

Efficacy of a Formulation Containing Imidacloprid and Moxidectin Against Naturally Acquired Ear Mite Infestations (*Psoroptes cuniculi*) in Rabbits

Olaf Hansen, DVM, PhD¹

Yvonne Gall, PhD²

Kurt Pfister, DiplEVPC, PhD²

Wieland Beck, DiplEVPC, PhD²

¹*Bayer Vital GmbH
Leverkusen, Germany*

²*Institute for Comparative Tropical Medicine and Parasitology, Faculty of Veterinary Medicine
Ludwig-Maximilians-University Munich
Leopoldstrasse, Munich, Germany*

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ABSTRACT

The purpose of this study was to evaluate the efficacy of a topical formulation containing imidacloprid and moxidectin for eradication of *Psoroptes cuniculi* in rabbits. Fourteen adult rabbits from a rabbit husbandry were enrolled in the study. Rabbits were treated with 40 mg imidacloprid and 4 mg moxidectin monthly as spot-on on Days 0, 30, and 60. No other treatment or environmental decontamination was performed during the trial. On Days 0, 30, 60, and 90, all rabbits were examined, and epidermal debris was collected from both auricular areas and the external ear canal for microscopic examination. Clinical signs had subsided by Day 30 in 13/14 rabbits and almost no signs of recurrence were apparent in the following weeks. All epidermal samples were negative by Day 90. No adverse reac-

tions were observed. Under the conditions of our study, topical formulation of imidacloprid and moxidectin was a practical and well-tolerated means of treatment for ear mange in rabbits.

INTRODUCTION

Astigmated *Psoroptes* mites are cosmopolitan external parasites of mammalian hosts and are of economic significance as the agents of mange in several domesticated animals, particularly with regard to the psoroptic mange of sheep caused by *Psoroptes ovis* (Hering).¹⁻³ Another ear mite, *Otodectes cynotis* (Hering), causing otodectosis, is an obligate parasite that inhabits the vertical and horizontal ear canals of dogs and cats,⁴ although other species such as ferrets may become infested.⁵ A fairly frequent species of veterinary importance is *Psoroptes cuniculi* (Delafond) responsible for otodectosis in different farm animals, mainly affecting rabbits, goats, horses,

antelopes, cattle, and sheep.⁶⁻⁹ The ear mite is mainly found in the external auricular meatus of the ear and inside the ear pinnae; it is common to discover that only one ear is affected. *Psoroptes cuniculi* infestations in domestic rabbits are recognized in 2 clinical pictures: characteristic psoroptic “ear canker” causing puff pastry-like crusts, excoriations, massive pruritus, and occasionally aural hematomas due to intense head shaking or scratching^{10,11}; and “extra-auricular” mange extensively described by Ribbeck and Ilchmann¹² and Guilhon.¹³ Cutler¹⁴ reported an ectopic *P. cuniculi* infestation in a pet rabbit, with severe lesions on the skin of the caudoventral abdomen. Bates³ observed the ectopic form in 5% of all *P. cuniculi*-infested rabbits of his study, showing lesions extending to the base of the ears, the cheeks, dewlap, face, and between the digits of both hind feet.

A new dermal product has been developed containing imidacloprid and moxidectin (Advocate[®], Bayer) that is administered as a viable topical application to the skin at a single site on dogs and cats. No information is available on the efficacy of this preparation in rabbit “ear canker.” There are currently no licensed veterinary products specifically indicated for the therapy of ectoparasites in rabbits. Thus, veterinarians need to rededicate pharmaceuticals normally used for other animal species. The present clinical study was conducted to evaluate the efficacy and tolerance of a spot-on formulation with imidacloprid and moxidectin in the treatment of *P. cuniculi* mange in naturally infested rabbits.

MATERIALS AND METHODS

Fourteen adult rabbits with a naturally occurring *P. cuniculi* infestation were enrolled in this field study. All rabbits were from the same rabbit husbandry in the western Bodensee area (Baden-Wuerttemberg) and kept exclusively in cages indoors during the treatment period. Ages ranged from 6 months to 1 year with a mean age of 9 months. On Day 0, all animals were individ-

ually weighed. Body weight of the measured rabbits ranged from 2.1 to 3.7 kg with a mean body weight of 2.65 kg. In the course of this study, one female was pregnant. Owners reported about reduced appetite and increasing restlessness in their animal husbandry over the last weeks. Moreover, remarkable crusts in the pinnae were observed.

