Evaluation of Delafloxacin in Rat Granuloma Pouch Infections Caused by Gram-negative Pathogens
Andrea Marra, Elizabeth Bortolon, David Molstad, Yuhong Wu, Hongwu Jing, and Eric Burak
Rib-X Pharmaceuticals, Inc., New Haven, CT, USA

ABSTRACT

Background: Delafloxacin is a novel synthetic fluoroquinolone derivative with excellent in vivo activity against a wide range of Gram-negative pathogens including multidrug-resistant strains. This in vivo activity and excellent therapeutic index in preclinical models make delafloxacin an attractive candidate for the treatment of human infections caused by Gram-negative bacteria. This study aimed to characterize the in vivo activity of delafloxacin against a panel of Gram-negative bacteria known to cause human infections.

Methods: A panel of Gram-negative bacteria, including Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, and Salmonella typhimurium, was cultured and infectivity was measured in a granuloma pouch infection model in rats. The bacterial load was determined by colony counting. Delafloxacin was administered at various doses to rats infected with the corresponding bacterial strain, and the bacterial load was measured at different time points post-administration.

Results: Delafloxacin showed significant activity against all the tested bacteria, with a concentration-dependent decrease in bacterial load. The MIC values were determined for each bacterium, and delafloxacin was found to be highly potent against all tested strains.

Conclusions: Delafloxacin is an effective treatment for Gram-negative infections in a granuloma pouch model. Further studies are needed to evaluate its potential for clinical use.

INTRODUCTION

Granuloma pouch infections are a model for patient infections caused by Gram-negative bacteria, including multidrug-resistant strains. The granuloma pouch model is an ex vivo system that allows for the study of bacterial growth and antibiotic efficacy under conditions that mimic the human body. Delafloxacin is a novel synthetic fluoroquinolone with excellent in vivo activity against a wide range of Gram-negative pathogens. This study aimed to evaluate the in vivo activity of delafloxacin against a panel of Gram-negative bacteria known to cause human infections.

METHODS

Bacterial strains: A panel of Gram-negative bacteria, including Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, and Salmonella typhimurium, was cultured.

Granuloma pouch infection model: The granuloma pouch model was used to measure bacterial infectivity and antibiotic efficacy. The pouches were infected with the corresponding bacterial strain, and the bacterial load was determined by colony counting.

Drug administration: Delafloxacin was administered at various doses to rats infected with the corresponding bacterial strain.

Bacterial load measurement: The bacterial load was determined by colony counting at different time points post-administration.

RESULTS

Delafloxacin showed significant activity against all tested bacteria, with a concentration-dependent decrease in bacterial load. The MIC values were determined for each bacterium, and delafloxacin was found to be highly potent against all tested strains.

CONCLUSIONS

Delafloxacin is an effective treatment for Gram-negative infections in a granuloma pouch model. Further studies are needed to evaluate its potential for clinical use.