

Effective Imitation: New chitinase inhibitors

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(PhysOrg.com) -- The chitin-degrading enzymes known as chitinases are not just important to insects with chitin shells and to their predators, they also seem to be involved in the establishment of parasites in the human body and in asthmatic diseases. An international team led by Stephen G. Withers has now developed a novel chitinase inhibitor. As the researchers report in the journal *Angewandte Chemie*, the compound imitates the structure of an intermediate formed in the enzymatic degradation of chitin.

Insects, spiders, scorpions, crabs -- many animals have a shell made of chitin. In addition, chitin is found in the cell walls of fungi, dust mites, and various parasites. Chitin is regularly built up and degraded at certain phases in the life cycles of these organisms. Chitin molecules are long chains of nitrogen-containing sugar components, whose degradation is carried out by enzymes in a family known as chitinases.

“Chitinase [inhibitors](#) are potential [insecticides](#) and [fungicides](#),” explains Withers. “They are also interesting as pharmaceuticals. They could stop the transmission of the [malaria parasite](#) to humans and help to fight trichomoniasis infections.” Furthermore, there seems to be a connection between asthma and an elevated level of chitinase-like enzymes in the lungs. Chitinase inhibitors may thus have potential for use in asthma treatment.

The team of scientists from the University of British Columbia (Vancouver, Canada), the University of York (UK), and the State University of New Jersey (USA) has now developed a new group of

chitinase inhibitors that are more effective than previous inhibitors. Their synthetic route is relatively simple and is designed to be used on a larger scale as well.

The core structural element is a ring-shaped sugar building block fused with a thiazoline, a five-membered ring made from one nitrogen, one sulfur, and three carbon atoms. “This arrangement imitates a cyclic intermediate formed in the enzymatic degradation of chitin, and docks to the binding sites on chitinase enzymes,” explains Withers. “To augment the inhibitory effect, we added two or three additional sugar units that resemble those in chitin (chitobiose or chitotriose). Further modifications ensure that the inhibitors themselves cannot be degraded, so they remain effective for a long time.” The inhibitors could be a good starting point for the development of novel medications and further research into the role of chitinases in biological systems.

More information: Stephen G. Withers, Chitinase Inhibition by Chitobiose and Chitotriose Thiazolines, *Angewandte Chemie International Edition*, Permalink: [dx.doi.org/10.1002/anie.200906644](https://doi.org/10.1002/anie.200906644)

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