

# Antifolate Compound as Multi-Drug Resistant Pathogens

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## A antifolate compound with demonstrated specificity for DHFR of *E. coli*

Georgia Tech inventors have discovered a novel antifolate compound with demonstrated specificity for DHFR of *E. coli*. The inventors report high affinity binding with DHFR using a thermal shift assay to reveal an extreme increase in the thermal stability of DHFR in the presence of this compound. Furthermore, the inventors have reported significant growth inhibition of numerous drug-resistant pathogens including bacterial and fungal species. This compound is entirely novel with its tricyclic heterocycle and with the demonstrated ability to bind DHFR.

### Summary Bullets

- Novel structure with high binding affinity for DHFR
- Demonstrated growth inhibition of numerous pathogens
- Demonstrated antibacterial activity for multi-drug resistant strains of *E. coli*, methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant *E. faecalis* & antifungal activity against amphotericin-resistant *Candida albicans*

### Solution Advantages

- Novel structure with high binding affinity for DHFR
- Demonstrated growth inhibition of numerous pathogens
- Demonstrated antibacterial activity for multi-drug resistant strains of *E. coli*, methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant *E. faecalis* & antifungal activity against amphotericin-resistant *Candida albicans*

### Potential Commercial Applications

- Topical medication for MRSA skin infections
- Treatment for systemic infections
- Fighting community or hospital-acquired infections
- Sterilizing agent in healthcare settings
- Tool to elucidate the cellular mechanism of action of DHFR

## Background and More Information

Overuse and misuse of current drugs has allowed for rapid emergence of resistance among numerous pathogens. Consequently, there has been a serious decline in treatment efficacy for common infections and an increase in severe opportunistic infections caused by antibiotic-resistant pathogens. Multi-drug resistant bacterial pathogens are associated with nosocomial infections in healthcare settings and have gained prominence as the causative agents of community-acquired infections. Separately, there is an unmet need for more effective antifungal treatments. The increased use of medical devices correlates with heightened incidence of fungal infections. In addition, transplantation, chemotherapy drugs, and radiation for cancer patients increases susceptibility to opportunistic infections. Dihydrofolate reductase (DHFR) is an essential enzyme involved in folic acid metabolism. To date, antifolate drug compounds have been developed to bind to and block the function of DHFR for the treatment of various cancers and malaria. Resistance to current antifolate drugs necessitates the need for new compounds with specificity for DHFR.

## Inventors

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## IP Status

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