Researchers develop new method to synthesize antimalarial drug

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SwRI Senior Research Scientist Dr. Shawn Blumberg and UTSA Professor Dr. Doug Frantz have developed a method to synthesize highly potent derivatives of the antimalarial drug artemisinin, which could lead to a more cost-effective treatment for deadly disease. Credit: The University of Texas at San Antonio

Southwest Research Institute (SwRI) and The University of Texas at San

Antonio (UTSA) have developed a method to synthesize the highly potent antimalarial drug artemisinin, which could lead to a more cost-effective treatment for malaria.

The work was recently featured on the cover of the journal *Organic Letters*.

In 2021, 247 million cases of malaria led to 619,000 deaths worldwide. The most effective malaria treatments utilize the drug artemisinin, which is derived from the sweet wormwood plant, Artemisia annua. However, the process of isolating artemisinin from the plant is time-consuming, and crop yields are susceptible to weather patterns, insect pests and other factors. Despite scientific advancements in treatment methods, the cost of artemisinin still burdens the countries most affected by malaria.

"We were able to develop a novel way of synthesizing artemisinin that mimics how it's made in nature," SwRI Senior Research Scientist Dr. Shawn Blumberg said. "Our method mimics the biosynthetic pathway of how artemisinin is made in the plant where it originates, Artemisia annua. We studied the intermediate compounds along that pathway and then used chemistry to create those same intermediates and recreate the pathway."

"There was nothing in public scientific literature that suggested this would work," Frantz said. "This was challenging chemistry that we were trying to pull off, but we let science tell us where to go. It enabled us to design a process of taking a common intermediate in the biosynthetic pathway for artemisinin and converting it all the way to Artemisinic acid, which is the direct precursor to artemisinin."

Blumberg and Frantz hope drug companies will take advantage of their work and offer a more potent and cost-effective malaria treatment to the impoverished countries that need it the most, especially considering the

inherent risks of drought, wildfire and insects that come with depending on a plant that can only grow in certain parts of the world.

"The supply of artemisinin is still kind of erratic, which causes prices to be erratic as well, and countries dealing with this endemic need a stable, cost-effective solution," Blumberg said. "While the new process we've created might not completely supplant current methods, it can complement other approaches and help to stabilize the world's supply of artemisinin."

More information: Nicholas A. Clanton et al, Site-Selective Functionalization of Unactivated Allylic C–H Bonds via Direct Deprotonation with KTMP: Application to the Formal Total Synthesis of (+)-Artemisinin from Amorphadiene, *Organic Letters* (2023). DOI: 10.1021/acs.orglett.2c04145

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