Treatment

Each rabbit received 3 spot-on treatments 30 days apart on study Days 0, 30, and 60. Dermal application was performed using a 40-mg imidacloprid and 4-mg moxidectin topical solution (Advocate[®], Bayer) at the base of the neck. Due to the animal welfare within this field trial of heavily mite-infested animals, a placebo treatment group was not enrolled. No other treatment or environmental decontamination was performed during the trial. The success of the treatment was assessed by clinical as well as parasitological examination.

Clinical Examination

General health of all treated animals was observed daily by the farm owners from Day 0 for the duration of the study, except for Days 30, 60, and 90 when a detailed clinical check-up was conducted by the veterinarian. At these particular assessment dates, ear lesions were judged for each rabbit. During the course of the trial, ear lesion evaluations and observed side effects were recorded. Clinical signs were evaluated by scoring from absent (-), mild (+), moderately (++) , or profoundly (+++) on Days 0, 30, 60, and 90 with respect to appearance of scaling and crusting in the pinnae and in the external auricular meatus.

Parasitological Examination

On Days 0, 30, 60, and 90, all rabbits were examined, and epidermal debris was collected from both auricular areas and the external ear canal for microscopic examination. The ear canal swabs sampled were examined for mites, their eggs, and other developmental stages each time by at least 2 of the following methods: (1) stereomicro-



Figure 1. Mild scaling/crusting in the pinnae due to *P. cuniculi* infestation in a rabbit prior to treatment with the imidacloprid/moxidectin combination.



Figure 2. Rabbit from Figure 1 on Day 90 of the trial.

scope: epidermal debris and hairs were placed in a petri dish and examined at 25 \times magnification; (2) epidermal debris and hairs from one sample, respectively, were diluted in ~1 mL of a 10% KOH solution and heated for 20 minutes to macerate scales and hairs. The mixture was stirred, centrifuged, and the supernatant discarded. A concentrated sucrose solution was then added to the sediment, a cover slip was applied to the surface of the solution, the samples were again centrifuged, and, finally, the cover slip was transferred to a slide and inspected under a microscope at 40 \times magnification; or (3) direct check up under the microscope: epidermal debris and hairs were applied directly onto a microscope slide, covered with a few drops of mineral oil and a cover slip, then inspected at 40 \times magnification. The KOH and flotation technique was used in all rabbits on Day 0, because a relatively large portion of pattern material was collected with a sharp spoon.

RESULTS

On Days 30, 60, and 90, the quantity of ear canal swaps sampled was generally much less than on Day 0, which appeared to correlate with clinical improvement. Clinical signs were absent by Day 30 in 13/14 rabbits, and no signs of recurrence were apparent in the following weeks (Figures 1 and 2). Thus, for all further examinations performed on Days 30, 60, and 90, the stere-

omicroscope and direct microscopic procedure were the only techniques used.

The eggs and mites recovered from the ears were documented for each rabbit to produce geometric mean egg and mite counts on each assessment day (0, 30, 60, and 90). For each treatment and/or assessment day within the study, the number of rabbits with or without eggs/mites in the skin scrapings was established in order to specify the efficacy of the used antiparasiticide (Table 1). Live mites and eggs were numerous in all animals on Day 0, but had declined on Day 30 prior to the second treatment. A moderate recurrence of mean mite counts was observed from Day 30 to Day 60 despite repeated treatment. Only 4/14 rabbits still harbored eggs and/or mites on Day 30 and Day 60. Thus the evaluated efficacy of the imidacloprid/moxidectin combination was 71.4%. No eggs or mites (dead or alive) in any rabbit were detected on assessment Day 90. Efficacy of the imidacloprid/moxidectin spot-on formulation rated 100% at this point of time, accordingly. Clinical signs of the rabbits during the study are summarized in Table 2. There were no adverse drug experiences or treatment-related mortalities during the trial.

DISCUSSION

Although our study does not allow us to conclude where the mite infestation is usually acquired, the fact that new rabbits are

Table 1. Parasitological Examination of Rabbits With Naturally Acquired *P. cuniculi* Infection Before and After Treatment With an Imidacloprid/Moxidectin Combination.

