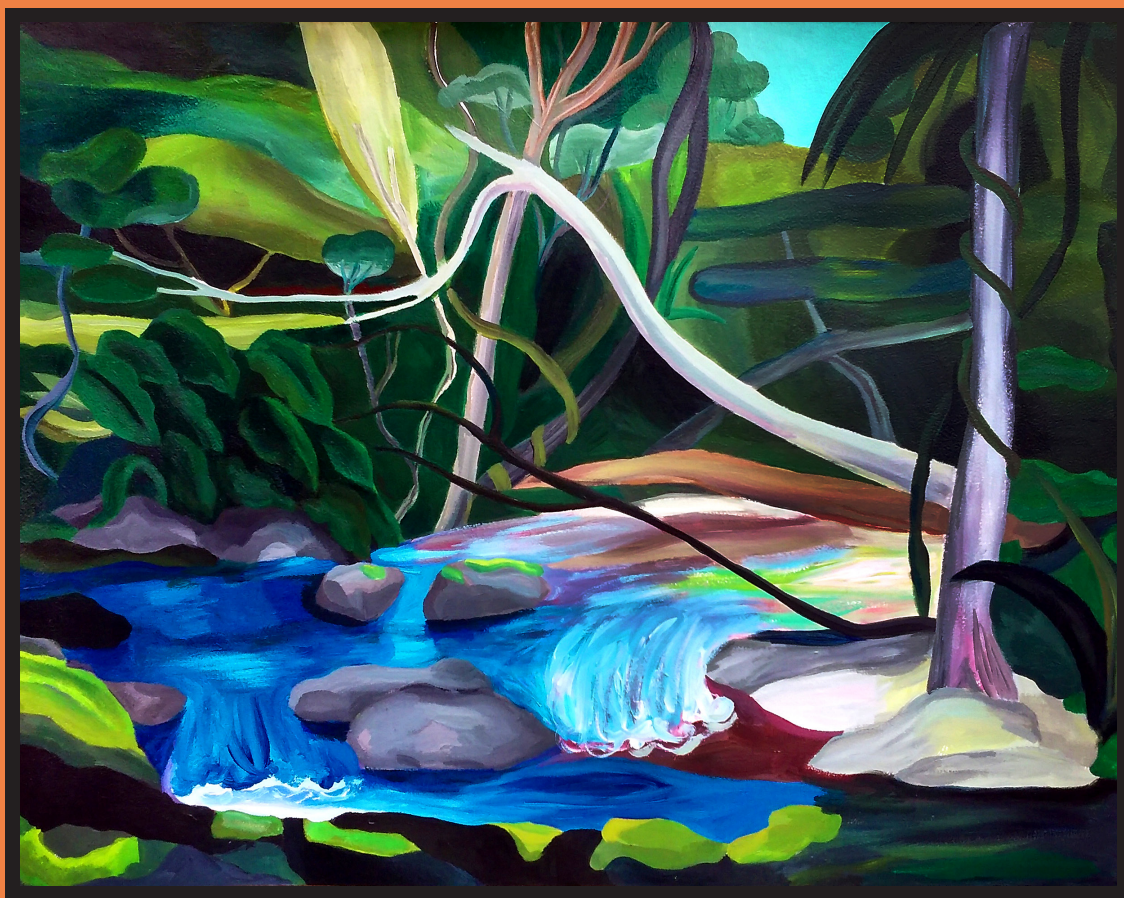


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opening of the mKATP, which prevent mitochondrial dysfunction. Moreover, the NO pathway does not participate

in the lack of cardioprotection when perfusing Amd.

IN-FEED DRUG MEDICATION IN PIG PRODUCTION: EFFECTS ON XENOBIOTIC METABOLIZING ENZYMES

Paula Ichinose^{1,2}, **Karen Larsen**^{1,2}, **María Victoria Miró**^{1,2}, **Adrián Lifschitz**^{1,2}, **Guillermo Virkel**^{1,2}

