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Bioavailability and efficacy of orally administered flunixin, carprofen and ketoprofen in a pain model in sheep

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Pain caused by routine husbandry practices performed on sheep can last several days. Sheep often do not receive therapeutic interventions to provide pain relief for routine husbandry procedures. Attractive candidates for long acting pain relief are non-steroidal anti-inflammatory drugs (NSAIDs). If NSAIDs can be shown to alleviate pain and inflammation when administered orally in sheep, it may be applicable to incorporate them in feed, providing producers with a quick and easy method to deliver extended pain relief.

The aim of this research was to test the bioavailability and efficacy of carprofen, ketoprofen and flunixin administered orally in a model of inflammation and pain associated with a turpentine injection. The model (Colditz *et al.* 2011) was recently developed to enable objective quantitative assessment of the analgesic, antipyretic and anti-inflammatory actions of NSAIDs in sheep.

Forty Merino ewes were randomised into four treatment groups (n = 10/group). Treatment was given orally at 24 h intervals for 6 days at dose rates expected to achieve therapeutic levels in sheep: carprofen (8.0 mg/kg), ketoprofen (8.0 mg/kg) and flunixin (4.0 mg/kg). Oil of turpentine (0.1 mL) was injected into a forelimb of each sheep. Responses (force plate pressure, skin temperature, limb circumference, haematology and plasma cortisol) were measured at 0, 3, 6, 9, 12, 24, 36, 48, 72, 96 h post-injection. NSAID concentrations were determined by Ultra High Pressure Liquid Chromatography. Data were analysed using a repeated measures model.

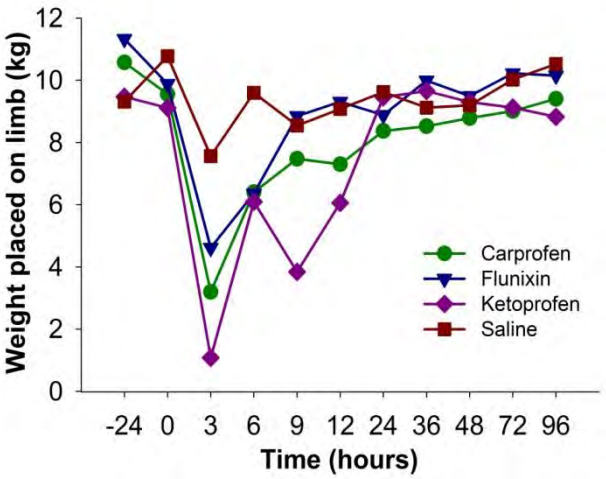

Figure: Weight placed on the oil of turpentine injected limb

The NSAIDs were detectable in ovine plasma 2 h after oral administration, with average concentrations between 4.5 - 8.4µg/mL for ketoprofen, 2.6 - 4.1µg/mL for flunixin and 30 - 80µg/mL for carprofen, concentrations dropped 24 h after administration. Placebo sheep placed more weight on their forelimbs at 3 h ($P<0.05$, Figure), compared to other treatments. Animals receiving flunixin had lower lameness scores than placebo sheep at 12, 24 and 48 h ($P<0.05$). There was no significant effect of NSAIDs on haematology variables.

The study showed the NSAIDs reached inferred therapeutic concentrations in blood, 2 h after oral administration. Pain response to an oil of turpentine injection was assessed using the measures with flunixin showing greatest efficacy in alleviating responses to turpentine injection. Some paradoxical responses in placebo sheep made interpretation of efficacy difficult. This was due to contrasting results to previous results with this model, placebo sheep continued to place weight on the oil of turpentine-treated limb despite tissue inflammation.

Colditz I.G. *et. al* (2011) *Australian Veterinary Journal* (89): 297-304.