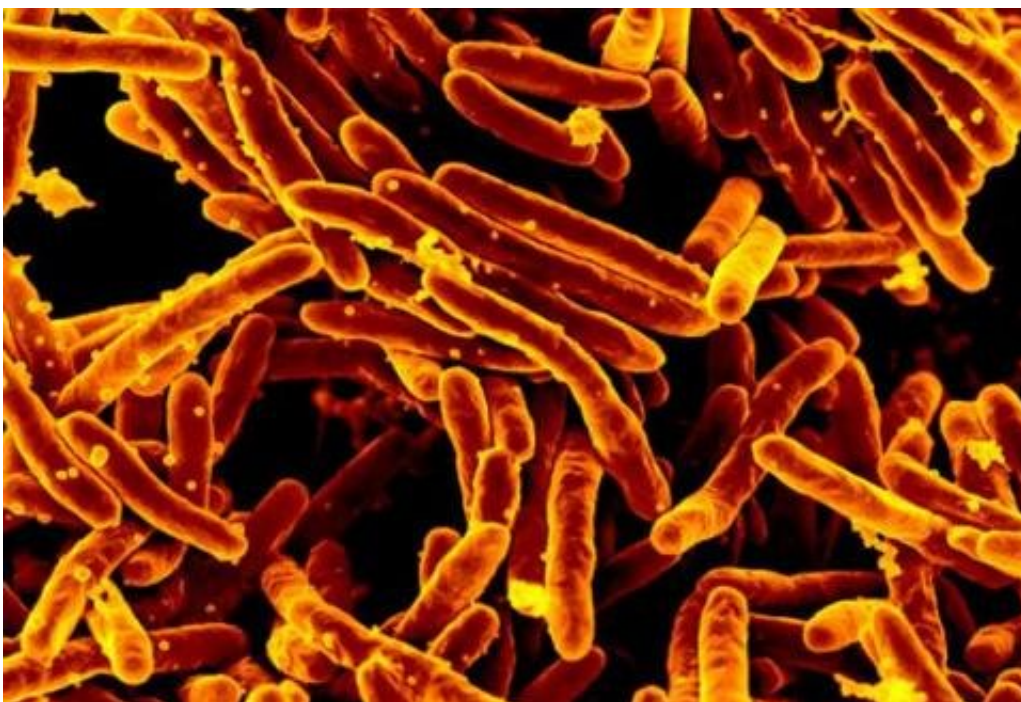


# A new antibiotic could be a better, faster treatment for tuberculosis

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Scanning electron micrograph of *Mycobacterium tuberculosis* bacteria, which cause tuberculosis. Credit: NIAID

Tuberculosis is a sneaky disease. The bacteria hide from antibiotics inside the very immune cells that are supposed to kill them, making treatment long and difficult. But in the November issue of *ACS Infectious Diseases*, UConn chemists report a new antibiotic that can find and kill tuberculosis bacteria where they hide.

Tuberculosis is the number one cause of death from infectious disease worldwide. About 25 percent of people on the planet are currently infected. Most of those infections will stay dormant, but one in 10 will become active, infectious, and often fatal if untreated.

Tuberculosis is caused by a bacteria called *Mycobacterium tuberculosis*. Because of *Mycobacterium*'s unique lifestyle, in which they allow themselves to be eaten by macrophage [immune cells](#) and then grow inside of them, they are very hard to treat. People infected with tuberculosis must typically take a cocktail of antibiotics diligently over many months, because the bacteria are only susceptible to the drugs when they break out of the macrophage in which they were born and search out a new one to invade.

UConn chemist Alfredo Angeles-Boza and his then-graduate student, Daben Libardo, and colleagues from the Indian Institute of Science, the Max Planck Institute, and MIT, decided to make an antibiotic that could make its way into the macrophages and hit the Mycobacteria where they hide. Angeles-Boza and Libardo had previously worked with antibiotics produced by fish, sea squirts, and other sea creatures. Many of these sea creatures make antibiotic [peptides](#) - small pieces of protein-like material - with a special chemical talent: when they bind to copper atoms, they enable the copper to shift its electrical charge from +2 to +3 and back. Copper with this ability becomes aggressive, ripping electrons away from some molecules and adding them to others, particularly oxygen-containing molecules. The oxygen-containing molecules become free radicals, dangerous chemicals that attack anything they encounter, including Mycobacteria.

Human macrophages infected with Mycobacteria also use copper to attack the bacteria, but they do so in a less sophisticated way. They trap the bacteria in a bubble and then inject copper +1 ions—that is, plain copper atoms with a plus one charge (Cu+) - into the bubble. But

the Mycobacteria can handle that. To them, the bubble is a safe haven, and the  $\text{Cu}^+$  ions are mere annoyances. The bacteria can steal an extra electron from the  $\text{Cu}^+$  to make it  $\text{Cu}^{2+}$ . The copper becomes unreactive and safe that way. And when enough  $\text{Cu}^{2+}$  surrounds the Mycobacteria, other, more dangerous kinds of copper can't get close.

Surrounded by defanged copper, "the bacteria can grow in peace. It's elegant!" says Angeles-Boza. But if Angeles-Boza and Libardo have their way, the copper camouflage will become *Mycobacteria's* downfall. If the antibiotic peptides can get close to the bacteria, they can grab onto one of the [copper](#) ions and weaponize it. The trick is getting the peptide close to the bacteria.

To do that, the chemists put the peptides into little bubbles similar to the kind cells use to move around packets of protein ingredients and other tasty stuff. When the [bacteria](#) snags one for a snack, the peptide works its chemistry and kills it.

The antibiotic peptide developed by Libardo and Angeles Boza effectively kills Mycobacteria living in macrophages in the lab, but they haven't been able to cure [tuberculosis](#) in mice yet—peptide drugs have various problems that make them tricky to use in mammals. The next step in the research is to use the same chemistry in smaller molecules that can be taken as pills like more typical [antibiotics](#).

**More information:** M. Daben J. Libardo et al, Phagosomal Copper-Promoted Oxidative Attack on Intracellular Mycobacterium tuberculosis, *ACS Infectious Diseases* (2018). [DOI: 10.1021/acsinfecdis.8b00171](#)

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