

Unusual sugar from cyanobacteria acts as natural herbicide

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Cyanobacteria in the lab: The new active ingredient was isolated from cultures of the freshwater cyanobacterium Synechococcus elongatus. Credit: Klaus Brilisauer

Researchers at the University of Tübingen have discovered a natural substance that could compete with the controversial herbicide glyphosate: a newly discovered sugar molecule synthesized from

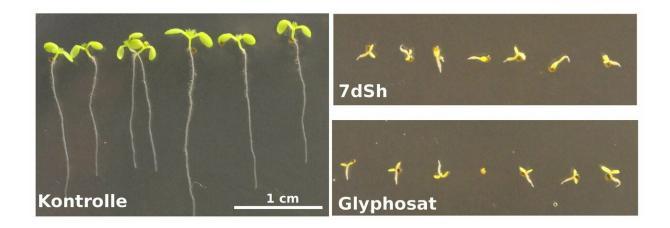


cyanobacteria that inhibits the growth of various microorganisms and plants but is harmless to humans and animals. The joint study was led by Dr. Klaus Brilisauer, Professor Stephanie Grond (Institute of Organic Chemistry) and Professor Karl Forchhammer (Interfaculty Institute of Microbiology and Infection Medicine). It was published in the journal *Nature Communications* on Friday.

Active ingredients for pharmaceutical or agricultural use often originate from natural substances. These substances can consist of complex chemical structures, but can also be relatively simple. The ingenuity of such <u>active ingredients</u> often lies in their simplicity: Antimetabolites interact with vital processes in the cell by mimicking metabolic products. This disrupts the biological process, which can inhibit <u>cell growth</u> or even kill the cell.

Chemists and microbiologists at the University of Tübingen discovered an unusual antimetabolite with a simple chemical structure: a <u>sugar</u> <u>molecule</u> with the scientific name 7-deoxy-sedoheptulose (7dSh). Unlike ordinary carbohydrates, which usually serve as an energy source for growth, this substance inhibits the growth of plants and microorganisms, such as bacteria and yeasts. The sugar molecule blocks a key enzyme of the shikimate pathway, a metabolic pathway that occurs only in microorganisms and plants. For this reason, the scientists classify the substance as harmless for humans and animals, and have already demonstrated this in initial studies.





Arabidopsis thaliana seedlings after germination and 7-day growth: While the control group (left) developed normally, growth was inhibited by 260 μ M glyphosate (figure below) or 7dSh (fig-ure above). (scaling identical in all images) Image: Klaus Brilisauer

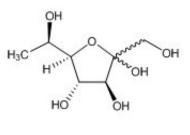
The rare deoxy sugar was isolated from cultures of the freshwater cyanobacterium Synechococcus elongatus, which is able to inhibit the growth of related bacterial strains. While searching for the cause of this growth inhibition, scientists deciphered the structure of the natural compound. Through a newly developed method for the production of 7dSh – a chemoenzymatic synthesis – the scientists were able to conduct extensive studies to determine the molecular mechanism of 7dSh.

The scientists used coupled high-resolution mass spectrometry to obtain precise insights into the inhibition mechanism and discovered that 7dSh blocks Dehydroquinatesynthase (DHQS), an enzyme of the shikimate pathway. One of the best-known inhibitors of this metabolic pathway to date is the controversial herbicide glyphosate. "In contrast to glyphosate, the newly discovered deoxy sugar is an entirely natural product that is believed to have good degradability and low ecotoxicity," says Dr. Klaus Brilisauer. So far, 7dSh inhibits plant growth promisingly. "We see an



excellent opportunity here to use it as a natural herbicide."

Scientists hope to replace controversial herbicides in the <u>long term</u> and thus reduce herbicide metabolites, which pose a health risk. However, effectiveness in the field, degradability in the soil and harmlessness to livestock and humans would have to be further investigated in comprehensive long-term studies for 7dSh.



7-desoxy-Sedoheptulose

Chemical structure of 7dSh. Credit: Klaus Brilisauer

More information: Klaus Brilisauer et al. Cyanobacterial antimetabolite 7-deoxy-sedoheptulose blocks the shikimate pathway to inhibit the growth of prototrophic organisms, *Nature Communications* (2019). DOI: 10.1038/s41467-019-08476-8

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