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**Some aspects of ivermectin resistance in gastrointestinal
nematodes of goats and sheep**

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REQUIRMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
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ABSTRACT

Experiments were conducted to determine whether sheep are at risk from grazing pasture previously grazed by goats harbouring ivermectin-resistant *Ostertagia* spp. by monitoring the level of resistance with faecal egg count reduction tests and larval development assays. Ivermectin resistance emerged rapidly in goats grazed on the paddocks previously grazed by goats or sheep. In contrast, resistance was never consistently identified in sheep grazed on paddocks previously grazed by sheep although ivermectin resistance emerged after about 5 months in sheep grazed on paddocks previously grazed by goats.

Ivermectin resistance was suspected in *Trichostrongylus colubriformis* and *Ostertagia* species on a goat farm in Northland, New Zealand. A controlled efficacy study was conducted in lambs (n=12) and young Angora goats (n=10) with this isolate. The establishment rate of *T. colubriformis* and *Ostertagia* spp. was similar ($p>0.05$) in the sheep and goats. Following ivermectin treatment (0.2 mg/kg b.wt. per oral) to half of the lambs and goats, the burdens of *T. colubriformis* were reduced by 39% and 13% in lambs and goats respectively whereas *Ostertagia* spp. burdens were reduced by 33% and 0% in lambs and goats respectively.

In series of larval development assays with ivermectin aglycone, ivermectin and avermectin B₂, this isolate of *T. colubriformis* had a resistance ratio of 37, 4-5 and 3-4 respectively indicating ivermectin aglycone is the drug of choice for detecting ivermectin resistance in *T. colubriformis*. However, both ivermectin and avermectin B₂ were still able to discriminate between resistant and susceptible *T. colubriformis* under controlled experimental conditions. The LC₅₀ values of ivermectin were found to be influenced by the age of the infection of *T. colubriformis* in sheep. These LC₅₀ values were relatively constant at 23 to 37 days after infection, then rose about four fold to peak between 51 to 58 days post infection, followed by a decline close to the original starting values by 72 days post infection. The resistance ratios recorded with thiabendazole were also high (14 to 15) suggesting that the ivermectin-resistant strain of *T. colubriformis* was also resistant to benzimidazoles.

The LC₅₀ values of ivermectin for *T. colubriformis* in a larval development assay for the two reciprocal first generation (F₁) crosses of ivermectin-resistant and -susceptible

parents were slightly lower than the LC_{50} values for ivermectin-resistant parents but greater than the ivermectin-susceptible parents suggesting that ivermectin resistance in *T. colubriformis* is inherited as an incompletely dominant trait.

The fitness of the ivermectin-resistant strain of *T. colubriformis* was investigated and there was no significant differences ($p>0.05$) in infectivity, longevity of infection, fecundity and development of eggs to larvae under natural or laboratory conditions between the ivermectin-resistant strain and two susceptible field isolates. The survival of ivermectin-resistant strain larvae was intermediate between the two susceptible field isolates at 10°C, 20°C, 25°C and 30°C under laboratory conditions.

An efficacy study in sheep indicated that the moxidectin oral formulation (0.2 mg/kg b.wt.), moxidectin injectable formulation (0.2 mg/kg b.wt.) and ivermectin oral formulation were 98%, 4% and 62% effective against this ivermectin-resistant strain of *T. colubriformis* respectively. These findings indicate that formulation of an anthelmintic plays an important role in the efficacy against resistant nematodes.

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