	Treatment* and Assessment Days			
	Day 0*	Day 30*	Day 60*	Day 90
Geometric mean mite counts	10.4	4.5	15.5	0
Geometric mean egg counts	7.5	4	4	0
Number of rabbits with mites and eggs in the ear swabs	14	4	4	0
Efficacy (%)	—	71.4	71.4	100

*Days of treatment.

Table 2. Clinical Efficacy of an Imidacloprid/Moxidectin Combination Against Naturally Acquired Infestations by *P. cuniculi* in Rabbits: Clinical Signs of Mite Infestation Before and After Treatment.

Clinical Signs	Number of Rabbits With Particular Scaling/Crusting (+, ++, +++)			
	Day 0	Day 30	Day 60	Day 90
Scaling/crusting				
Absent (-)	—	13	12	14
Mild (+)	12	1	2	—
Moderate (++)	2	—	—	—
Profound (+++)	—	—	—	—
Clinical efficacy (%)	0 (0/14)	92.9 (13/14)	85.7 (12/14)	100 (14/14)

purchased permanently in this husbandry may be seen as a constant source of infestation with *P. cuniculi* mites. Twelve of the 14 rabbits showed a mild form of “ear canker” accompanying moderate pruritus and head shaking. There had been no evidence for ectopic ear mite infestation. The skin lesions were margined to the pinnae and the external ear canal. All animals suffered from bilateral otitis externa parasitaria. On Day 0, all 14 rabbits showed a clinical picture compatible with “ear canker.” Pruritus, which was present in 14/14 rabbits, was considered mild to moderate in 12 rabbits and severe in 2 rabbits. Fourteen rabbits presented mild to moderate ear scaling and crusting. Alopecia, excoriations, or hematomas were not detectable. On Day 30, a great clinical improvement was noted. Only one rabbit still exhibited mild scaling. Pruritus and head shaking had resolved in all of the small mammals. On Day 60, with the exception of 2 rabbits, all clinical signs disappeared, even though a total of 4 rabbits still harboured eggs and mites on this day. On Day 90, all rabbits were free from clinical

signs and mites or developmental stages. Significantly increased mite counts from Day 30 to Day 60 may be due to reinfestation from the contaminated environment. This might be supported by the ability of *P. cuniculi* to survive off the host for 4 to 21 days at relative humidities between 20% and 99% and temperatures between 5°C and 30°C.¹⁵ Smith and colleagues¹⁶ quantified the probability of transmission of psoroptic mites from the environment to the animal and emphasized its fundamental importance for the design and implementation of effective control strategies.

In this trial, the spot-on formulation containing imidacloprid and moxidectin was 100% effective against naturally acquired aural infestations of *P. cuniculi* mites in rabbits. Although there was no control group, the treatment regimen appeared effective and tolerable in the clinical control of ear mite infestations. A lack of licensed antiparasitics for this indication in rabbits requires an off-label use of adequate pharmaceuticals.¹⁷ The simple dosing protocol used here, with a spot-on

formulation topically administered at the base of the rabbit's neck, facilitates owner compliance with the treatment protocol. "Ear canker" is seen predominantly in large agricultural rabbit husbandries. It is in contrast to the otic preparations currently available for the therapy of ear mites that demand applications into the external auricular meatus once or twice daily for up to 4 weeks. Because of more applications and a higher incidence of recurrence, topical administration into the ear canal is much more time-consuming and laborious. The off-label use of another macrocyclic lactone of the avermectin subclass, ivermectin, administered subcutaneously, has been reported to be successful in the control of *P. cuniculi* in rabbits.¹⁸⁻²² Although there are topical and injectable acaricidal products available for the treatment of psoroptic mange in rabbits, most of them require frequent and careful application to control or eradicate the mites. Several authors report that efficacy of injections with the preferred ivermectin appears to vary with several populations of *P. cuniculi* in rabbits. According to Wilkins and colleagues²³ in Texas, USA, and Pandey¹⁹ in the UK, a single injection of ivermectin (200 µg/kg body weight) eliminated all *P. cuniculi* mites. Animals studied by Wright and Riner¹⁸ required injections at a higher dose rate of 400 µg/kg body weight to cure psoroptic "ear canker." In a German trial, neither 200 nor 400 µg/kg body weight failed to eradicate *P. cuniculi* completely.²⁴ Moreover, the injection route seems to be a determining factor. Rabbits infested with *P. ovis* and *P. cuniculi* were injected intramuscularly (IM) or subcutaneously (SC) with ivermectin. A single application of 200 µg/kg body weight either IM or SC was inadequate to eliminate all mites in the ears of the rabbits. However, a single injection of 400 µg/kg body weight, regardless of the route of application, eradicated all *P. cuniculi* mites, but eliminated *P. ovis* in only 50% of the rabbits.¹⁸ Results of a study from McTier and colleagues²⁵ suggest that a single topical application of selamectin at a dose of 6

