

Efficacy and safety of topical administration of selamectin for treatment of ear mite infestation in rabbits

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Objective—To evaluate the efficacy and safety of topical administration of selamectin in rabbits naturally infested with *Psoroptes cuniculi*.

Design—Randomized controlled trial.

Animals—48 mixed-breed domestic rabbits with active *P cuniculi* mite populations and clinical ear lesions.

Procedures—Rabbits were randomly allocated to 1 of 6 treatment groups. On day 0, rabbits in groups 1 and 2 were given vehicle, rabbits in groups 3 and 4 were given selamectin at a dose of 6 mg/kg (2.7 mg/lb), and rabbits in groups 5 and 6 were given selamectin at a dose of 18 mg/kg (8.2 mg/lb). On day 28, rabbits in groups 2, 4, and 6 were given a second dose of vehicle or selamectin. Otoloscopic examinations were performed and ear lesion size was measured weekly for 8 weeks. Quantitative viable mite counts were performed on day 56.

Results—On days 7 through 56, lesion sizes for all selamectin-treated groups were significantly lower than sizes for control groups; there were no significant differences in lesion sizes among selamectin-treated groups. All rabbits in the 2 control groups had viable adult *P cuniculi* mites for the duration of the study, as determined by otoscopic examination, whereas all rabbits in the 4 selamectin-treated groups were free from *P cuniculi* mites on days 7 through 56. No adverse reactions associated with selamectin treatment were observed.

Conclusions and Clinical Relevance—Results suggest that topical application of selamectin at a dose of 6 or 18 mg/kg can completely eliminate mites from rabbits naturally infested with *P cuniculi*. (*J Am Vet Med Assoc* 2003;223:322–324)

Selamectin is a macrocyclic lactone of the avermectin subclass. Percutaneous absorption of selamectin following topical administration in dogs and cats is rapid, and plasma and tissue concentrations are sustained for at least several weeks.¹ A major advantage of selamectin is that topical application of a single dose is effective against a variety of ectoparasites in dogs and

cats. For instance, in 2 studies,^{2,3} topical administration of a single dose of selamectin (minimum dose, 6 mg/kg [2.7 mg/lb]) was found to be effective for treatment of naturally acquired aural infestations of *Otodectes cynotis* in dogs and cats. Selamectin has also been shown to be effective in the prevention and control of flea (*Ctenocephalides felis*) infestations in dogs and cats^{4,7} and for the treatment of sarcoptic mange (*Sarcoptes scabiei*) in dogs.⁸

Psoroptes cuniculi is a common parasite that causes infestations in the body and ears of rabbits.⁹ As many as 10,000 mites may inhabit a single pinna, creating a gray-brown mass of crusts and scabs that consists of live and dead mites, their wastes, and inflammatory exudates.¹⁰ Removing the crusts and treating topically may be painful, and cross-resistance to topically applied parasiticides is not uncommon.¹¹

Psoroptes mites are generally sensitive to macrocyclic lactones, and SC injections of ivermectin (50 to 800 µg/kg [23 to 364 µg/lb]) have been used to treat *P cuniculi* ear mite infestations in rabbits.¹²⁻¹⁸ However, multiple injections are typically needed. In 1 study,¹² for instance, eradication of ear mites was demonstrated in rabbits treated with 2 doses of ivermectin 2 weeks apart. In another study,¹³ SC or IM administration of a single dose of 200 µg of ivermectin/kg (91 µg/lb) did not eliminate mites, but administration of a single dose of 400 µg of ivermectin/kg (182 µg/lb) did. In rabbits with mild mite infestations, mites were completely eliminated after 2 weekly injections of ivermectin (200 µg/kg), but in rabbits with moderate or severe infestations, mites were still present after 4 weekly injections.¹⁴ Other studies^{17,18} have also confirmed the need for multiple doses of ivermectin to control *P cuniculi* infestations in rabbits.

Given the response to treatment with ivermectin in rabbits with ear mite infestations, it seems likely that selamectin would also be effective. To our knowledge, however, the efficacy of topical administration of selamectin or ivermectin in rabbits with ear mite infestations has not been determined. The purpose of the study reported here was to determine the efficacy and safety of topical selamectin administration in rabbits naturally infested with *P cuniculi*.

