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## **A first insight into the effect of Lotilaner on GABA-gated channels from the european tick *Ixodes ricinus***

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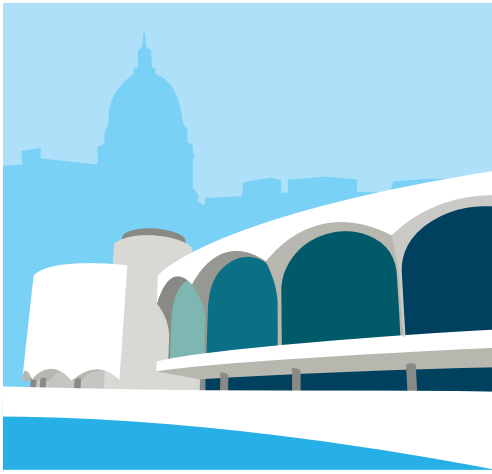
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# WAAVP

27<sup>th</sup> Conference of the World Association for  
the Advancement of Veterinary Parasitology

**JULY 7 - 11, 2019 | MADISON, WI, USA**

Dedicated to the legacy of Professor Arlie C. Todd

*Sifting and Winnowing the Evidence in Veterinary Parasitology*



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# Abstract Book

*Joint meeting with the 64<sup>th</sup> American Association of Veterinary Parasitologists  
Annual Meeting & the 63<sup>rd</sup> Annual Livestock Insect Workers Conference*

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humidity). Geometric means of combined live tick counts were calculated for attachment intervals of 1-2 hours, 3-4 hours, 5-6 hours, and 7-8 hours, and least squares means were compared by ANOVA with a two-sided significance level set at  $\alpha=0.05$ . Significantly fewer live *I. scapularis* were removed from treated than control dogs after 3-4 hours of attachment ( $p=0.0012$ ); upon holding 24 hours, significantly fewer *I. scapularis* that had previously been attached to treated dogs for 1-2 hours were alive ( $p=0.0049$ ). Significantly fewer live *A. americanum* were removed from treated than control dogs after 7-8 hours of attachment ( $p=0.0254$ ); upon holding 24 hours, significantly fewer *A. americanum* that had previously been attached to treated dogs for 3-4 hours were alive ( $p=0.0003$ ). These data indicate that acaricidal activity of sarolaner against *I. scapularis* and *A. americanum* begins after 1-2 hours and 3-4 hours of attachment, respectively, on sarolaner treated dogs.

#### OA13.04 A First Insight Into the Effect of Lotilaner on GABA-Gated Channels From the European Tick *Ixodes Ricinus*

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Ticks are strict blood-feeding arthropods (Acari), which represent a major health issue for wild or domesticated animals and humans, due to their potential to transmit disease agents. Control of ticks is increasingly difficult due to the development of drug-resistant parasites. Ligand-gated ion channels of the tick central nervous system are the primary targets of acaricides. Among those receptors, the  $\gamma$ -aminobutyric acid-gated chloride ion channels (GABACs) are the main synaptic inhibitory receptors. Lotilaner is a recently developed parasiticide from the isoxazoline chemical class that was shown to be a non-competitive antagonist of GABACs from the livestock tick *Rhipicephalus microplus*. In the

present study, we characterized the GABACs from the European tick species *Ixodes ricinus*.

We extracted RNAs from *Ixodes ricinus* nymphs. Taking advantage of the phylogenetic closeness of *I. ricinus* and *R. microplus* in the Arthropoda phylum, we identified the *I. ricinus* GABAC subunit homologue. The cDNA encoding the Iri-GABAC was cloned and the corresponding in vitro synthesized cRNAs were micro-injected into *Xenopus laevis* oocytes to investigate its pharmacological properties. Functional expression and two-electrode voltage clamp studies demonstrated that the GABAC subunit formed a homomeric receptor gated by GABA. Importantly, the insecticides like lotilaner, fipronil and picrotoxin efficiently blocked the GABA currents as previously observed for the *R. microplus* GABAC. Surprisingly, *I. ricinus* GABAC was not sensitive to the pesticide dieldrin, suggesting a potential naturally existing resistance mechanism involving alternative exons.

Here we report the functional characterization of the first GABAC of *I. ricinus* demonstrating that it is an important molecular target for lotilaner. Transcriptomic analysis of *I. ricinus* are in progress to identify new acaricidal targets.

#### OA13.05 Clinical Efficacy of Afoxolaner in Dogs Naturally Infected With *Sarcoptes Scabiei* and Concomitant Modifications of the Skin Microbiota

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Infection by *Sarcoptes scabiei* remains a common disease in dogs, especially in tropical countries where most of stray or non-controlled dogs show cutaneous