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Promising malaria drug to undergo clinical trials

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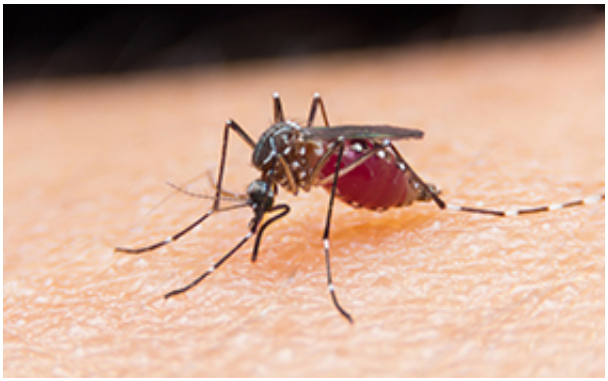

Parasites that infect mosquitoes cause malaria, which has plagued people for millennia. Credit: PlotPhoto

Malaria killed about 440,000 people – mostly young children – last year, but a new drug candidate discovered at Rutgers may help fight the long-dreaded disease.

The compound, which literally blows up malaria parasites in the blood stream, is about to undergo clinical trials, said Spencer Knapp, a chemistry professor in the Department of Chemistry and Chemical Biology at Rutgers University-New Brunswick.

"That's actually a very exciting development," said Knapp, who has been at Rutgers for 38 years and works in the School of Arts and Sciences. "The drugs that are out there are starting to encounter resistance, so this is a new drug candidate just now entering trials. We don't know how

effective it will be yet in humans."

The compound, code-named SJ733, works in a novel way, said Knapp, who first prepared the chemical in his lab. It binds to a malaria parasite protein that serves as a sodium (salt) pump. The pump is designed to get rid of sodium, but the compound blocks or interferes with the protein, and sodium ions build up. That allows water to rush in, blowing up the parasite inside human blood cells.

"It's really quite interesting," he said, noting that Rutgers is co-holder (with St. Jude Children's Research Hospital in Memphis, Tennessee, and Medicines for Malaria Venture in Geneva) of a U.S. patent that is pending.

Malaria, a mosquito-borne disease, can make people very sick. Fever, chills and flu-like illness are common symptoms, according to the U.S. Centers for Disease Control and Prevention. More severe cases of malaria can lead to seizures, coma, severe anemia, acute respiratory distress, kidney failure and other problems.

The United States was deemed malaria-free in 1949, according to the CDC.

But last year, an estimated 214 million people worldwide contracted malaria, according to the World Health Organization. The scourge is particularly lethal to children under five, who accounted for 70 percent of the roughly 440,000 deaths.
Africa is essentially ground-zero for malaria. Last year, 88 percent of malaria cases and 90 percent of deaths linked to the disease were there, according to WHO.

Still, malaria cases and deaths have dropped a lot in recent years. Between 2000 and 2015, new malaria cases fell by 37 percent globally

and 42 percent in Africa, according to WHO. Malaria death rates plunged by 60 percent globally and 66 percent in Africa.

Three key reasons are greater use of insecticide-treated mosquito nets, indoor spraying and artemisinin-based combination therapies. The latter medicines are very effective against P. falciparum, the deadliest and most common malaria parasite.

According to Knapp, the National Institutes of Health awarded $1.5 million to Rutgers over five years as part of a collaborative effort to fight malaria. Aside from Knapp, the lead scientists include: James Duffy of the Medicines for Malaria Venture (MMV) in Geneva, Switzerland; R. Kiplin Guy at St. Jude Children's Research Hospital; and David M. Floyd of MMV and a Rutgers consultant.

St. Jude, MMV and Eisai Inc. have been working to deliver the preclinical studies and clinical trials through phase 2, according to Knapp, with funding from the Global Health Innovation Technology Fund.

Large amounts of SJ733 – 4 kilograms, or 8.8 pounds – were synthesized by contract for the clinical trials, he said.

The compound has been tested successfully in preclinical safety studies, with no side effects detected so far. "There are plenty of compounds that don't make it through animal studies, but ours has made it through," Knapp said.

The clinical trials could last as long as two years, he said. During phase 1, SJ733 – in the form of pills – will be given to healthy volunteers to assess the safety and pharmacokinetics of the compound. Pharmacokinetics refers to how drugs are absorbed, distributed, metabolized and eliminated by the body, according to the National

Institutes of Health.

Then SJ733 would be tested in two phases of human malaria studies to find out if it works and if it's safe.

"The thing about malaria is that really, really poor people have it, so the medicine has to be very inexpensive," Knapp said. "We think that ours is going to be inexpensive."

Provided by Rutgers University