Materials and Methods

Rabbits—Forty-eight male and female mixed-breed domestic rabbits were used in the study. Rabbits were between 6 and 24 months old at the time of the study and weighed between 1.95 and 4.67 kg (4.3 and 10.3 lb). Rabbits were obtained from a local colony where ear mite infestations were known to be a persistent problem and maintained in a facility approved by the AAALAC. Animal husbandry was in

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accordance with standard operating procedures of the institution and applicable guidelines. Rabbits were housed individually in wire cages (0.3 to 0.4 m² [3 to 4 ft²]) and grouped by treatment; no contact was permitted between treatment groups. Cages were housed in an enclosed barn equipped with forced air heat and natural ventilation. Commercial rabbit pellets (17% protein) and water were available ad libitum. Rabbits were not known to have had any prior treatment with an ectoparasiticide. Rabbits were selected on the basis of overall health and the presence of clinical ear lesions and active *P cuniculi* mite populations, as determined by means of otoscopic examination.

Experimental design—Prior to inclusion in the study, rabbits were evaluated for severity of *P cuniculi* infestation. Ear lesion size was recorded as the sum of the area of the lesions in each ear, measured to the nearest 0.25 cm². Rabbits were grouped according to lesion size and randomly allocated to 1 of 6 treatment groups (8 rabbits/group) so that each treatment group contained rabbits with a similar range of lesion severity.

Three days after assignment to the treatment groups (day 0), rabbits were treated topically with vehicle or selamectin. Rabbits in groups 1 and 2 were given vehicle at a dose of 0.1 mL/kg (0.045 mL/lb; 0.25 mL for rabbits weighing ≤ 2.5 kg [5.5 lb], 0.75 mL for rabbits weighing 2.6 to 7.5 kg [5.7 to 16.5 lb], and 1 mL for rabbits weighing > 7.5 kg). Rabbits in groups 3 and 4 were given selamectin^a at a dose of 6 mg/kg (2.7 mg/lb; 0.25 mL for rabbits weighing ≤ 2.5 kg, 0.75 mL for rabbits weighing 2.6 to 7.5 kg, and 1 mL for rabbits weighing > 7.5 kg). Rabbits in groups 5 and 6 were given selamectin at a dose of 18 mg/kg (8.2 mg/lb; 0.75 mL for rabbits weighing ≤ 2.5 kg, 2.25 mL for rabbits weighing 2.6 to 7.5 kg, and 3 mL for rabbits weighing > 7.5 kg). On day 28, rabbits in groups 2, 4, and 6 were reweighed and given a second dose of vehicle or selamectin. Selamectin or vehicle was applied directly to the skin at the base of the neck, cranial to the scapulae. Treatments were supplied in plastic unit-dose tubes (0.25 or 0.75 mL of selamectin at a concentration of 60 mg/mL and 0.25 or 0.75 mL of vehicle). The vehicle consisted of isopropyl alcohol and glycol methyl ether.

The general health of all rabbits was monitored daily throughout the study, and detailed clinical observations were made approximately 4 and 24 hours after treatment on days 0 and 28.

Otosopic examinations for viable adult *P cuniculi* mites were performed on all rabbits on days 7, 14, 21, 28, 35, 42, 49, and 56. Ear lesion size was also determined for each rabbit on days 7, 14, 21, 28, 35, 42, 49, and 56. At the conclusion of the study (day 56 or 57), rabbits were euthanized, and quantitative counts of viable *P cuniculi* mites (larvae, nymphs, and adults) were performed on all rabbits.

Statistical analyses—Data for ear lesion size were analyzed with a general linear repeated-measures model. If a significant treatment or treatment-by-day effect was found, appropriate contrasts among treatments on each day of the study were performed. Ear lesion sizes were transformed to natural logarithms prior to analysis, and least-squares means were back-transformed to geometric means for tabular presentation.

Data for ear mite counts (representing the number of mites in both ears) were analyzed with a general linear mixed model. If a significant treatment effect was found, appropriate contrasts among treatments were performed. Mite counts were transformed to natural logarithms prior to analysis, and the least-squares means were back-transformed to geometric means.

