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Abstract (poster session)

Activity of XF-73 against methicillin-resistant and sensitive Staphylococcus epidermidis

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Objectives: XF-73 is undergoing clinical trials for the nasal decolonisation of Staphylococcus aureus. The frequency of nasal colonisation by Staphylococcus epidermidis is significantly higher than for S. aureus and recent studies have demonstrated that the presence of S. epidermidis inhibits colonisation by S. aureus. S. epidermidis is also a significant source of nosocomial infections. The effect of XF-73 decolonisation against nasal bacteria other than S. aureus is therefore an important consideration. This study aimed to investigate the activity of XF-73 against both methicillin-sensitive and methicillin-resistant S. epidermidis and to investigate the mechanism of action of XF-73 against S. epidermidis Methods: Planktonic MICs for five S. epidermidis strains (2 methicillin-sensitive; 3 methicillin-resistant) was determined by broth microdilution according to British Society for Antimicrobial Chemotherapy (BSAC) specifications. Time-kill studies using exponentially growing S. epidermidis ATCC35984 were undertaken at 4x MIC against XF-73 with samples taken every 30 minutes. Membrane damage after exposure to lethal concentrations of test compounds was determined using the BacLight™ assay. The leakage of intracellular potassium was determined by atomic absorption spectroscopy and a luciferin/luciferase assay was used to quantify the leakage of intracellular ATP. Results: The MIC for the five S. epidermidis strains tested were found to be 0.5 - 1 µ g/mL and the presence of methicillin resistance was found to not have any effect on the MIC. Time-kill experiments demonstrated a rapid bactericidal activity against S. epidermidis ATCC35984 with a 99.99% reduction in viable cell numbers after only 30 minutes incubation. Bacterial membrane integrity was found to be completely lost after 10 minutes incubation and >78% of the internal potassium and >90% of the internal ATP was found to have leaked out of the cells after 60 minutes exposure. Conclusions: XF-73 demonstrated similar rapid bactericidal activity against S. epidermidis to that previously demonstrated for S. aureus. The presence of methicillin resistance had no effect on the potency of XF-73 and the mechanism of action appears to be identical to that determined against S. aureus. The results suggest that XF-73 has broader utility than just the potential for nasal decolonisation of S. aureus.