

Healing plants inspire new compounds for psychiatric drugs

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Treatments used by traditional healers in Nigeria have inspired scientists at Northwestern University to synthesize four new chemical compounds that could one day lead to better therapies for people with psychiatric disorders.

In a paper published online in the journal *Angewandte Chemie International Edition*, the scientists detail how they created these [natural compounds](#) by completing the first total syntheses of two indole alkaloids—alstonine and serpentine. These alkaloids, found in various plant species used by healers in Nigeria to treat people with conditions such as schizophrenia and [bipolar disorder](#), have antipsychotic properties that have potential to improve mental disorder treatments.

The current drugs used for schizophrenia effectively treat delusions and hallucinations but are only partially effective for cognitive impairment. Early experimental research of these new compounds in animal models shows promise in improving cognitive impairment, the Northwestern scientists said.

"After billions of years of evolution, nature has given us a great starting point for generating new types of molecules that could end up being used as innovative drugs," said Karl Scheidt, lead author of the paper. "We've learned how to make these natural products in the lab and can now evaluate what are the most effective parts of these natural products for potential therapies."

Scheidt is a professor of chemistry at Northwestern University's Weinberg College of Arts and Sciences and professor of pharmacology at Northwestern University Feinberg School of Medicine. He collaborated on this study with Dr. Herbert Meltzer, professor in psychiatry and behavioral sciences, pharmacology and physiology at Feinberg. They are both members of Northwestern's Chemistry of Life Processes Institute (CLP), which helps foster collaboration between schools and lowers the barriers to scientific discovery.

Meltzer, who has spent much of his career researching drug therapies now in use for schizophrenia and bipolar disorder, approached Scheidt about the possibility of creating these compounds. Meltzer's longtime research goal is to improve treatment outcomes and develop knowledge of brain mechanisms in [mental disorders](#). Scheidt's expertise is in designing novel methods and strategies for the construction of complex natural products with important biological attributes.

"The synthesis of these alkaloids, which we have now just achieved, was exceedingly difficult," said Meltzer, second author of the paper and an attending physician at Northwestern Memorial Hospital. "Karl Scheidt's expertise in the synthesis of natural products was crucial to the success of this project and is the first step in getting a new drug ready for clinical trials."

Traditional healers boil these special plants and produce an extract that they administer to people with symptoms of mental illness. However, this extract isn't pure, and it contains other compounds and materials that may not be beneficial to people with mental disorders.

"Nature did not intend this plant to produce an antipsychotic drug on its own," Meltzer said.

The collaborative work to create the compounds took place in the Center

for Molecular Innovation and Drug Discovery (CMIDD) at Northwestern, using high-level purification resources and state-of-the-art research instrumentation and equipment. Scheidt is the director of CMIDD.

Through an efficient and stereo-selective synthesis, Scheidt and his team created four separate but related [natural products](#). Now a template exists to continue making these compounds as needed for future studies and ultimately for use in clinical drug trials.

"We can make multi-gram quantities of any of the compounds we want," Scheidt said. "We built the assembly line and are now uniquely positioned to explore their potential."

Meltzer is already using these compounds in animal studies in his lab to better understand how they affect brain biology and chemistry in the schizophrenia disease model. Early results from his lab show that the [compounds](#) may increase the ability of other antipsychotic drugs to improve [cognitive impairment](#).

More information: Younai, A., Zeng, B.-S., Meltzer, H. Y. and Scheidt, K. A. (2015), Enantioselective Syntheses of Heteroyohimbine Natural Products: A Unified Approach through Cooperative Catalysis. *Angew. Chem. Int. Ed.*.. [DOI: 10.1002/anie.201502011](https://doi.org/10.1002/anie.201502011)

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