Antibacterial Agents Effective Against Intracellular Pathogens

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- Pharmaceuticals

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- Non-Toxic
- Pharmaceuticals
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- Vancomycin

Researchers at Purdue University have developed therapeutics against methicillin-resistant staphylococcus aureus (MRSA) that penetrate through host cells and retain their antibiotic activity, effectively reducing the intracellular MRSA levels with no adverse effects on the host. Antibiotic resistance is a global problem accruing a cost of $20 billion in associated medical costs and taking the lives of 23,000 patients in the US each year. MRSA is a bacterial infection that commonly acquires resistance through infecting macrophages and other phagocytic host cells. Many antibiotics used to treat MRSA, including vancomycin, cannot penetrate through host cell membranes at lethal doses, thus leaving the MRSA infection free to proliferate in the intracellular compartment. The Purdue technology addresses this shortcoming of existing therapeutics while also addressing the need for a therapy that will not encourage bacterial resistance.

Multiple strains of MRSA did not display any resistance characteristics when treated with these therapeutic molecules over time. Preliminary data indicate that these compounds exhibit decreased MRSA load in mice to the same degree as vancomycin. Additionally, these molecules underwent an Ames test and displayed no mutagenic characteristics. When screened at 10x MIC, they showed no toxicity to red blood cells in in vitro experiments. Initial mechanistic studies show these molecules reduce levels of bacterial DNA, RNA, and cell wall biosynthesis with similar or better potencies relative to antibiotics commonly used to reduce these macromolecules.

Advantages:
- No adverse effects to host cells
- No acquired bacterial resistance
Potential applications:
- Antimicrobial resistance
- Antibiotic therapy
- MRSA therapeutic

Related Publication:
Inhibitors of Intracellular Gram-Positive Bacterial Growth Synthesized via Povarov–Doebner Reactions
ACS Infect. Dis. 2019, 5, 11, 1820-1830
DOI: 10.1021/acsinfecdis.9b00022

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