registration process.

OBJECTIVE

The goal of the current work was to assess the OFZ safety in pigs orally treated at 30 mg kg^{-1}. Complementary, the OFZ systemic exposure was measured.

MATERIALS AND METHODS

Thirty-two healthy pigs (57 ± 6.9 kg) were used in the current study. The animals were divided into four experimental groups: OFZ_{30}, OFZ_{90}, OFZ_{150}, which received OFZ (Synanthic® 9.06% oral suspension, Merial) at 30, 90 and 150 mg kg^{-1}, respectively, and an untreated Control Group. Treatments were performed by the oral route over three (3) consecutive days. Potential OFZ toxicity was assessed following VICH guidelines. Additionally, OFZ/metabolites plasma concentrations were quantified by HPLC at 3, 5 and 10 days after the first treatment. Parametric/non-parametric methods were used for the statistical comparison.