or 18 mg/kg body weight can completely eliminate mites from rabbits naturally infested with *P. cuniculi*. Wagner and Wendlberger²⁶ treated rabbits with psoroptic mites with moxidectin 0.2 mg/kg body weight SC and orally twice 10 days apart, respectively. After this period, neither excessive cerumen nor mites could be identified in the external ear canal. All rabbits were cured and did not show clinical signs during the next 6 months. No side effects occurred in any of these rabbits. Fourie and colleagues⁴ figured out that a single therapy with an imidacloprid/moxidectin solution applied at a dosage of 0.1 mL/kg body weight resulted in a treatment success rate of 80% as assessed 50 days after application in *O. cynotis*-infested cats. Two treatments with the imidacloprid/moxidectin combination 4 weeks apart and at the same dosage was efficacious in curing all cats from the ear mites as assessed 22 days after the second application (Day +50). Pullium and colleagues²⁷ found that in mice infested by *Myocoptes musculus*, there was a total eradication of mites without any toxic effect or clinical signs of illness in the patients after one topical treatment with moxidectin 0.5%. Avermectins are not currently approved for use in rabbits in Germany or elsewhere in the world. Interest is developing in the use of biocompatible products such as lavender oil for the therapy of external parasites in rabbits.²⁸ Macchioni and colleagues²⁹ tested acaricidal activity of aqueous extracts of camomile flowers against *P. cuniculi* and showed its efficacy.

CONCLUSIONS

Under the conditions of our trial, topical formulation containing imidacloprid and moxidectin was a practical and well-tolerated means of treatment for ear mite infestation in rabbits. The results indicate that imidacloprid in addition to moxidectin at a dosage of 10 and 12 mg/kg body weight, respectively, percutaneously thrice 4 weeks apart is effective and a good alternative for the control of "ear canker" in rabbits.

