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Advancing Towards Safe and Effective Topical Mosquito Repellents Against Dengue

Researchers uncover the multifaceted potential of low viscosity polydimethylsiloxane, a silicone polymer, for effective mosquito repellence on human skin.

Topical mosquito repellents are effective in limiting mosquito-borne disease transmission. Most widely used repellents, however, lose effectiveness in the short-term due to volatilization and in the long-term due to mosquito cognate receptor mutations. Now, researchers have enhanced repellent effectiveness by combining them with low viscosity silicone oil, significantly improving their adhesiveness to mosquito legs and reducing bites on human skin. Moreover, silicone oil prevents object tracking and makes mosquitoes avoid co-applied odors, providing added protection.

Mosquito-borne diseases, such as dengue and malaria, are persistent threats to human health in many parts of the world. Acting as a defense and offering personal protection, topical mosquito repellents can effectively reduce mosquito bites and consequently prevent the transmission of mosquito-borne diseases. However, many widely used topical mosquito repellents lose their efficacy over time due to resistance development in mosquitoes caused by mutations. Developing new and effective repellent products that are as comfortable to use as everyday skin care products is crucial for preventing frequent waves and outbreaks of mosquito-borne diseases like dengue and malaria around the world.

Working towards the development of unique repellent technologies, researchers from Japan have uncovered the effects of low viscosity polydimethylsiloxane (L-PDMS), commonly known as silicone oil, on mosquito behavior and sensory abilities. The study, conducted in affiliation by researchers from Kao Corporation and RIKEN, was published on 5 March 2024, in Volume 14 of *Scientific Reports*.

Elaborating on the motivation behind this study, Bianca Wiedemann, a full-time researcher of human health care products at Kao Corporation, Japan, says, "*We have been working towards repellent technologies for preventing the spread of mosquito-borne diseases, and in doing so, we aim to protect the lives of our future generations, particularly children. In fact, this research is part of our "GUARD OUR FUTURE" project. Through this initiative, we have launched the innovative "Bioré GUARD Mos Block Serum" for blocking mosquito bites in Thailand, and will expand it to Singapore, Taiwan, Hong Kong, and Malaysia this year.*"

Interestingly, the results of this study revealed that, when used as a mixture with a topical repellent, L-PDMS improves the adhesive properties of the topical mosquito repellent, helping it to stick for a longer time on mosquitoes' legs and reduce bites. L-PDMS was also

found to compromise mosquitoes' visual object tracking ability and induce aversive learning to the simultaneously applied odorant. These results suggest that silicone oil not only inhibits mosquito landing on human skin, but also exerts multifaceted effects by enhancing its effectiveness when used in combination with the topical repellents and by modulating mosquito behavior in a sustained manner.

The study was led by a team of researchers, including Bianca Wiedemann, Kohei Takeuchi, Aya Kato-Namba, Masayuki Yabuki, and Takao Nakagawa at Kao Corporation, and Kazumi Ohta and Hokto Kazama at RIKEN. Notably, the team had earlier identified that several hydrophobic solutions like L-PDMS are capable of preventing mosquito bites by efficiently wetting even the hydrophobic scales of mosquito legs. In turn, this wetting generates a capillary force, restraining mosquitoes every time they try to bite and escape a human. Since mosquitoes require energy to escape this force, applying L-PDMS on skin keeps them at bay, preventing them from biting the human skin.

In the current study, three innovative experimental paradigms were employed to understand and identify the mechanisms by which L-PDMS operates. Using an "arm-in-cage" experimental setup, human volunteers were asked to place their arms inside a cage filled with female *Aedes albopictus* mosquitoes. Researchers then compared the number of mosquito bites in two scenarios — one, where the arm was covered with both a mosquito repellent and L-PDMS, and the other, where the arm was covered with repellent alone.

"*When combined with topical repellents and administered to human skin, L-PDMS amplified the efficacy of the repellent by effectively transferring it to mosquito legs upon contact, thereby reducing mosquito bites,*" explains Wiedemann.

To examine the effects of L-PDMS on mosquitoes, the researchers employed a virtual flight arena, where individual tethered mosquitoes behaved based on visual and olfactory inputs. The virtual arena was fitted with an LED screen, a high-resolution camera, and microphones to capture all variations in behavior. "*We established a virtual space for mosquitoes to detect even small behavioral changes in response to sensory stimulation. As a result, we found sustained behavioral changes induced by silicone oil*," notes Kazama.

In one variation of the experiment, the researchers measured the mosquito's orientation relative to a virtual object that appeared on the screen in the virtual arena. They observed that the mosquitoes' ability to track the object on the screen was notably reduced when their legs were wetted with L-PDMS.

