In Vivo Efficacy of Finafloxacin in Difficult to Treat Animal Models of Infection

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Abstract

Introduction

Finafloxacin (FIN, Figure 1) is a novel, broad-spectrum fluoroquinolone (FQ) that belongs to a new chemical series [1]. FIN contains a novel chiral base component and exhibits improved antibacterial activity under slightly acidic pH values (pH 5.0–6.0) under which other marketed FQs exhibit significantly reduced activity [2]. FIN also exhibited excellent activity against adherent bacteria in vitro [3].

Additionally, FIN displayed an excellent safety profile in a wide range of predictions in vivo, toxicity screens [4] and was well tolerated in healthy human volunteers [5]. These attributes suggest that FIN warrants clinical investigation for bacterial infections that are associated with extremely acidic sites such as Helicobacter pylori infection and rheumatoid arthritis [5].

FIN was also shown to be clinically active in rodent models of infection that were selected to offer a wide range of infection sites and to mimic the type of infections that are difficult to treat in humans, including those involving formation of adherent bacterial populations.

Figure 1. Finafloxacin hydrochloride.

Methods

Thigh Infection Model - S. aureus: Mice were inoculated intramuscularly by the subcutaneous (s.c.) administration of cytopathic Staphylococcus aureus. Day 1 drug treatment was initiated at 10 mg/kg FIN or 50 mg/kg CIP. The effect of the FQs on reducing the numbers of staphylococci in the thigh is shown in Figure 2. FIN produced a dramatic half-log (50 CFU) reduction in the thigh homogenate at 10 mg/kg, far more than was seen with the other compounds. FIN and MOX had the lowest MICs (0.125 mg/L) but FIN, although being more active than CIP, was less active at all dose levels than FIN.

Results and Discussion

Figure 2. S. aureus infected thigh model – CFU reduction in thigh tissue.

Imprinted Foreign Body Model - S. aureus: Infection of the right hind leg was cut into pieces 1 x 1 cm and incubated overnight in sterile PBS, pH 7.4. The following day these were implanted s.c. on the back of mice. Within 3 days a capsule formed around the implant and this was infected with 1 x 10^5 S. aureus DSM 11823 culture. The catheter was rinsed and then implanted s.c. in the thigh muscle. Within 3 days the catheter was removed and the abscesses were measured. The results of all the experiments are summarised in Table 1.

Table 1. Summary of in vivo test results

Conclusions

In general, the efficacy of FIN was superior to that of CIP, LVX and MOX.

The efficacy of FIN was better than expected from its MIC at all three concentrations tested and also in ascending pyelonephritis using infected catheter – CFU reduction in various tissues.

References