Researchers at the University of South Florida have identified novel inhibitors against bacteria resistance to carbapenemases and other beta – lactam antibiotics.

One of the most extensively studied bacterial resistance mechanisms is resistance to beta-lactam antibiotics such as pencillins, cephalosporins, and carbapenems. Betalactam antibiotics are among the most commonly prescribed antibiotics in the clinical setting. Beta-lactam antibiotics target the cross-linking of the bacterial cell wall, which ultimately results in cell death.

Despite the numerous successes of the beta-lactam antibiotics, bacteria have developed resistance to them, most often through the production of enzymes known as betalactamases.

Combining a beta-lactamase inhibitor with a beta-lactam antibiotic has been the most successful approach in extending the efficacy of beta-lactam antibiotics; however, the clinically relevant beta-lactamase inhibitors, clavulanic acid, sulbactam, and tazobactam are most effective only against class A beta-lactamases. In addition, these inhibitors possess a beta-lactam ring, which can induce beta-lactamase expression and increase their susceptibility to hydrolysis.

USF inventors have discovered coumarin phosphonates and related derivatives, which act as inhibitors of the class A KPC-2 and class B NDM-1 betalactamases.

The compounds would be useful in potentiating the action of beta-lactam antibiotics in the treatment of multi-drug resistant bacterial infections. In particular, the compounds can be combined with a beta-lactam antibiotic such as benzylpenicillin, cefotaxime, or meropenem to target bacteria resistant to beta-lactam antibiotics as a result of KPC-2 and/or NDM-1 betalactamase production.

Advantages:

- Effectively inhibits multiple targets
- Extends efficacy of beta-lactam antibiotics

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