7. Summary

Ultrastructural investigations in Fasciola hepatica after the therapy with albendazole sulphoxide with Rattus norvegicus and with sheep

In the course of this study several tests were out into whether, and in what concentrations, albendazole sulphoxide is suitable for use in therapy against *F. hepatica*. It was also determined whether the use of an enhancer results in an improvement of efficacy and allows the reduction of the active substance. The study also investigated the effects of albendazole sulphoxide on the morphology of the parasite. Parasite tissue was analysed using both transmission electron and scanning electron microscopy in order to determine whether morphological changes occurred under exposure to the active substance.

In the animal experimental part of the study, it was found that albendazole sulphoxide has a fasciolide effect whether administered orally, subcutaneously or intraperitoneally to rats in a dosage of 30 mg per kg bodyweight. In combination with the enhancer, the quantity of active substance in the aforementioned forms of administration can be reduced to 20 mg per kg bodyweight. For pour- on treatment of the infected rats, a dose of 130 mg per kg bodyweight was found to be necessary if albendazole sulphoxide was applied by itself. In combination with enhancer the albendazole sulphoxide dose for pour- on treatment could be reduced to 90 mg per kg bodyweight. The studies showed that the enhancer itself had no fasziolide effect. It allowed a reduction of the quantity of the active substance required and stoped the secretion of eggs faster. The effective quantity of the active compound in the oral application in sheep was found to be 20 mg albendazole sulphoxide per kg bodyweight. The pour- on dosage determined as being necessary in sheep was 20mg to be 200 mg albendazole sulphoxide per kg bodyweight in combination with the enhancer.

For the electron microscope examinations, rats were treated with 20 mg and 40 mg albendazole sulphoxide per Kg bodyweight. Treatment was given both in the form of albendazole sulphoxide alone and in combination with the enhancer. The worms were examined after 24 and 48 hours. Both scanning and transmission electron microscopy showed that the higher the dose, the more substantial the damage caused to the worm. It was also found that the damage to the parasite increased the longer it was exposed to the active substance. With use of the enhancer, the damage

to *F. hepatica* was greater and more marked than under treatment with albendazole sulphoxide alone.

Examination under the scanning electron microscope revealed that the treatment evidently causes marked damage to the surface of the worm. In all the worms exposed to treatment, swelling of the tegument could be seen, causing the hooks located on top to appear sunken in. Additionally, an accumulation of small blisters and cytoplasmatic debris was observed on the tegument. Under higher dosages and with additional application of the enhancer, furrows occurred in the tegument, with loss of hooks from the worm`s surface. The examinations revealed no differences in reaction between the ventral and the dorsal tegument. However, the damage to the rear end of the worm was more marked than to the front end.

With the aid of the TEM images, it was possible to examine the damage caused by albendazole sulphoxide alone and in combination with the enhancer to the tegument, intestine and ovary. In all the tissue examined, treatment with the active substance was found to cause damage in the form of extensive vacuole formation. The most severe damage in all the tissue examined was observed in the area of the basal lamina in the form of merging vacuoles. Use of the enhancer intensified the damage, with additionally fissuring. Mitochondrial changes in morphology such as swelling and bursting occured. In some cases, the basal lamina broke away from the surrounding tissue, creating large cavities in the worm tissue in some cases being completely lysed.