REFERENCES

1. Pfister K: Epizootological views on the occurrence of *Psoroptes mangle* and other ectoparasites in the sheep in the canton Bern. *Schweiz Arch Tierheilk* 1978;120:561–567.
2. Bates PG: Epidemiology of subclinical ovine psoroptic otacariasis in Great Britain. *Vet Rec* 1996;138:388–393.
3. Bates PG: Subclinical ovine psoroptic otacariasis in Great Britain: an abattoir survey. *Vet Rec* 1996;139:235–236.
4. Fourie LJ, Kok DJ, Heine J: Evaluation of the efficacy of an imidacloprid 10%/moxidectin 1% spot-on against *Otodectes cynotis* in cats. *Parasitol Res* 2003;90:112–113.
5. Beck W: Otacariasis in ferret caused by *Otodectes cynotis* (Acari: Psoroptidae)—Biology of *Otodectes cynotis*, pathogenesis, clinical features, diagnosis and treatment. *Kleintierprax* 2001;46:31–34.
6. Rafferty DE, Gray JS: The feeding behaviour of *Psoroptes* sp. on rabbits and sheep. *J Parasitol* 1987;73:901–906.
7. Friel J, Greiner EC: Ear mites from domestic goats in Florida. *Exp Appl Acarol* 1988;4:345–351.
8. Wright FC, Glaze RL: Blackbuck antelope (*Antilope cervicapra*), a new host of *Psoroptes cuniculi* (Acari: Psoroptidae). *J Wildl Dis* 1988;24:168–169.
9. Bates PG: Inter- and intra-specific variation within the genus *Psoroptes* (Acari: Psoroptidae). *Vet Parasitol* 1999;83:201–217.
10. Curtis SK, Housley R, Brooks DL: Use of ivermectin for treatment of ear mite infestation in rabbits. *J Am Vet Med Assoc* 1990;196:1139–1140.
11. Beck W: Ear mange in domestic rabbit caused by *Psoroptes cuniculi* (Acari: Psoroptidae)—Biology of *Psoroptes cuniculi*, pathogenesis, clinical features, diagnosis and treatment. *Kleintierprax* 2000;45:301–308.
12. Ribbeck R, Ilchmann G: Complications of *Psoroptes cuniculi* of domestic rabbits. *Monatsh Veterinärmed* 1969;24:377–381.
13. Guilhon J: Extension corporelle de l'otacariose cuniculine à *Psoroptes cuniculi* (generalisation of otacariasis in rabbits with *Psoroptes cuniculi*). *Recueil Méd Vétérin* 1990;166:119–123.
14. Cutler SL: Ectopic *P. cuniculi* infestation in a pet rabbit. *J Small Anim Pract* 1998;39:86–87.
15. Arlian LG, Kaiser S, Estes SA, Kummel B: Infestivity of *Psoroptes cuniculi* in rabbits. *Am J Vet Res* 1981;42:1782–1784.
16. Smith KE, Wall R, Berriatua E, French NP: The effects of temperature and humidity on the off-host survival of *Psoroptes ovis* and *Psoroptes cuniculi*. *Vet Parasitol* 1999;83:265–275.
17. Beck W: Common endo- and ectoparasitic diseases in small mammals—clinical feature, diagnosis and treatment. A review of the literature and own experiences. *Tierärztl Prax* 2004;32:311–321.
18. Wright RC, Riner JC: Comparative efficacy of injection routes and doses of ivermectin against *Psoroptes* in rabbits. *Am J Vet Med* 1985;46:752–754.
19. Pandey VS: Effect of ivermectin on the ear mange mite, *Psoroptes cuniculi*, of rabbits. *Brit Vet J* 1989;145:54–56.
20. Bowman DD, Fogelson ML, Carbone LG: Effect of ivermectin on the control of ear mites (*Psoroptes cuniculi*) in naturally infested rabbits. *Am J Vet Res* 1992;53:105–109.
21. Ferrero O, Rebuelto M, Albarellos G, Hallu R: Efficacy of ivermectin in the treatment of rabbit ear cancer. *Veterinaria Argent* 1994;11:242–244.
22. Harikrishnan TJ, David BP, Sarathchandra G, Albert A: Efficacy of ivermectin against rabbit mange. *J Vet Med Sci* 1996;27:145–147.
23. Wilkins CA, Conroy JA, O'Shanney WJ, Egerton JR: Treatment of psoroptic mange with avermectins. *Am J Vet Res* 1980;41:2112–2113.
24. Prosl H, Kanout A: Treatment of ear mange in rabbits with ivermectin. *Berl Münch Tierärztl Wschr* 1985;98:45–47.
25. McTier TL, Hair JA, Walstrom DJ, Thompson L: Efficacy and safety of topical administration of selamectin for treatment of ear mite infestation in rabbits. *J Am Vet Med Assoc* 2003;223:322–324.
26. Wagner R, Wendlberger U: Field efficacy of moxidectin in dogs and rabbits naturally infested with *Sarcoptes* spp., *Demodex* spp. and *Psoroptes* spp. mites. *Vet Parasitol* 2000;93:149–158.
27. Pullium J, Brooks W, Langley A, Huerkamp M: A single dose of topical moxidectin as an effective treatment for murine acariasis due to *Myocoptes musculinus*. *Cont Top Lab Anim Sci* 2005;44:26–28.
28. Perrucci S, Cioni PL, Flamini G, Morelli I, Macchioni G: Acaricidal agents of natural origin against *Psoroptes cuniculi*. *Parasitologia* 1994;36:269–271.
29. Macchioni F, Perrucci S, Cecchi F, Cioni PL, Morelli I, Pampiglione S: Acaricidal activity of aqueous extracts of camomile flowers, *Matricaria chamomilla*, against the mite *Psoroptes cuniculi*. *Med Vet Entomol* 2004;18:205–207.