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Beautyberry leaf extract restores drug's power to fight 'superbug' MRSA

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"We decided to investigate the chemical properties of the American beautyberry because it was an important medicinal plant for Native Americans," says Emory ethnobotanist Cassandra Quave, a senior author of the study. Credit: Tharanga Samarakoon

Scientists discovered a compound in the leaves of a common shrub, the American beautyberry, that boosts an antibiotic's activity against antibiotic-resistant staph bacteria. Laboratory experiments showed that the plant compound works in combination with oxacillin to knock down the resistance to the drug of methicillin-resistant Staphylococcus aureus, or MRSA.

The American Chemical Society's Infectious Diseases published the finding, led by scientists at Emory University and the University of Notre Dame.

The American beautyberry, or *Callicarpa americana*, is native to the southern United States. Prolific in the wild, the shrub is also popular in ornamental landscaping. It's known for showy clusters of bright purple berries that begin to ripen in the summer and are an important food source for many species of birds.

"We decided to investigate the chemical properties of the American beautyberry because it was an important medicinal plant for Native Americans," says Cassandra Quave, co-senior author of the study and an assistant professor in Emory University's Center for the Study of Human Health and Emory School of Medicine's Department of Dermatology. Quave is also a member of the Emory Antibiotic Resistance Center and a leader in the field of medical ethnobotany, studying how indigenous people incorporate plants in healing practices to uncover promising candidates for new drugs.

Micah Dettweiler, a recent Emory graduate and a staff member of the Quave lab, is first author of the study. Christian Melander, professor of chemistry at Notre Dame, is co-senior author.

The Alabama, Choctaw, Creek, Koasati, Seminole and other Native American tribes relied on the American beautyberry for various medicinal purposes. Leaves and other parts of the plant were boiled for use in sweat baths to treat malarial fevers and rheumatism. The boiled roots were made into treatments for dizziness, stomachaches and urine retention, while bark from the stems and roots were made into concoctions for itchy skin.

Previous research found that extracts from the leaves of the beautyberry

deter mosquitoes and ticks. And a prior study by Quave and colleagues found that extracts from the leaves inhibit growth of the bacterium that causes acne. For this study, the researchers focused on testing extracts collected from the leaves for efficacy against MRSA.

"Even a single plant tissue can contain hundreds of unique molecules," Quave says. "It's a painstaking process to chemically separate them out, then test and retest until you find one that's effective."

The researchers identified a compound from the leaves that slightly inhibited the growth of MRSA. The compound belongs to a group of chemicals known as clerodane diterpenoids, some of which are used by plants to repel predators.

Since the compound only modestly inhibited MRSA, the researchers tried it in combination with beta-lactam antibiotics.

"Beta-lactam antibiotics are some of the safest and least toxic that are currently available in the antibiotic arsenal," Quave says. "Unfortunately, MRSA has developed resistance to them."

Laboratory tests showed that the beautyberry leaf compound synergizes with the beta-lactam antibiotic oxacillin to knock down MRSA's resistance to the drug.

The next step is to test the combination of the beautyberry leaf extract and oxacillin as a therapy in animal models. If those results prove effective against MRSA infections, the researchers will synthesize the plant compound in the lab and tweak its chemical structure to try to further enhance its efficacy as a combination therapy with oxacillin.

"We need to keep filling the drug-discovery pipeline with innovative solutions, including potential combination therapies, to address the

ongoing and growing problem of antibiotic resistance," Quave says.

Each year in the U.S., at least 2.8 million people get an antibiotic-resistant infection and more than 35,000 people die, according to the Centers for Disease Control and Prevention.

"Even in the midst of the COVID-19, we can't forget about the issue of antibiotic resistance," Quave says. She notes that many COVID-19 patients are receiving antibiotics to deal with secondary infections brought on by their weakened conditions, raising concerns about a later surge in antibiotic-resistant infections.

More information: Micah Dettweiler et al. A Clerodane Diterpene from Callicarpa americana Resensitizes Methicillin-Resistant Staphylococcus aureus to β-Lactam Antibiotics, *ACS Infectious Diseases* (2020). DOI: 10.1021/acsinfecdis.0c00307

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