Researchers synthesize antimalaria molecules found in a fungus from Nunavut

June 5 2019

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The solution to the problem of increasing drug resistance among malaria-causing parasites could come from the North, according to a study published in *Chemical Communications* by researchers from Université

Laval and the CHU de Québec Research Centre. The team successfully synthesized molecules discovered in a microscopic fungus from Nunavut and demonstrated their *in vitro* efficacy against the parasite responsible for malaria.

The researchers observed that molecules from a microscopic fungus discovered in 2017 in sediments from Frobisher Bay, Nunavut, showed structural similarities with known antimalarial compounds. However, only very small amounts of these molecules, called mortiamides, were present in the fungi. "To study the efficacy of these molecules against malaria we needed more, and the only way to get more was to synthesize them," explained Normand Voyer, head of the study and professor of chemistry at Université Laval's Faculty of Science and Engineering. We were able to obtain sufficient amounts of mortiamides thanks to a new approach developed in our laboratory."

Once that step was completed, Dr. Voyer asked malaria expert Dave Richard, professor at Université Laval's Faculty of Medicine, to evaluate the activity of mortiamides against Plasmodium falciparum, the parasite responsible for about 50% of all malaria cases. "Our premise was that the parasite could not be resistant to these northern molecules because it had never been exposed to them," said Professor Voyer. Tests using a common strain of the parasite and a multi-drug resistant strain proved the researchers right: in less than 72 hours, three of the four mortiamides stopped the growth of both parasite strains.

"The antimalarial efficacy of these molecules is moderate for now, but our results suggest it is possible to create analogues that, at lower doses, would be more effective against the parasite," Professor Voyer maintained. "In addition, since we can now synthesize these molecules, it will be easier to determine their mode of action. Once we know why they are toxic to the parasite, we can develop better-targeted drugs."

More information: Christopher Bérubé et al, Total synthesis and antimalarial activity of mortiamides A–D, *Chemical Communications* (2019). DOI: 10.1039/C9CC02864A

Provided by Laval University