SYNTHESIS, STRUCTURE, AND IN VITRO ACTIVITY OF THE NEOGLYCOSIDE ACHN-490


ABSTRACT

Background: The rapid emergence of drug resistance in Gram-negative bacteria is causing alarms in hospitals and healthcare facilities around the world. With few new agents in the pipeline to address this growing threat, nanomolar to sub-micromolar antibacterial activities against drug-resistant (DR) strains of Gram-negative bacteria are extremely valuable. Additional activity against drug-resistant (DR) strains may be translated to effective treatments for patients with nosocomial pathogens, such as the multidrug-resistant (MDR) Acinetobacter baumannii (AB). ACHN-490 is a cephalosporin analog with reduced activity against Gram-negative and extended Gram-positive bacteria. Unlike other AEs, ACHN-490 retains effectiveness against widespread and increasing resistance to the existing antibiotics (β-lactams).

Methods: ACHN-490 was synthesized in 6 steps from 8-bromo-7-mercapto-2,3-di-4-nitrobenzoyl cephalosporin. ACHN-490 was tested for antibacterial activity using the CLSI broth microdilution method against a panel of 26 organisms with characterized AG resistance mechanisms (AGRM). The minor AMEs found in GNB were illustrated with ACHN-490.

Conclusion: ACHN-490 is a broad-spectrum, rapidly bactericidal agent with excellent potency against drug-resistant (R) strains of Gram-negative bacteria are desperately causing alarm in hospitals and health care facilities around the world. With few new agents in the pipeline to address this growing threat, nanomolar to sub-micromolar antibacterial activities against drug-resistant (DR) strains of Gram-negative bacteria are extremely valuable. Additional activity against drug-resistant (DR) strains may be translated to effective treatments for patients with nosocomial pathogens, such as the multidrug-resistant (MDR) Acinetobacter baumannii (AB). ACHN-490 is a cephalosporin analog with reduced activity against Gram-negative and extended Gram-positive bacteria. Unlike other AEs, ACHN-490 retains effectiveness against widespread and increasing resistance to the existing antibiotics (β-lactams).

INTRODUCTION

An imipenem-like ACHN was a well-established class of antibiotics that are being bridged by the Ac-490. The traditional approaches and interfacing with existing products is synthons. Since then, introduction of 19 years ago, susceptibility to AEs has emerged. The most significant contribution to clinical AG resistance is represented by the discovery of Amp C-resistant extended spectrum β-lactamases (ESBL) (490). The mechanism of action of this class has been identified, often occurring in combinations that can impart broad AG resistance. As increasing resistance

RESULTS

The antibacterial activity of ACHN-490 was determined using the CLSI broth microdilution method against a panel of 26 organisms with characterized AG resistance mechanisms (AGRM). The minor AMEs found in GNB were illustrated with ACHN-490.

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