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Background: Clostridium difficile infection (CDI) represents a scourge to society with serious consequences that result in disease in the gut and pseudomembranous colitis. It is difficult to treat due to its antibiotic-mediated resistance. The presence of antibiotic-resistant and pan-MRSA strains of CDI has been observed in the gut flora at levels as high as 10% and has been associated with increased levels of antibiotic resistance and the development of multidrug-resistant strains.

Methods: Minimal inhibitory Concentration (MIC) assays were performed against a series of anorectal fecal isolates and various isolates of C. difficile, including antibiotic-resistant and pan-MRSA subsets. MIC was determined using standard techniques. The efficacy of the novel compound, MBX 259C, was characterized against C. difficile, with promising results.

Results: MBX 259C displayed potent activity against multiple C. difficile isolates, including those resistant to metronidazole, with an MIC of 0.54-µg/mL. A collection, lacking the tetracycline resistance gene, was efficacious in multiple in vivo models given orally. First, in two separate studies, in a hamster model of CDI, MBX 259C was observed to be equally efficacious with the comparator, vancomycin. Second, in a mouse CDI model, MBX 259C behaved in a manner superior to vancomycin, protecting mice from infection by 12 days after treatment, whereas 20% of vancomycin-treated mice succumbed to infection. Finally, in a pig model of CDI, MBX 259C was efficacious when dosed at 100 or 200 mg/kg.

Conclusions: The AU/FQ hybrid antibacterial MBX 259C exhibits potent activity against drug-resistant and drug-sensitive C. difficile in vivo and in three animal infection models.

INTRODUCTION

Antibiotic resistance, a threat to the health of our society, continues to be a serious threat to the health of our society. The emergence of antibiotic-resistant strains of Clostridium difficile has led to increased rates of hospitalization, treatment complications, and increased healthcare costs. The development of novel antibiotics is critical to address this global health challenge.

RESULTS

Mouse Model

Hamster Model

Piglet Model

REFERENCES