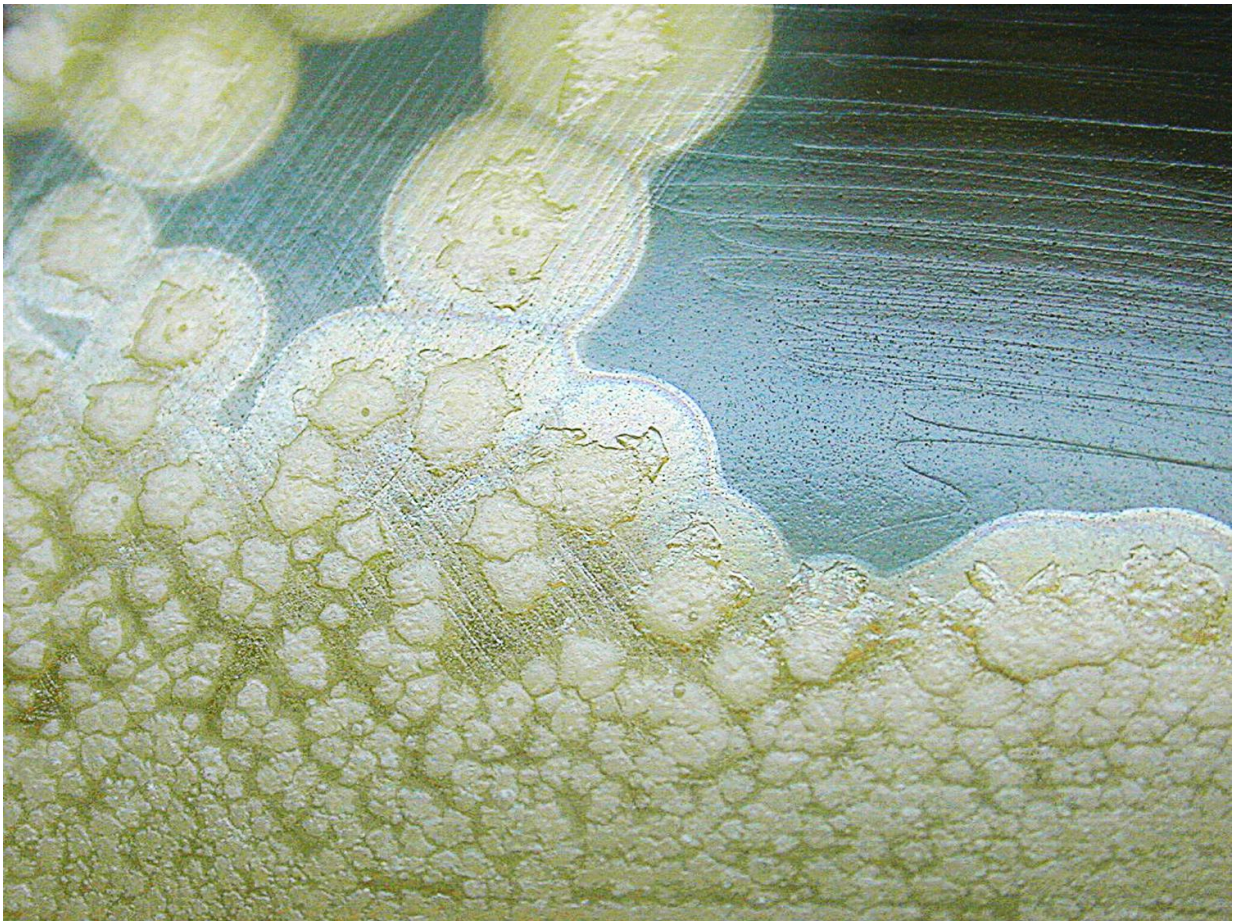


Researchers discover potential antidote to botulism

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The *Clostridium botulinum* bacterium (shown here in colonies) can cause foodborne illnesses and potentially deadly effects due to the neurotoxin it produces. Credit: CDC

Researchers have identified a compound that strongly inhibits botulinum neurotoxin, the most toxic compound known. That inhibiting compound, nitrophenyl psoralen (NPP), could be used as a treatment to reduce paralysis induced by botulism. Botulinum neurotoxin is considered a potential bioweapon because there is no FDA-approved antidote. The research is published in *Applied and Environmental Microbiology*, a journal of the American Society for Microbiology.

In the study, the investigators' first step was to identify the enzyme within [botulinum neurotoxin](#) that damages neurons, causing paralysis. They then screened a library containing more than 300 natural compounds from extracts of Indian medicinal plants, searching for enzymes that could neutralize the neuron-damaging activity.

"Using high throughput screening, we identified one of the compounds, nitrophenyl psoralen, as having particularly strong activity against the neuron-damaging enzyme," said corresponding author Bal Ram Singh, Ph.D., Professor and Director, Botulinum Research Center, Institute of Advanced Sciences, Dartmouth, MA.

The investigators then tested NPP's activity in vitro and in cell culture against [botulinum neurotoxin](#) type A, which is the most potent serotype among the seven serotypes of botulinum toxin. NPP type A had powerful anti-[botulinum toxin](#) activity, with low toxicity to human cells. (image: molecular model of botulinum neurotoxin)

"NPP also showed activity to reverse the mouse muscle paralysis induced by botulinum neurotoxin type A," said Dr. Singh.

Although fewer than 200 botulism cases occur worldwide, annually, "these cost more to treat than the millions of salmonella outbreaks that occur, making botulism the most expensive form of food poisoning," said Dr. Singh. Botulinum toxin is produced by *Clostridium botulinum*, a

soil bacterium that is ubiquitous, and hard to kill. The spores can survive being boiled.

Botulism can be acquired through routes other than food poisoning, such as through wound contamination, and via colonization of the digestive tracts of children and infants.

Psoralen derived drugs are already approved by the FDA in the United States. That would likely hasten the drug approval process for NPP, said Dr. Singh.

The research originated from Dr. Singh's group's work on biochemical basis of Ayurveda, an herbal medicine system widely used in India. Natural products, such as those used in Ayurveda, have more diversified structures, lower toxicity, and better drug-like properties than synthetics. As Founding Director with the Center for Indic Studies at UMass Dartmouth, he considered natural herbal [compounds](#) as source of countermeasures against botulism. This led to discussions, and then to a collaboration on this work with Professor Virinder Parmar, head of the Chemistry Department at the University of Delhi.

Provided by American Society for Microbiology

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