

A poisonous cure

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A team of Michigan State University scientists has discovered an enzyme that is the key to the lethal potency of poisonous mushrooms. Credit: G.L. Kohuth

Take two poisonous mushrooms, and call me in the morning. While no doctor would ever write this prescription, toxic fungi may hold the secrets to tackling deadly diseases.

A team of Michigan State University scientists has discovered an enzyme that is the key to the lethal potency of poisonous mushrooms. The results, published in the current issue of the journal *Chemistry and*

Biology, reveal the enzyme's ability to create the mushroom's molecules that harbor missile-like proficiency in attacking and annihilating a single vulnerable target in the human liver.

The team revealed how the enzyme contributes to the manufacture of chemical compounds known as [cyclic peptides](#), a favorite type of molecule that pharmaceutical companies use to create new drugs. These findings could lead to single-minded medicines with zero side effects, said Jonathan Walton, professor of plant biology and co-lead author.

"Mushrooms are prolific chemical factories, yet only a few of their peptides are poisonous," he said. "These toxins survive the high temperatures of cooking and the acids of digestion, and yet they're readily absorbed by the bloodstream and go directly to their intended target. These are the exact qualities needed for an effective medicine."

Walton published the paper with fellow MSU scientists Hong Luo, Sung-Yong Hong, R. Michael Sgambelluri and Evan Angelos. Working with the mushroom species *Amanita*, Walton and his teammates disassembled one of its poisonous peptides, which can be compared to a laser-guided missile with a nuclear warhead.

By removing the molecular equivalent of the deadly warhead, they now have a sturdy, precise delivery system that can supply medicine - rather than poison - to a single target. By taking a laser, rather than a shotgun approach, scientists could develop medicines capable of curing disease without the patient suffering any side effects.

The enzyme the team discovered is called POPB, and it converts toxins from their initial linear shape into cyclic peptides, fortress-like molecular circles comprising eight amino acids.

Harnessing the distinct properties of POPB will allow scientist to create

billions of variant molecules, which can be tested against many different medical targets such as pathogenic bacteria and cancer.

"We've found some variables that are key," said Walton, an AgBioResearch scientist. "By making more variants, we can add or replace molecules that may or may not work. To date we've created a library of a hundred or so, and we eventually plan to create millions."

The challenge of the next stage of research, though, is testing the variants against diseases such as cancer. The bottleneck lies in the screening process. While Walton's team has discovered a missile capable of carrying a million different potential medicines, as of yet the payload that will be effective remains a mystery.

Provided by Michigan State University

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