

Comparison of Postantibiotic Effects of Finafloxacin and other Fluoroquinolones

C. Y. GOH¹, S. B. NG¹, M. EVERETT¹ and A. VENETE²

¹MerLion Pharmaceuticals, Singapore ²MerLion Pharmaceuticals, Berlin, Germany

Contact information:

Andreas Vente
MerLion Pharmaceuticals GmbH
Robert-Rössle-Str. 10
13125 Berlin
Phone : +49-(0)30-9489-4050
info@merlionpharma.de

Abstract

Background: Finafloxacin (FIN) is a novel member of the fluoroquinolone (FQ) class of antibiotics. Specifically, FIN belongs to a new 8-cyano subclass. The agent contains a novel base component which confers improved antibacterial activity under acidic conditions, where the activity of many existing FQs is impaired.

Post-antibiotic effect (PAE) has been named as a parameter by both Food and Drug Administrations (FDA) and European Medicines Agency (EMA) guidance for investigation of new drugs. Literature reviews also indicate a clinical impact on dosing regimens; drugs without PAEs needing to be administered more frequently than those with PAEs. The aim of these experiments was to investigate the PAEs of FIN against various microorganisms under both acidic and neutral conditions.

Methods: Mid-logarithmic phase bacterial cultures of *S. aureus*, *E. coli* and *P. aeruginosa* were exposed to FQ for 1 hour and the treatment was then removed by dilution. The diluted cultures were further incubated and the growth monitored by performing viable counts up to 24 hours. Experiments were performed using FIN, ciprofloxacin (CIP), levofloxacin (LVF) and moxifloxacin (MXF). PAE was defined as $PAE = T - C$, where T is the time required for the viable count of an antibiotic-exposed culture to increase by 1 log and C is the corresponding time of the growth control, immediately after dilution.

Results: All FQs showed increasing PAEs with increasing drug concentrations. FIN exhibited longer PAEs under acidic conditions against all 3 strains, compared to the other FQs. Under neutral conditions and at low concentrations the PAEs of FIN were comparable to the other FQs, whereas at higher concentrations, FIN exhibited more than 6 hours of growth suppression.

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Organism and antibiotic	PAE (h)									
	pH 5.8					pH 7.2				
	MC	1x	2x	4x	10x	MC	1x	2x	4x	10x
<i>E. coli</i> ATCC 25922										
Finafloxacin	0.008	0.2	1.3	2.5	>6	0.063	0.5	1.4	>6	>6
Ciprofloxacin	0.063	0.1	0.8	2.5	4.5	0.008	0.5	1.8	2.1	3.0
Levofloxacin	0.125	0.2	0.9	2.4	>6	0.015	0.8	1.1	2.6	>6
<i>P. aeruginosa</i> ATCC 27853										
Finafloxacin	1	3.0	>6	>6	>6	4.0	0.4	1.2	4.0	>6
Ciprofloxacin	1	NE ¹	NE ¹	0.2	>6	0.5	1.0	3.5	>6	>6
<i>S. aureus</i> ATCC 29213										
Finafloxacin	0.031	0.4	0.6	1.3	3.2	0.125	0.3	0.8	1.2	>6
Moxifloxacin	0.125	0.1	0.2	0.6	0.9	0.063	0.6	0.9	1.4	3.4
Levofloxacin	0.25	0.2	0.5	1.0	2.5	0.25	0.3	0.8	2.5	2.7

¹NE: No effect

Introduction

Finafloxacin (FIN) is a novel member of the fluoroquinolone class of antibiotics. Specifically, FIN belongs to a new 8-cyano subclass. The agent contains a novel base component which confers improved antibacterial activity under acidic conditions¹, where the activity of many existing fluoroquinolones is impaired.

Post-antibiotic effect is described as the suppression of bacterial growth that persist after a short exposure of the organism to the antimicrobial agent². PAE has been named as a parameter by both FDA and EMA guidance for investigation of new drugs. Literature reviews also indicated a clinical impact on dosing regimens; drugs without PAEs may require more frequent dosing than those with PAEs³. In addition, reducing the dosing frequency may also help to lower the possibility of adverse events³.