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In-feed medication with the anthelmintic fenbendazole (FBZ) is routine in pig husbandry. This drug undergoes hepatic metabolism through cytochrome P450 (CYP) and flavin-monooxygenase (FMO) enzyme families. Also, FBZ and its metabolite oxfendazole (OFZ) may induce the CYP1A subfamily. This work aimed to evaluate the effect of FBZ administration on i) CYP1A-dependent enzyme activities; ii) its own pattern of hepatic S-oxidation; iii) the metabolism of enrofloxacin (ERF) and aflatoxin B1 (AFB1). Female Landrace piglets remained untreated (n=5) or received a pre-mix of FBZ in feed as usually is recommended for 9 days (n=6). Liver microsomes from control and FBZ-treated animals were used for i) CYP content determination; ii) monitoring CYP1A-dependent enzyme activities, 7-ethoxyresorufin O-deethylase (EROD) and methoxyresorufin O-demethylase (MROD); iii) measurement of FBZ (50 µM) S-oxidation, ERF (50 µM) conversion into ciprofloxacin (CPF) and AFB1 (16 nM) disappearance. In liver microsomes from treated

animals, EROD and MROD increased 20-fold (p=0.002) and 19-fold (p=0.001), respectively. An enhanced (3-fold, p=0.0037) participation of the CYP pathway in the hepatic S-oxidation of FBZ into OFZ was observed in the liver of piglets receiving FBZ compared to controls. ERF conversion into CPF increased (p=0.014) from 26.5±8.4 pmol/min.nmol CYP (controls) to 139.4±60.1 pmol/min.nmol CYP (FBZ-treated). The rate of disappearance of AFB1 in FBZ-treated pigs was 79% higher (p=0.036) compared to control animals. An auto-induction of the CYP1A-dependent S-oxidation of FBZ towards its active metabolite OFZ was observed. The in-feed medication with FBZ may cause potential metabolic interactions with the antimicrobial ERF and the mycotoxin AFB1. Enzyme induction caused by the anthelmintic may modify the pharmacokinetic behaviour of ERF and CPF. In addition, induction of the CYP1A-dependent metabolism of AFB1 may increase the production of a hepatotoxic AFB1-derived epoxide.

ANTIMICROBIAL ACTIVITY OF THE NOVEL BACTERIOCIN AP7121: FROM *IN VITRO* ASSAYS TO AN *IN VIVO* PRELIMINARY INTRANASAL TREATMENT APPROACH

Laureano Schofs^{1,3,4}, **Mónica Sparo**^{2,3,4}, **Sabina Lissarrague**^{2,4}, **Mariana Bistoletti**^{2,4}, **María Guadalupe de Yaníz**^{1,3}, **Sergio Sánchez Brun**^{1,3,4}

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The impact of staphylococci infections on human and animal health increased as result of its ability to become resistant to antimicrobials. Most *Staphylococcus* spp. (*Staph*) infections are endogenously acquired, and treatment of nasal carriage is one strategy for prevention. AP7121 bacteriocin, showed *in vitro* bactericidal activity against *Staph*. The main goals of this study were: a) to assess the nasal carriage of *Staphylococcus* species in asymptomatic dogs, and b) to test the effect of intranasal administration of AP7121 in the staphylococci population. Dogs were randomly allocated in two groups (n=3) and two intranasal administration protocols were evaluated as follows: *protocol A*: canines received one dose of either 150 µL of sterile saline solution (SSS) (*control group*) or 150 µL of AP7121 solution (330 µg/mL) (*AP7121 group*); *protocol B*: dogs received 100 µL every 24 h for 3 days of SSS or AP7121 (330 µg/mL). Previous to each

treatment (*T0*) and 24 h after the topical treatment (*T1*), standardized nasal swabs samples of both nasal vestibules were taken. Swabs were systematically inoculated and cultured in Mannitol salt agar and Blood agar. *Staph* isolates were phenotypically characterized according to antimicrobial sensibility using the disk diffusion method and VITEK® 2 system. Fischer exact Test was used for statistical analysis of treatments. Variability in *Staphylococcus* species was found in many cases among individual dogs in *T0* and *T1*. Fifty *Staph* strains were isolated, being 58% (29/50) resistant to Penicillin and 4% (2/50) showing inducible macrolide and lincosamide resistance. *Protocol A* treatment failed to reduce the viability of the nasal staphylococci population. However, *protocol B* (3 doses of AP7121) showed a significant 50% of decolonization (p<0.01). In conclusion, the antimicrobial effect of AP7121 against *Staph* could be explored as a potential