For rabbits treated with selamectin, the percentage reduction in mite counts was determined by use of the following formula: percentage reduction = 100 × (mite count for control group – mite count for selamectin-treated group)/mite count for control group. All mite counts were geometric mean counts, estimated for each group as the least-squares mean value for the logarithm of total mite count + 1. For this evaluation, group 1 was used as the control group for groups 3 and 5, and group 2 was used as the control group for groups 4 and 6.

Results of otoscopic examinations for mites were summarized and evaluated with appropriate descriptive statistics. For all analyses, values of $P \leq 0.05$ were considered significant.

Results

Prior to the initial treatment (day –3), mean ear lesion size was not significantly different among groups (Table 1), and no significant differences in mean ear lesion size were observed between the 2 control groups (groups 1 and 2) at any time during the study. Mean ear lesion sizes for the selamectin-treated groups were significantly lower than lesion sizes for the corresponding control groups on days 7 through 56 after treatment. However, there were no significant differences in mean ear lesion size at any time among the 4 selamectin-treated groups.

All rabbits in the control groups had viable adult *P cuniculi* mites for the duration of the study, as determined by otoscopic examination, whereas all rabbits in the 4 selamectin-treated groups were free from *P cuniculi* mites on days 7 through 56. Geometric mean live mite counts, determined at the end of the study, were not significantly different between the 2 control groups (geometric mean live mite counts for groups 1 and 2

Table 1—Size of ear lesions in rabbits naturally infested with *Psoroptes cuniculi* and treated topically with vehicle or selamectin

Group	Mean ear lesion size (cm ²)								
	Day –3	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56
1	6.4	7.2	7.4	8.3	8.1	9.2	8.8	9.7	9.4
2	7.1	7.4	8.3	8.2	8.8	8.9	9.3	9.8	9.6
3	5.9	1.7	0.5	0.2	0.4	0.3	0.5	0.2	0.1
4	5.7	1.1	0.6	0.4	0.7	1.0	0.9	0.2	0.1
5	9.0	2.0	0.6	0.2	0.3	0.3	0.3	0.0	0.0
6	6.0	1.0	0.5	0.7	0.1	0.1	0.2	0.1	0.1

On day 0, rabbits in groups 1 and 2 were given vehicle, rabbits in groups 3 and 4 were given selamectin at a dose of 6 mg/kg (2.7 mg/lb), and rabbits in groups 5 and 6 were given selamectin at a dose of 18 mg/kg (8.2 mg/lb). On day 28, rabbits in groups 2, 4, and 6 were given a second dose of vehicle or selamectin. On days 7 through 56, mean lesion sizes for all selamectin-treated groups were significantly lower ($P \leq 0.05$) than sizes for control groups; there were no significant differences in mean lesion sizes among selamectin-treated groups.

were 2,033 and 2,029, respectively). No live mites were recovered from any selamectin-treated rabbits; therefore, for all 4 selamectin-treated groups, geometric mean live mite counts were 0, and mean percentage reductions in mite counts were 100%. Mean live mite counts were significantly lower for the selamectin-treated groups than for the corresponding control groups.

No adverse clinical signs associated with treatments were observed during the study.

Discussion

Results of the present study suggest that a single topical application of selamectin at a dose of 6 or 18 mg/kg can completely eliminate mites from rabbits naturally infested with *P. cuniculi*. In the present study, no live ear mites were recovered from any selamectin-treated rabbits, whereas all control rabbits remained heavily infested with viable *P. cuniculi* mites. The substantial decrease in mean ear lesion size 7 days after treatment for the 4 selamectin-treated groups was particularly remarkable, considering the size of the lesions and amount of scabbing in some of the more heavily infested rabbits prior to treatment.

Although detailed toxicity studies in rabbits have not been reported, selamectin has been shown to be safe in dogs and cats.^{19,20} In the present study, although additional treatments were not necessary for elimination of mites, 1 or 2 topical applications of selamectin at a minimum dose of 6 mg/kg and 1 or 2 topical applications of selamectin at a minimum dose of 18 mg/kg with a 28-day interval between treatments did not result in any adverse clinical signs. Selamectin is not currently approved for use in rabbits in the United States or elsewhere in the world.

^aRevolution/Stronghold, Pfizer Animal Health, New York, NY.

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