Antibiotic for Veterinary Staphylococcal Infections

Technology #018-033-dowd

New bacteriostatic compounds treat Staphylococcal strains that infect bovine, cat, and dog populations. Staphylococcal infections affect an estimated 20% of bovine populations in the dairy industry, and are the single largest indication for antibiotic use on dairy farms. Staphylococcal infections lead to a cost of greater than $1 billion per year to U.S. farms.

Isoprenoids are an ancient, large, and essential class of biomolecules critical for electron transport, cell membranes, pigments, signaling, and more. Isoprenoids are synthesized via two biochemical pathways, the MEP pathway and the mevalonate pathway. Mammals use the mevalonate pathway, but many bacteria use only the MEP pathway. This makes enzymes in the MEP pathway safe drug targets for overcoming pathogenic bacteria. The malaria drug candidate, fosmidomycin, targets the Dxr enzyme in the MEP pathway. Fosmidomycin was safe, but not very effective in human trials.

Researchers from GW and Washington University in St. Louis developed fosmidomycin derivatives with more drug-like properties. They found that some of these new compounds had great activity against Staphylococcal strains relevant to farm animals and pets. The researchers validated the new Dxr inhibitors against recombinant Dxr enzyme and by treating bacteria in vitro. The compounds reached IC50 as low as 40 nM against Staphylococcus strains. Lipophilic prodrug MEPicides (compounds 2 and 4) showed significant inhibition for glpT mutant strains that are resistant to fosmidomycin.

Applications:

- Treatment of Staphylococcal infections in cattle, cats, and dogs

Advantages:

- Active against drug resistant bacteria
- Safer treatment through targeted pathway not found in animals
Inventors

Cynthia S. Dowd, Ph.D.

Dr. Cynthia Dowd focuses on antibiotic drug discovery and structure-based design. The main focus is on Mycobacterium tuberculosis, causing TB, Plasmodium falciparum, the primary organism causing malaria, and the ESKAPE pathogens. Dowd's lab focus on vulnerabilities in microorganism metabolism that might be targeted by small-molecule therapeutic agents.

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