**ABSTRACT**

Background: The bactericidal action of FQs is generally concentration dependent and requires actively growing cells. However, during infection, bacterial pathogens grow slowly and therefore, the conventional kinetic studies with fast growing cultures might not represent actual in vivo kinetics.

Methods: WCK 771 A ketolides were performed against MRSA 032 and 5003 at 0.25, 0.5, 1, 2, 4 and 8X MIC in two In-carbon supplemented Mueller Hinton Broth (MHB) to evaluate initial KD effect of WCK 771A against slow and fast growing staphylococci. A study was undertaken wherein growth rates were modulated through appropriate supplementation to yeast Nitrogen base (YNB) medium. YNB medium supplemented with 0.5% glucose resulted in slow growth, whereas further supplementations with 1.7% tryptone resulted in fast growing cultures. KD kinetic of WCK 771 A in and without modfluoros (Mox) were performed against slow and fast growing staphylococci or s. aureus ATCC 29213, S. aureus 11998 (NovA) and S. haemolyticus 203 0.5, 1.0 and 2.0 mcg/ml respectively. Similarly, against MRSA 032, WCK 771 A and Mox were studied in YNB medium supplemented with 3.12 and 12.5 mcg/ml respectively. To assess the effect of growth rate on KD, MIC of cultures were determined up to 24 h.

Results: MRSA killing by WCK 771 A in MHB was comparable at 2 4 and 8X MIC. Both Mox and Mox were killed to the extent of 2 log at 4 h and 3 log at 8 h. For S. aureus 203 0.5, 1.0 and 2.0 mcg/ml respectively. Similarly, against MRSA 032, WCK 771 A was only killed to fast growing cultures but also to slow growing cultures (2 log reduction), whereas Mox failed to kill slow growing strains (1 log reduction).

Conclusions: MRSA killing by WCK 771 A is independent of concentration dependence on duration of exposure. Effective killing of slow growing staphylococci by WCK 771 A would have in vivo relevance.

**INTRODUCTION**

It is generally believed that unlike E. coli, KD's cidal action on bacteria is concentration dependent and hence necessitating administration of higher doses with the aim of achieving high serum levels for maximum bacterial eradication. However, recently it has been shown that pharmacodynamic efficacy of vancomycin action against pneumococcus is neither a function of MIC driven nor driven by time > MIC. Gemifloxacin in ketolide kinetics study has been shown to not be affected by proportional increases in concentrations. Similarly, we studied cidal potential of WCK 771 A at various concentrations against 4 staphylococcal strains with the objective to determine the manner in which WCK 771 A acts on cell wall and cell envelope.