

New way to bump off ticks: Dry up their saliva

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Saliva from a tick's bite can transmit pathogens that cause serious illnesses, such as Lyme disease, and significant agricultural losses. Current insecticides have drawbacks, so scientists have been seeking new ways to prevent these pesky arachnids from spreading pathogens. Now, researchers report that compounds they previously identified can dry up ticks' saliva by upsetting the balance of ions in the salivary gland, reducing feeding and potentially limiting pathogen transmission.

The researchers will present their results today at the American Chemical Society (ACS) Fall 2019 National Meeting & Exposition.

"Lyme disease is exploding in the northeastern U.S.," says Daniel Swale, Ph.D., the project's principal investigator. "Most methods to kill ticks in the agricultural sector involve the use of neurotoxic insecticides, but it's difficult to effectively use these insecticides to control ticks in residential areas. So we wanted to identify a new way to control these disease-carrying ticks."

"We knew that the salivary gland is critical to the biological success of ticks, suggesting it had potential as a target for a pesticide that works through a new mechanism," Zhilin Li, a doctoral student who is presenting the work at the meeting, says. The researchers, who are at Louisiana State University, reasoned that if they could stop ticks from producing [saliva](#), then they could prevent them from feeding—a situation that would be incompatible with sustaining life.

Li and Swale focused on a [potassium ion channel](#), known as a Kir channel, which has been shown to be important for the excretory systems of arthropods—a classification of animals that includes mosquitoes, as

well as ticks. These microscopic channels allow potassium to move in and out of cells in the salivary gland and elsewhere in the ticks, maintaining an ionic balance essential to saliva secretion and the ticks' health.

In their current work, they fed ticks [blood](#) laced with two compounds known to act on the Kir channels. Two of the molecules—known as VU0071063 and pinacidil, a human hypertension drug—were effective, reducing saliva secretion by 95% or more and reducing blood ingestion by approximately 15-fold. Importantly, ticks that fed on bovine blood infused with either of these compounds were dead within 12 hours. That timeframe is significant because transmission of pathogens via ticks' saliva into their human or animal hosts typically takes at least 12 hours and sometimes as many as 40 hours. These initial studies were conducted in artificial host feeding systems that contained a blood meal. Next, the researchers plan to test whether their treatment can in fact prevent pathogen transmission when ticks feed on rodents.

Ticks removed from the blood meal before they died were obviously sick, the researchers report. The ticks were uncoordinated and lethargic, and they couldn't walk well. The researchers attribute this behavior to an imbalance of potassium, sodium and chloride ions in the ticks. Normally, when a tick feeds, its saliva returns excess water and ions from human or animal blood back into the host. But the treated ticks were spitting out more ions despite producing much less saliva, disrupting their biological functions. "We think their nervous system wasn't working normally, and we suspect that's why we saw high mortality in the treated ticks," Li says.

Li and Swale will follow up on initial results suggesting that the ion channel is expressed in the salivary gland only during blood feeding and then disappears. And the researchers are zeroing in on the exact type of cells in which the ion channels are produced within the [salivary gland](#). Once they have a more complete understanding of the reliance of blood

feeding and pathogen transmission on Kir channel function, they hope industry can use their findings to create a commercial product such as a spray for gardens, or an injection or oral treatment for the agricultural industry for those animals at risk of getting [tick](#) bites. Swale notes that the method also seems to reduce saliva production and feeding in aphids and fruit flies, so it could potentially be used to control these agricultural pests, too.

More information: Giving ticks 'dry mouth' through chemical modulation of inward rectifier potassium channels as a mechanism to prevent blood feeding, the American Chemical Society (ACS) Fall 2019 National Meeting & Exposition.

Abstract

Ticks are competent vectors for multiple pathogens that induce extreme morbidity and mortality to humans and livestock worldwide. The salivary gland is critical to the biological success of ticks indicating it may hold potential as a target tissue for acaricides. Therefore, we directly tested the hypothesis that tick salivary gland function is reliant upon epithelial transport of potassium ions and chemical modulation of inward rectifier potassium (Kir) conductance will have deleterious consequences to tick biology. Confocal fluorescent microscopy was performed to determine the spatial and temporal localization patterns of Kir channels expressed in the salivary gland. Imaging analysis indicates expression of Kir proteins in basal cells of Type III acini, which are responsible for fluid and protein secretion. Correspondingly, activation of Kir channels reduced fluid secretion from 81 ± 11 nL to less than 3 ± 1 nL with IC50 values in the low micromolar range. Interestingly, analysis of Kir protein expression in ticks that blood fed for >5 days showed no expression of Kir channels, indicating Kir channels are dynamically regulated and are critical for the initial blood feeding phase but not the later. In vivo feeding assays were performed to test the hypothesis that reduced secretory activity of the salivary gland will

reduce blood ingestion and that altered osmoregulation will induce mortality due to an inability to deal with the cation rich mammalian blood. Indeed, exposure to Kir channel modulators reduced the ingested volume of blood by up to 15-fold. Further, exposure to Kir channel modulators during blood feeding significantly increased the the rate of mortality with ET50 values of

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