Researchers identify and shut down makers of fake anti-malarial medications

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Facundo Fernandez, an assistant professor in Georgia Tech's School of Chemistry and Biochemistry, was part of an international effort to halt the production of counterfeit anti-malarial drugs. Georgia Tech Photo: Gary Meek

Georgia Institute of Technology researchers were part of a three-continent, multi-organizational effort known as "Operation Jupiter" that successfully identified and shut down manufacturers who were flooding Southeast Asia with counterfeit – and ineffective – anti-malarial drugs.

With 11 different organizations, including the Centers for Disease

Control and Prevention (CDC), the World Health Organization (WHO), the Wellcome Trust – and ultimately the international law enforcement agency INTERPOL – the global effort provided Chinese officials with enough information to shut down the drug makers.

Beyond the human health cost of failing to effectively treat hundreds of thousands of malaria cases, the fake drugs could be fueling development of malarial strains that may become resistant to the most sophisticated drug now available to treat the disease: artesunate. That's because counterfeiters sometimes include small quantities of the real drug in their fakes, possibly as part of an effort to fool simple quality tests. By not killing the malaria parasites, the small amount could facilitate development of drug resistance.

As their part of the investigation, Georgia Tech researchers used sensitive mass spectrometry techniques to analyze nearly 400 drug samples provided by public health authorities. They also developed methods to speed up analysis, including an ionization process that reduced the time required to test a drug sample from half an hour to just a few seconds.

Activities aimed at addressing the widespread problem of counterfeit anti-malarial drugs were reported February 12th in the journal PLoS Medicine. Georgia Tech's efforts to develop faster analytical techniques were sponsored by the U.S. National Science Foundation, while the sample analysis was supported by a small grant from WPRO/WHO.

Malaria kills more than a million people each year worldwide, and is a risk for about 40 percent of the world's population. Most victims would survive – if they had access to the proper drugs.

"About 50 percent of the samples obtained from the field in Southeast Asia were fakes," said Facundo Fernandez, an analytical chemist and

assistant professor in Georgia Tech's School of Chemistry and Biochemistry. "They look very real, even down to the hologram in the packaging. It's very difficult to tell which ones are the fakes and which ones are real."

When Fernandez began analysis of the drug samples, he assumed that they would not include any real active ingredients. But his graduate students Christina Hampton and Leonard Nyadong soon discovered that the counterfeiters were making their fake anti-malarials with a broad range of mostly expired pharmaceuticals.

"We found old and ineffective anti-malarials like chloroquine," he said. "We found antibiotics like erythromycin. We found all sorts of drugs that basically have no effect on resistant malaria parasites. Acetaminophen was one of the most common chemicals we found."

Fernandez speculates that the makers chose certain compounds, like acetaminophen, because they could temporarily make patients feel better by lowering the fever associated with malaria.

Mass spectrometry provides a very effective means of identifying samples by determining their accurate molecular weight. But the conventional analysis can be time-consuming – especially in the preparation of samples.

Fernandez and his Georgia Tech group developed a faster method that allows them to analyze hundreds of samples in a single day. Their goal was to make mass spectrometry analyses responsive within the time constraints that surveys in developing countries and law enforcement agencies involved in anti-counterfeiting tasks require.

"These are methods that let you analyze a solid sample without any significant preparation," he explained. "You can take a tablet, put it in

front of the instrument with an ionization source, and you get a quick snapshot of what's in the sample. It provides a very high throughput pipeline to identify samples quickly."

Ultimately, Fernandez hopes to help develop high-accuracy instrumental tests that could be used in the field to save the time and expense of shipping suspected fakes to labs.

Beyond the mass spectrometry, the effort also relied on analysis of pollen found in the drugs – a discipline known as forensic palynology – which was done by scientists in New Zealand who were part of Operation Jupiter. A study of calcium carbonate isotopes in the compounds, together with the pollen and active ingredients in the samples, pointed to two main groups of samples originating in different geographic regions of Asia.

"This is absolutely CSI – the techniques they use on the television program really do work in real life," Fernandez said.

The team provided enough information that Chinese authorities were able to shut down the manufacturers, which were sophisticated operations able to accurately mimic the packaging and holographic seals of legitimate pharmaceutical companies.

Fernandez and his students remain involved in anti-counterfeiting activities and hope to obtain additional funding to continue supporting the efforts. They are now investigating fake anti-malarials sold in Africa, analyzing assortments of drugs sold in markets there, and studying other faked drugs, such as tamiflu.

Fernandez got involved in the project in 2003 because of a chance encounter with Michael Green, a parasitic disease specialist at the CDC. He soon began working with Green and with Paul Newton, a physician

from the University of Oxford in the United Kingdom who is based in Laos.

Large pharmaceutical companies can afford to pursue counterfeiting themselves, Fernandez noted, but in many cases, drugs sold for use in developing nations come from small companies that cannot afford private investigators and law firms to go after the counterfeiters.

“The problem is not over,” he cautioned. “There are more fakes and more fake producers. But at least this is a beginning. Having an opportunity to do some good in this area is very satisfying.”

Source: Georgia Institute of Technology