Friulimicin B Shows Good Efficacy in a Staphylococcal Murine Abscess Infection

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Methods

The test compounds were obtained from the following sources: FRI (Combinatie Biopharm AG, Germany), VAN (Lilly Deutschland GmbH, Germany), DAP (Novartis Pharma GmbH, Germany).

Bacterial strain: The staphylococcal strain DSM 11823, a clinical isolate, was taken from the culture collection of Bayer HealthCare AG, Germany. MIC values for FRI, VAN and DAP were determined by agar dilution method. Mueller-Hinton agar substituted with 184 mg/l CaCl₂ was used. Agar plates were inoculated with bacterial spots using a Denley multipoint inoculator, containing ~1 - 5 x 10⁴ colony forming units (CFUs) each. Plates were incubated for 16-20 hrs. at 37°C under 5% CO₂. The lowest antibiotic concentration yielding no growth was read as the MIC.

Test compounds: The test compounds were obtained from the following sources: FRI (Combinatie Biopharm AG, Germany), VAN (Lilly Deutschland GmbH, Germany), DAP (Novartis Pharma GmbH, Germany).

Conclusions: In this study, FRI shows good efficacy in a mouse model of SSTI, the granuloma pouch, caused by MSSA.

Introduction

Friulimicin B (FRI) is a novel lipopeptidic antibiotic agent that exhibits potent activity against a variety of Gram-positive bacteria. It is structurally similar to the lipodepsipeptide (DAP) but has a distinct mode of action. Its chemical structure is shown in Figure 1.

The aim of this study was to investigate the potential of FRI in experimental skin and soft tissue infections (SSTI). The efficacy of FRI in the murine granuloma pouch model using a susceptible Staphylococcus strain was determined in comparison with that of vancomycin (VAN) and DAP. This model is regarded as an example of an SSTI.

Results and Discussion

In this study, FRI shows good efficacy in a mouse model of SSTI, the granuloma pouch, caused by MSSA.

The MIC values for the three test compounds are shown in Table 1. The therapeutic efficacy of compounds in the granuloma pouch model was measured by the reduction of the number of staphylococci in the exudates. Figure 3 shows the counts in the individual granuloma pouches of each group at 2 days post infection and Table 2 shows the change in the numbers of viable organisms compared with control animals receiving no therapy. The growth of the infecting organism in the control group was consistent and reached approximately 6 x 10⁸ CFU/ml of homogenate by 2 days post-infection. All test compounds showed a dose-dependent reduction of the bacterial load. DAP was more active than the comparators. Compared with VAN, the bactericidal efficacy of FRI was higher over the whole dose range (1.25 - 10 mg/kg).

Overall friulimicin B showed a higher reduction in the bacterial counts in the exudates than vancomycin, but was less potent than daptomycin at the lower doses.