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Scientists identify plants that combat MRSA infections

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With antimicrobial resistance (AMR) a continued threat to global public health, a recent study by Dominican University of California researchers has identified two plants commonly used in Native American remedies as having potential to treat antibiotic-resistant infections, including methicillin-resistant Staphylococcus aureus (MRSA) infections.

The study by Dr. Maria Graciela Carranza, assistant professor of chemistry, and Dr. Mary B. Sevigny, assistant professor of biology, in the Department of Natural Sciences and Mathematics in the School of Health and Natural Sciences examined *Rhamnus californica* (coffeeberry) and *Umbellularia californica* (California bay or California laurel), two indigenous California plant species historically used by Native Americans to treat skin, respiratory, and gastrointestinal infections.

"Our research was inspired by the use of plants in Native American culture," Carranza said. "Our results give scientific credence to the traditional medicinal uses of plants by the indigenous peoples of California."

Over a period of two years, the research team assessed the antimicrobial activity of extracts of leaves and bark of R. and U. *californica* against MRSA and other bacteria commonly found in health care settings.

The results, published earlier this summer in *The Annals of Clinical Microbiology and Antimicrobials*, are the first to report the antibacterial activity of extracts from these two plant species and illustrate their promising anti-MRSA potential.

"Most intriguing was the discovery that these plant extracts were effective at controlling the growth of MRSA, one of the most ominous AMR strains," Carranza said.

"Our research indicates that the plant extracts could be helpful in overcoming antimicrobial resistance, as the fight against resistance will not be won by any one miracle drug, but by a combination of multiple agents that together can combat infection."

The plants' leaves and bark were separated, oven dried, and ground into fine powder or shavings. After being dissolved in a solvent using methanol, doses of plant extracts were applied to the various bacterial species. Extract doses ranging from 1 to 25 mg were tested on the Gram-negative organisms *Escherichia coli* and *Pseudomonas aeruginosa* and on the Gram-positive bacteria *B. cereus, M. smegmatis, S. pyogenes, S. aureus*, and MRSA.

"While the Gram-negative bacteria were virtually unaffected by the extracts, all extracts completely inhibited the growth of MRSA and other Gram-positive bacteria at concentrations ranging between 3.3 and 6.0 mg/ml. *B. cereus* exhibited the greatest sensitivity to the three extracts, and the California bay extracts, rather than the coffeeberry extract, appeared to be most active," Carranza said.

"The fact that the two Gram-negative organisms *E. coli and P. aeruginosa* were virtually unaffected by these extracts indicates that the antimicrobial effects on the Gram-positive organisms are specific and significant," co-author Sevigny said. "The complete lack of activity on the Gram-negative organisms is most likely due to the protective nature of the outer membrane of their cell walls."

"Our study is also the first to detect the presence of quinones, alkaloids, flavonoids, cardenolides, tannins, and saponins in *R. californica*," Carranza said. "In addition, alkaloids, flavonoids, cardenolides, saponins, tannins (leaves), and steroids (bark) were detected in *U. californica*."

These secondary metabolites are present in other plants, and individually, each of these classes of compounds varies considerably in antimicrobial capacity. At the same time, some of the structural classes found in *R. and U. californica* have recently shown promising anti-MRSA potential.

The researchers maintain that the antimicrobial activity observed is due to the synergistic effects of all or most of the secondary metabolites present in each extract. Unlike the purified antibiotics commonly prescribed today, these extracts contain multiple compounds that may affect the bacteria via several different mechanisms, thus decreasing the likelihood of selecting for a resistant strain and averting the risk of AMR.

"Our findings suggest that extracts of *R. and U. californica* merit further chemical study as natural antibiotics to identify the secondary metabolites responsible for their antimicrobial activity, since such structures could serve as valuable therapeutic anti-MRSA leads," Carranza said.

Two former Dominican students are co-authors of the study. Lacie Fox-Cubley graduated in May 2013 with a BS in biological sciences, and Debashree Banerjee earned an MS in biology in December 2013.

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