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Selective inhibitors of vancomycin-resistant enterococcus

A novel, orally bioavailable compound builds on an existing scaffold to improve potency and pharmacokinetics for the treatment of vancomycin-resistant Enterococcus while reducing off-target toxicities.

Vancomycin-resistant Enterococci (VRE) is the second-most prevalent cause of hospital-acquired infections (HAIs), with most cases showing up in hospitals and long-term care facilities. The only FDA-approved treatment method for VRE is linezolid, which has known dose-limiting side effects and toxicity issues. Additionally, while linezolid is still therapeutically effective against VRE, the possibility of resistance mechanisms developing is very high. Thus, there is a need to develop new antibiotics to combat antimicrobial resistant pathogens like VRE. Researchers at Purdue University have improved upon previously disclosed technology with improved pharmacokinetic properties and reduced off-target inhibition of related human enzymes. These new leads build upon the previous AZM scaffold by adding in new functional groups to rotationally lock the molecule to maintain antibacterial potency while reducing binding to known human off-targets and improving plasma exposure for greater potency in vivo. Efficacy testing in mouse models is underway, but this is a promising new lead compound for treatment of VRE in an orally bioavailable formulation.

Technology Validation:

-Four lead compounds had 100-fold and 8-fold improvement in MIC compared to AZM and linezolid, respectively

-Lead compounds show minimal toxicity against mammalian cell line

-Lead compound 28 has greatly improved pharmacokinetic profile compared to previously developed AZM-derivatives

Advantages

-Compound is orally bioavailable

-Facile synthesis

Technology ID
2026-FLAH-71325

Category
Pharmaceuticals/Small Molecule Therapeutics
Pharmaceuticals/Drug Delivery & Formulations

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View online

-Minimal off-target toxicities

Applications

-Orally bioavailable drug formulation to treat vancomycin-resistant Enterococcus

Related Publications (if none, delete this section)

1.Kaur, J. et al. J Med Chem. 2020 Aug 11;63(17):9540â€“9562.

2.Holly, K. J. et al. J Med Chem. 2025, Aug 29; published online; doi: 10.1021/acs.jmedchem.5c01584

TRL: 3

Intellectual Property:

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