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VETERINARY ANTHELMINTICS:

THEIR EFFICACY AND EFFECTS ON ABOMASAL PHYSIOLOGY

A thesis presented in
partial fulfilment of the requirements
for the degree of
MASTER OF VETERINARY SCIENCE
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For Pauline, with all my love

ABSTRACT

PART 1. A Review of the Veterinary Anthelmintic Literature

A comprehensive review was undertaken of the pharmacology, efficacy, side effects and toxicity of veterinary anthelmintics used against nematode parasites. Anthelmintics reviewed for use in cattle, sheep, goats, horses, dogs and cats include copper, nicotine, arsenic, tetrachlorethylene, phenothiazine, diethylcarbamazine, piperazine, toluene, cyacethydrazide, bephenium, thenium, organophosphates, and methyridine. The review was limited to cattle for the benzimidazoles, pyrantel, morantel, tetramisole, levamisole, avermectin and milbemycins anthelmintics. Efficacy data is provided in a tabular format which classifies each anthelmintic according to method of administration and dose.

PART 2 Efficacy of two formulations of moxidectin pour-on and the effects of treatment on serum pepsinogen and gastrin levels and tissue gastrin in cattle

Three groups of eight yearling Friesian bulls were used to compare the efficacy of two 5 g/L pour-on formulations of moxidectin applied at 1ml/10kg (500 mcg moxidectin per kg bodyweight) in removing naturally acquired gastrointestinal parasites.

At slaughter, 14-16 days after treatment, the burdens of *Ostertagia* spp. and *Trichostrongylus axei* were significantly lower in both the treated groups versus the controls ($P < 0.01$). Anthelmintic efficacies (based on geometric mean worm burdens of treated and control groups) were all greater than 99.8% for *Ostertagia* spp. and *Trichostrongylus axei* in both treated groups compared with the controls. A significantly lower burden of adult *Cooperia* spp. was recorded for Formulation 1 ($P < 0.05$). The anthelmintic efficacy of the two treatments against *Cooperia* adults, early L4 and late L4 were 96.25% ($P < 0.05$), 97.31% and 91.08% respectively in calves treated with Formulation 1, and 71.44%, 67.14% and 64.29% respectively for calves treated with Formulation 2. Low numbers of large intestinal worms, *Trichuris ovis* and *Oesophagostomum* spp. in the control cattle precluded any valid efficacy assessment of these species.

Based on these results, Formulation 1 is distinguished from Formulation 2 by its significantly greater efficacy against adult *Cooperia* spp.

Serum pepsinogen and gastrin levels were monitored in the three groups of calves after treatment. All groups showed a steady decline in levels of both pepsinogen and gastrin until termination on day 14. On only one occasion was there a significant difference in serum pepsinogen between treated and untreated calves. Following treatment there was a more rapid and significant decrease in gastrin levels in calves treated with Formulation 1 than Formulation 2. At no stage was there a significant difference between the controls and calves treated with Formulation 2. There was no correlation between pepsinogen and gastrin levels for any of the groups. Neither was there a correlation between numbers of *Ostertagia* spp. and serum pepsinogen or gastrin. It is suggested that the decreases seen in the control group were due to lack of larval challenge and normal loss of adult worms resulting insufficient numbers to sustain a hypergastrinaemia.

Gastrin concentrations were also measured in tissue samples from the pyloric antrum or the proximal duodenum. There was no significant difference in antral and proximal duodenal gastrin concentrations between the treatment and the control groups. Antral levels were between 1148-1323 pM/g which were 25-35 times those found in duodenal tissue (32.3-50.9 pM/g).

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PART 1.

**A Review of the Veterinary Anthelmintic
Literature**

1.0 INTRODUCTION

The influence of helminth parasites on intensive agriculture production systems is considerable in terms of animal health and welfare. There is now a heavy reliance on the use of anthelmintics to maintain these farming practices, which more recently is starting to take a heavy toll on the continued efficacy of these compounds. Up until the 1960's, anthelmintics of various levels of efficacy were used to aid in the management of nematodes. With the discovery of the benzimidazoles (Brown *et al.* 1961), a new era in parasite control occurred. The success of this compound stimulated considerable research and as the knowledge of anthelmintic pharmacology has developed, so has the development of more potent drug analogues, and better and more effective methods of administration (Prichard, 1986a).

In order for parasites to exist in an animal, they must maintain an appropriate feeding site and ingest and move food through their digestive tracts. Anthelmintics can be divided into two general classes as to how they affect parasites. There are those which inhibit metabolic processes, and those which inhibit neuromuscular co-ordination. The benzimidazoles inhibit metabolic processes by binding to microtubules which results in disruption of normal cell processes, such as formation of the mitotic spindle in cell division, maintenance of cell shape, cellular motility, nutrient absorption and intracellular transport. Anthelmintics which have their effects on neuromuscular co-ordination can be divided into two groups. Those which inhibit the breakdown of excitatory neurotransmitters (cholinesterase inhibitors - organophosphates) or mimic the action of excitatory neurotransmitters (imidazothiazoles - levamisole, and pyrimidines - pyrantel and morantel) and result in spastic paralysis. The second group either mimic the inhibitory action of the inhibitor neurotransmitter or cause hyperpolarisation (piperazine, avermectins/milbemycins) resulting in flaccid paralysis. Any effect on parasite neuromuscular co-ordination, results in the parasite losing its ability to maintain its position within the gastrointestinal tract or pulmonary system, and is subsequently expelled.

The "ideal" anthelmintic should have a broad spectrum of activity against mature and immature (including inhibited larvae); be easy to administer to a large number of animals; have a wide margin of safety and be compatible with other compounds; result in minimal residues; and be economical to use.

The following review identifies anthelmintics which affect nematode parasites in cattle, sheep, horses, dogs and cats. It describes the history of each of the anthelmintics, their pharmacology and their efficacy against nematodes of the gastrointestinal tract and pulmonary system, and side effects and toxicity to the treated animals. For the four main action families, the benzimidazoles, imidazothiazoles, tetrahydropyrimidines and the avermectins/milbemycins, the review has been limited to cattle.