[volume 41 | supplement 1 | june 2018]

JOURNAL OF

Veterinary Pharmacology and Therapeutics

Including veterinary toxicology

14th International Congress of the European Association for Veterinary Pharmacology and Toxicology held in Wroclaw, Poland, June 24–27, 2018

Guest edited by Błażej Poźniak, Marcin Świtała and Johanna Fink-Gremmels

ISSN 0140-7783 (paper)
ISSN 1365-2885 (online)

Available online at wileyonlinelibrary.com/journal/jvp

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oxfendazole (5 mg kg^{-1} PO), triclabendazole (12 mg kg^{-1} PO) or their combination. Experiment 2: Lambs (two groups, n = 7 each) were treated with moxidectin (0.2 mg kg^{-1} SC) alone or in combination with loperamide (0.16 mg kg^{-1} PO) and pluronic 123. Experiment 3: Lambs (two groups, n = 10 each) were treated with abamectin (0.2 mg kg^{-1} SC) alone or in combination with ivermectin (0.2 mg kg^{-1} SC) and itraconazole (30 ml PO). Drug/metabolite concentrations in plasma were measured (days 0–15). The faecal egg count reduction test (FECRT) was used as a measure of nematodicidal efficacy.

Results: Experiment 1: Coadministration resulted in an increase in both the plasma $AUC_{0\text{-}LOQ}$ and MRT of the metabolite fenbendazole sulfone (p 0.05), whereas all the PK parameters for triclabendazole sulfone were significantly decreased. Efficacy rose from 47.2 and 55.4% (single administration) to 75.7% (coadministration). Experiment 2: No differences in PK parameters were observed upon coadministration. Efficacies were 77.1 and 71.2%, respectively, for the single and combined treatments. Experiment 3: Exposure to ivermectin and itraconazole resulted in an increase in abamectin C_{max} and $AUC_{0\text{-}LOQ}$ (not significant). Efficacies were 0% for both treatments.

Conclusions: Combination of active principles with modulators and other active compounds has been advocated as an alternative to enhance anthelmintic efficacy. However, clinical efficacy against resistant nematodes remains elusive in practical terms. In spite of proven *in vitro* pharmacological interactions, translation to clinical settings shows that *in vivo* trials are needed in order to assess the real impact of modulators and combined therapies in parasite control.

O22.3 | Old drugs for new uses: pharmacokinetic assessment to support oxfendazole repurposing as a flukicidal compound

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Introduction: Fascioliasis caused by *Fasciola hepatica* can cause considerable financial losses in livestock production. The main strategy for liver fluke control is based on the use of chemical-based treatments. However, the frequent use of effective flukicidal compounds had led to the development of drug resistance, largely to triclabendazole, the most extensively used drug. Oxfendazole (OFZ) is a broad spectrum anthelmintic used as nematodicidal, without flukicidal activity at therapeutic doses (5 mg kg^{-1}). However, activity against *F. hepatica* has been reported after a single OFZ dose of 30 mg kg^{-1} in both sheep and pigs. The goals of the current work were (i) to compare the plasma pharmacokinetic (PK) profile of different OFZ doses in non-infected sheep, and (ii) to evaluate the dose-related pattern of *in vivo* accumulation of OFZ/metabolites into adult *F. hepatica*.

Materials and Methods: (i)PK trial: sheep were allocated into two groups (n = 6 each) and orally treated with OFZ at a single dose of either 5 (OFZ_5) or 30 (OFZ_{30}) mg kg^{-1}. Blood samples were collected for 96 h post-treatment, and plasma analyzed for OFZ/metabolites by HPLC.

(ii)Drug accumulation trial: Animals (8) were each orally infected with seventy-five (75) metacercariae of *F. hepatica*. Sixteen weeks after infection, animals were randomly allocated into two experimental groups (n = 4) and orally treated with OFZ at either 5 or 30 mg kg^{-1}. Animals were killed at different times post-treatment and samples of blood, bile, liver and adult liver flukes were obtained. Samples were analyzed by HPLC.

Results and Conclusions: OFZ parent drug was the main analyte detected in plasma from OFZ treated sheep. The C_{max} and AUC_{0-t} values were approx. 4-fold higher in the OFZ_{30} group (2.5 ± 0.6 μg ml^{-1} and 83.7 ± 20.5 μg × h ml^{-1}, respectively), compared to that observed after the 5 mg kg^{-1} dose (0.6 ± 0.1 μg ml^{-1} and 18.0 ± 3.7 μg × h ml^{-1}, respectively). These differences were also reflected in the pattern of OFZ accumulation into *F. hepatica*, which results 332% higher after the 30 mg kg^{-1} dose (4.28 μg g^{-1}) compared to the lower dose (0.99 μg g^{-1}). The data shown here demonstrates that the OFZ dose increment is associated with a higher plasma drug exposure and accumulation into the target parasite, which help to explain OFZ efficacy against adult liver flukes at 30 mg kg^{-1} dose. The reported pharmacological data may contribute to assess OFZ repurposing for a new use as a flukicidal compound.

O22.4 | Efficacy of pyrantel and fenbendazole against *Parascaris univalens* infection in foals in Sweden

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Introduction: *Parascaris univalens* infection in foals is a common problem around the world. Resistance against the anthelmintic ivermectin is well established in the worldwide parascaris population. Also multi-resistance to ivermectin and pyrantel has been reported in North America and Australia. The aim of this study was to investigate the efficacy of pyrantel and fenbendazole on stud farms in Sweden. Previous Swedish studies from 2005 showed resistance to ivermectin on 5 out of 6 investigated farms, but that pyrantel and fenbendazole were still effective.

Material and Methods: A Fecal Egg Count Reduction Test (FECRT) was performed on a total of 158 foals on 17 stud farms in Sweden from September 2016 to December 2017. Foals were between 6 and 10 months of age. Individuals with a minimum of 150 eggs per gram feces were included in the study. Faecal samples were collected before treatment with pyrantel or fenbendazole, and 14 days post-treatment. Pyrantel embonat (Banminth® Pharmaxim) was used at a dose of 19 mg kg^{-1} bodyweight (equals 6.6 mg of pyrantel base) or