INTRODUCTION

ABSTRACT

The antibacterial activity of various novel derivatives of the new semisynthetic ESP was determined for 14 novel semisynthetic ESP derivatives and comparator antibiotics by broth microdilution (CLSI, M7-A9). The bacterial MIC50/90 were determined for eight compounds against Enterobacteriaceae (8-16 µg/mL), which were largely resistant to amoxicillin/sulbactam (MIC90 < 32 µg/mL), cefotaxime (MIC90 < 1 µg/mL), and moxifloxacin (MIC90 < 0.03 µg/mL). The novel ESP derivatives were fully active against TEM-, CTX-M and NDM-1 producing Enterobacteriaceae. All tested S. pneumoniae isolates were inhibited by ESP concentrations of 1/16-1/32 µg/mL, irrespective of resistance to macrolides or penicillins. Conclusions: The new generation of pleuromutilin antibacterials, demonstrated a potent antibacterial profile covering the most prevalent Gram-positive and Gram-negative bacterial organisms including multi-drug resistant and carbapenemase-producing strains. The novel ESP derivatives were fully active against NDM-1 metallo-ß-lactamase-producing Enterobacteriaceae. All tested S. pneumoniae isolates were inhibited by ESP concentrations of 1/16-1/32 µg/mL, irrespective of resistance to macrolides or penicillins.

RESULTS

A variety of novel ESP has been synthesised by the semi-synthetic modification of pleuromutilin (Figure 1) and tested for their activity against Enterobacteriaceae. The screened bacterial species included clinical isolates and CLSI reference strains of E. coli, K. pneumoniae, C. freundii, E. cloacae, S. aureus, S. pneumoniae and H. influenzae. Particularly carbapenem-resistant isolates producing metallo-ß-lactamases (NMD-1, KPC ß-lactamases or other ESBL were included to evaluate if ESP meet the high demand for new antibiotics being active against those pathogens.

REFERENCES


ACKNOWLEDGMENTS

The authors gratefully acknowledge the practical work of A. Gross and the kind provision of clinical isolates by H.N. Jones (JMI Laboratories, USA), D. Livermore (Health Protection Agency, UK) and F.J. Schmitz (Klinikum Minden, Germany).