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Lotilaner is a potent inhibitor of the novel GABA receptor of body lice *Pediculus humanus humanus*

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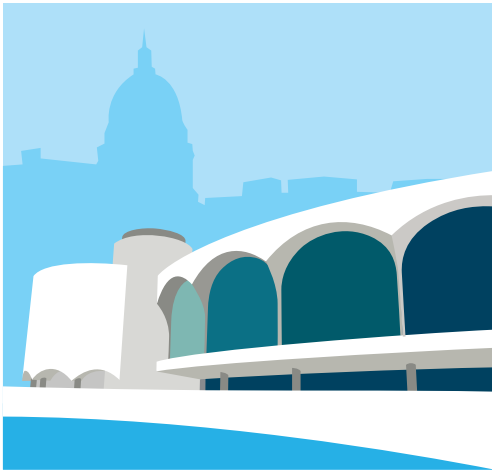
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the Advancement of Veterinary Parasitology

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Abstract Book

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the lesions. Twenty four hours after treatment all larvae were killed on all treated animals. Total amount of larvae recovered ranged from 3 to 327 larvae per animal (average of 67.7). Afoxolaner (NexGard®) at doses ranging from the minimum active dose of 2.5 mg/kg to the maximum dose 6.7 mg/kg (mean of 3.9 mg/kg) was rapidly efficacious for the treatment of 14 dogs with light, moderate and severe infestations with *Cochliomyia hominivorax* larvae, by eliminating all larvae within 24 hours after a single oral treatment.

OA13.02 Lotilaner Is a Potent Inhibitor of the Novel GABA Receptor of Body Lice *Pediculus Humanus Humanus*

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Drug resistance in the parasites field, including the cosmopolitan lice (*Pediculus humanus*), and the prevalence increasing despite the marketing of new therapies are an important challenge for our societies. The major pharmacological targets of insecticides like pyrethrins, malathion, spinosad and ivermectin (also used as nematicide and acaricide) are the ligand gated ion channels present in the nervous system of insects. Currently, targets of these molecules remain largely unknown in body lice. Among those channels receptors, -aminobutyric acid gated chloride ion channels (GABACl) are the main synaptic inhibitory receptors in insects, making them pertinent pharmacological targets.

In the present study, we identified and characterized the targets of insecticides in lice to decipher the mode of action of insecticides in Pediculidae. Research in the genomic databases of *Pediculus humanus* allowed us to identify a GABACl subunit encoded by the Resistance to dieldrin (Rdl) gene. We cloned the corresponding full-length cDNA into a transcription vector and performed in vitro

synthesis of the cRNAs, which were injected in the *Xenopus* oocysts system to reconstitute functional channels. Two-electrode voltage clamp recordings showed that Phh-RDL assemble into a homomeric receptor sensitive to different insecticides like fipronil, picrotoxin and lotilaner, a novel class of ectoparasiticide agent using to treat ticks and fleas of dogs (Credelio™, Elanco). These results correlated with the efficacy of these drugs on lice in vivo. In conclusion, we report the functional characterization of the first GABACl of *Pediculus humanus humanus*. These results contribute to our understanding of the mode of action of insecticide compounds and will allow the development of new therapeutic strategies to control lice infestations.

OA13.03 Early Oral Sarolaner (Simparica™, Zoetis) Acaricidal Activity Against *Ixodes Scapularis* and *Amblyomma Americanum* Adults After Monitored Attachment Intervals on Treated Dogs

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Acaricidal activity of oral sarolaner (Simparica™, Zoetis) against *Rhipicephalus sanguineus sensu lato* and *Dermacentor reticulatus* begins 4 and 8 hours, respectively, after induced infestations on treated dogs. Here, we evaluated *Ixodes scapularis* and *Amblyomma americanum* mortality in response to sarolaner after monitored, documented attachment time intervals within 1-8 hours of infestation. In duplicate, staggered infestation experiments, 6 treated and 6 control dogs were infested with 250 *I. scapularis* and 250 *A. americanum* adults. Ticks were allowed 60 minutes to embed mouthparts into the dermis. A ≤ 50% attachment rate was targeted. Subsets of ≤ 20 ticks were removed from dogs after documented attachment times of 1, 3, 5, and 7 hours or 2, 4, 6, and 8 hours. Live/dead status was assessed at the time of removal and 24 hours post-removal (live ticks incubated at ambient temperature (~70°F [21.1°C], 80-90%