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# Efficacy and safety of oral praziquantel against *Dicrocoelium dendriticum* in llamas

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ABSTRACT

*Dicrocoelium dendriticum* can cause severe pathological changes of the liver and bile system in camelids, and therapeutic options for treatment are limited. To address this problem, the efficacy of two different dose rates of praziquantel was investigated in llamas suffering from natural *D. dendriticum* infections. 53 llamas were examined under field conditions on two occasions: before and two weeks after treatment. At the beginning of the study, the animals were weighed, randomly allocated to one of the treatment groups ($n = 21$ each) or the control group ($n = 11$) and dosed orally using a praziquantel-containing paste (250 mg/ml) at a dose of either 25 mg (group 1) or 50 mg (group 2) per kg of body weight. Criteria for efficacy were faecal egg count reduction (FECR) and extensity effect.

Animals treated with 25 mg/kg of body weight showed a FECR of 85%. Therapy with 50 mg/kg led to a FECR of 91%. Almost twice the number of animals of group 1 (33%) still shed eggs two weeks after treatment compared with group 2.

The results of this study indicate that 50 mg/kg oral praziquantel is required for efficacious dosing and that this dose rate is safe in llamas and thus is recommended for the treatment of camelids naturally infected with *D. dendriticum*.



## 1. Introduction

There are unique specifications for veterinary medical care of domesticated South American camelids (SAC). Llamas and alpacas are raised in non-native countries for a variety of reasons, e.g. landscape management and preservation, as pack and trekking animals, for wool, for animal-assisted therapy, as guard animals for sheep ranges or simply as exotic pets. Camelids were traditionally farmed for meat in some parts of South America and are considered as "farmed game" (farmed land mammals; Annex I of Commission Regulation (EC) No. 853/2004) within the European Union and consequently classified as food-producing animals. Thus there are special guidelines governing their pharmacological treatment. In llamas and alpacas, drugs are used in an off-label manner, since the required veterinary medicinal products are solely authorised for domestic food producing species such as horses, goats, sheep and cattle, but not for camelids. Various medications are administered orally, a major challenge when medicinal products initially developed to treat equines or

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ruminants are used in camelids, with often very different rates of dose compared to the target species (Dadak et al., 2013).

Dicrocoeliosis is one of the most serious parasitic infections of llamas and alpacas in Europe, where the infection occurs ubiquitously in wild life species (Ducháček and Lamka, 2003; Hertzberg and Kohler, 2006) and domestic ruminants (Manga-González et al., 2001; Otranto and Traversa, 2003; Cranwell et al., 2010). In contrast to cattle, sheep and goats, which can cope with high burdens of the small liver fluke without major clinical and/or pathological changes (Theodoridis et al., 1991; Otranto and Traversa, 2002) SAC infected with *Dicrocoelium dendriticum* show severe pathological changes of the liver and bile system such as cirrhosis, abscesses and granulomas (Wenker et al., 1998; Gunsser et al., 1999).

There are limited therapeutic options for treatment or prevention of dicrocoeliosis in these animals and drugs need to be used off-label. It is difficult to determine whether anthelmintic drugs applied at dose rates and routes recommended for domestic animals lead to drug levels able to eliminate parasites in camelids as well. The potential risk of either underdosing (with ineffective levels and the danger of development of anthelmintic resistance) or overdosing (leading to toxic levels) is therefore high. Albendazole, which can be used to treat dicrocoeliosis in other species, has been reported to be toxic in camelids (Gruntman et al., 2009). Netobimin, a prodrug of albendazole, should thus also not be used in SAC. For other (pro)benzimidazoles further studies are required regarding the safety in camelids since higher dose rates need to be used against *D. dendriticum* than those used against tapeworms, lungworms and gastrointestinal nematodes (Otranto and Traversa, 2002). Praziquantel, an isoquinoline-pyrazino derivative, has anticestode and antitrematode (Redman et al., 1996) activities and was shown to be effective against trematode infections in sheep (Akkaya et al., 2006). No adverse drug effects have been reported in camelids so far (Hertzberg and Kohler, 2006). Thus it is presumed that this drug can be administered safely to llamas and alpacas infected with *D. dendriticum*.

There are very few published data relating to the appropriate dose of praziquantel in camelids. Hertzberg and Kohler (2006) report the frequent application of praziquantel for the control of dicrocoeliosis in SAC in Switzerland but without evidence of efficacy. To the authors' knowledge there is only one published report describing a praziquantel dose-related experimental study in SAC (Wenker et al., 1998). In this study praziquantel was administered to three llamas by gavage. The authors suggested a dose rate of 50 mg/kg body weight (BW) for the treatment of dicrocoeliosis, corresponding to 2 ml/kg (300 ml/150 kg) BW of a commercial solution registered for sheep. In routine practice it is extremely cumbersome to administer praziquantel to camelids by gavage as these animals become stressed more quickly than other species. To treat camelids by gavage would thus require prior sedation.

At present there is no authorised veterinary medicinal product on the market containing praziquantel in a concentration suitable for the treatment of camelids at the dose rate suggested in the literature. Since infections with *D. dendriticum* frequently have serious or even fatal outcome, however, treatment is required.

To address this problem a novel oral galenic formulation for the special needs of camelids was developed at the University of Veterinary Medicine Vienna. The key advantage of this patent-protected (EP11189706.2) oral paste formulation is that high concentrations of drugs (single or in combination) can be packed in a very small volume. Thus any substance can be applied in an easy and safe way. The individual drug dose is willingly swallowed by camelids without drug loss by spitting or dripping.

The use of this novel oral formulation enabled a study on efficacious dosing of camelids with the anthelmintic drug praziquantel under field conditions. Efficacy of two different dose rates was evaluated against an untreated control group in llamas suffering from natural infections with *D. dendriticum*.

## 2. Materials and methods

### 2.1. Animals

53 llamas (male, female, pregnant, non-pregnant) from two different farms located in Austria were included in the study. Animals were kept for landscape management purposes, as trekking animals and for breeding. Faecal examinations confirmed natural infection with *D. dendriticum*. For ethical reasons as well as for owner compliance, animals with deviating findings upon physical examination were excluded from the study. Animals had not been treated with anthelminthics at least five months before the trial.

### 2.2. Experimental protocol

Study procedures were discussed and approved by the institutional ethics committee of the University of Veterinary Medicine Vienna in accordance with Good Scientific Practice Guidelines and national legislation.

On study day (SD) 1 the animals were weighed accurately right before treatment by using a calibrated animal scale (MAS.VS-300, Rauch, Austria) and randomly allocated to the study groups. Llamas were dosed orally using a praziquantel-containing paste (250 mg/ml; Pharmacy at the University of Veterinary Medicine Vienna, Austria) at doses of 25 mg/kg BW ($n = 21$) or 50 mg/kg ($n = 21$) BW. For oral application of the calculated individual drug dose a calibrated drug dispenser was used to avoid any risk of underdosing.

An untreated control group ($n = 11$) was used for monitoring natural fluctuations in egg counts during the study. Faecal samples (taken on SD 1 and 14 days later, SD 2) were collected directly from the rectum of each animal and examined on the same day or stored at 4 °C for processing on the following day. Faecal examination was carried out in a blinded manner. The FEC was determined by using a modified McMaster technique employing saturated zinc sulphate solution with a specific density 1.3 (Bauer, 2006) with a lower threshold of 25 eggs per gram (EPG).