The aim of these experiments was to investigate the PAEs of FIN against various microorganisms under both acidic and neutral conditions.

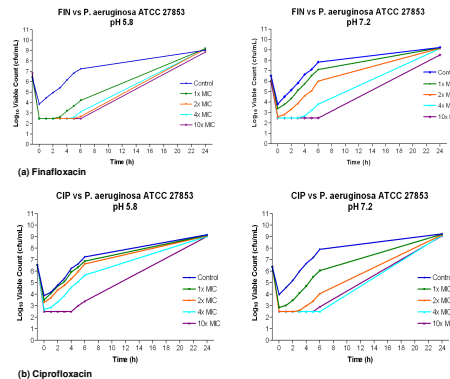


Figure 1. PAEs of (a) finafloxacin and (b) ciprofloxacin against *P. aeruginosa* ATCC 27853

Methods

Mid-logarithmic phase bacterial cultures of *S. aureus* ATCC 29213, *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were exposed to FQ for 1 hour and the treatment was then removed by diluting the culture 1000-times in pre-warmed cation-adjusted Mueller Hinton broth (CAMHB). The diluted cultures were further incubated and the growth monitored at hourly interval by performing viable counts up to 24 hours. Experiments were performed using FIN, ciprofloxacin (CIP), levofloxacin (LVF) and moxifloxacin (MXF), at pH 5.8 and 7.2.

PAE was defined as $PAE = T - C$, where T is the time required for the viable count of an antibiotic-exposed culture to increase by 1 log and C is the corresponding time of the growth control, immediately after dilution.

Conclusions

- Under both acidic and neutral conditions post-antibiotic effects were observed for FIN against all three organisms tested.
- In acidic conditions FIN exhibited longer PAEs compared to other FQs.
- In neutral conditions the PAEs of FIN are comparable to other FQs at low concentrations, whereas at higher concentrations, FIN exhibited more than 6 hours of growth suppression.

Literature

- ¹ Stubbings *et al.*, AAC 55 (2011) 4394-97
- ² Sprangler *et al.*, AAC 42 (1998) 1253-55
- ³ Athamna *et al.*, J Antimicrob Chemother. 53 (2004) 609-15

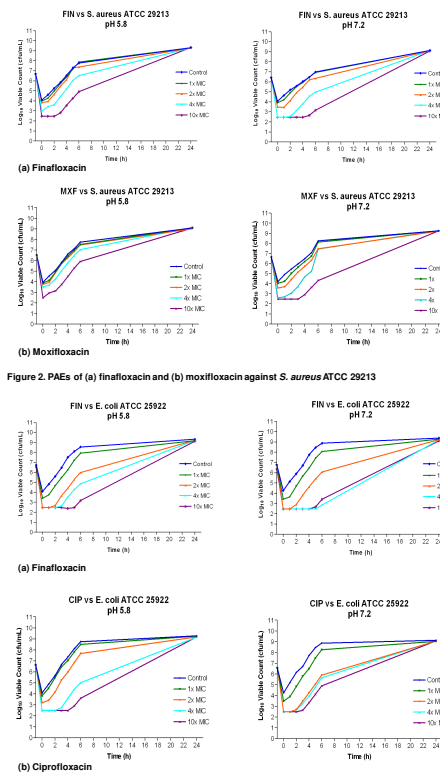


Figure 2. PAEs of (a) finafloxacin and (b) moxifloxacin against *S. aureus* ATCC 29213

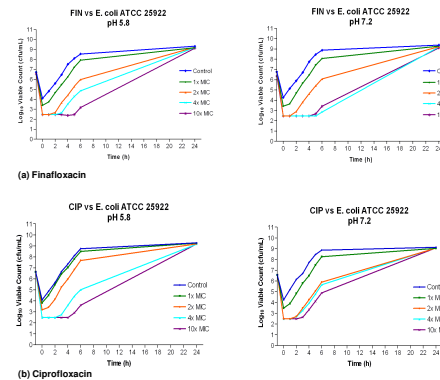


Figure 3. PAEs of (a) finafloxacin and (b) ciprofloxacin against *E. coli* ATCC 25922