In another experiment, the researchers applied a mixture of citronella oil (a widely used topical repellent) on mosquitoes' legs along with L-PDMS over several minutes. Once the mosquitoes learned to associate the odor of citronella oil with L-PDMS, they were placed in the virtual arena, and their flight paths in response to the odor of citronella oil were measured. The researchers discovered that when mosquitoes were pre-exposed to a combination of citronella oil and L-PDMS, their aversion to citronella oil increased.

"*Since L-PDMS confers an aversive meaning to a simultaneously presented odor, the mere presence of this conditioned odor may be enough to protect the local environment from*

mosquitoes following learning. In theory, the conditioned odor can be any odor, including those that are safe and perceptually pleasant for humans," suggests Kato-Namba.

Therefore, repellents containing L-PDMS can have a longer-lasting effect compared to most other repellents. Not only is L-PDMS more persistent in wetting mosquitoes and reducing their ability to track visual objects, but it can also create a learned aversion in mosquitoes towards the smell. Mosquitoes exposed to L-PDMS can form associative memories, causing them to avoid the odor of citronella oil more strongly after contact with the mixture.

In summary, these findings open up several unique and interesting possibilities for leveraging mosquito behavior for the development of more effective repellent products in the future. Not only are the implications of this study far-reaching, but they also offer hope for new strategies to combat mosquito-borne diseases and reduce the burden on healthcare systems worldwide.

Reference

Title of original paper:	Hydrophobic solution functions as a multifaceted mosquito repellent by enhancing chemical transfer, altering object tracking, and forming aversive memory
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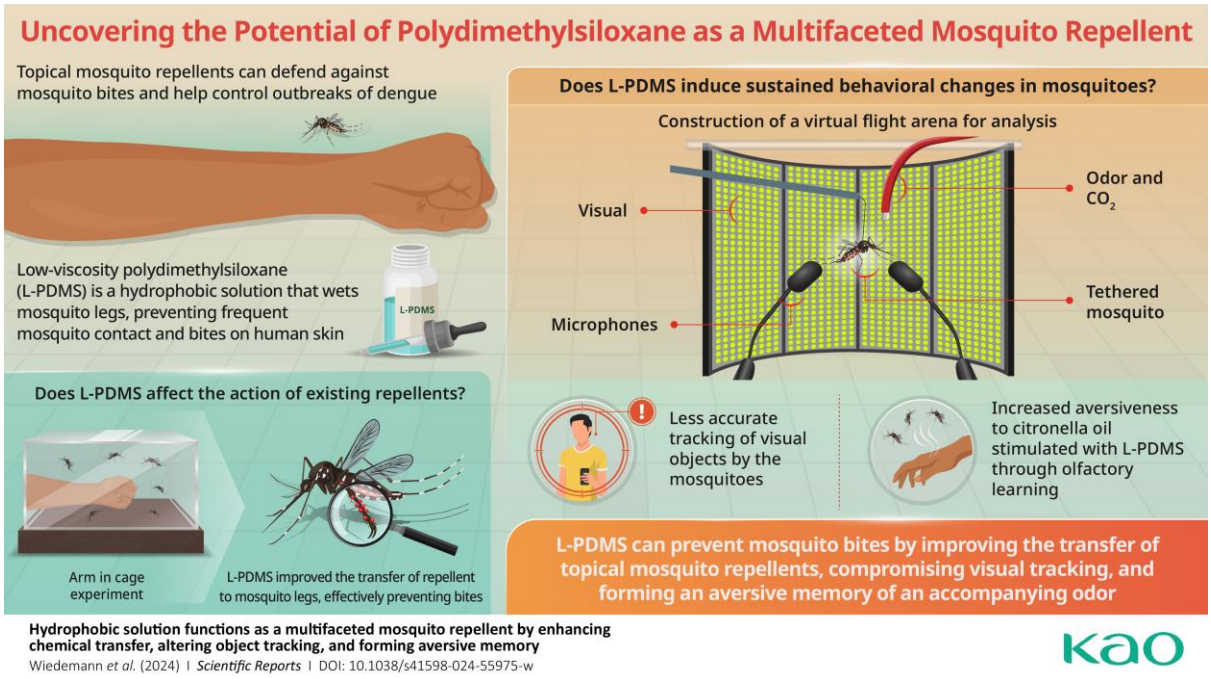

Image Title: Low viscosity polydimethylsiloxane (L-PDMS) can greatly improve the efficacy of widely used topical mosquito repellents

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life of all people and the planet. Through its portfolio of over 20 leading brands such as *Attack, Bioré, Goldwell, Jergens, John Frieda, Kanebo, Laurier, Merries, and Molton Brown*, Kao is part of the everyday lives of people in Asia, Oceania, North America, and Europe. Combined with its chemical business, which contributes to a wide range of industries, Kao generates about 1,530 billion yen in annual sales. Kao employs about 34,300 people worldwide and has 137 years of history in innovation. Please visit the Kao Group website for updated information.

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