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Activity of the Investigational Fluoroquinolone Finafloxacin and Seven Other Antimicrobial Agents Against 83 Obligately Anaerobic Bacteria.

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Abstract

Background: Finafloxacin (FIN) is a novel fluoroquinolone belonging to a 8-cyano subclass and exhibits enhanced activity at slightly acidic pH. FIN exhibited superior activity to comparator fluoroquinolones in a wide range of rodent infection models. With the present study the activity of FIN against 83 recently isolated strains of obligately anaerobic bacteria including reference strains was tested and compared to various other antimicrobials.
Methods: FIN was compared with moxifloxacin (MOX), levofloxacin (LEV), ciprofloxacin (CIP), clindamycin (CLI), imipenem (IMP), piperacillin/tazobactam (PIT) and metronidazole (MET) against 62 strains of the *Bacteroides fragilis* group and 21 *Clostridium difficile* strains. MICs were determined employing the microdilution technique in Wilkens-Chalgren broth supplemented with vitamin K1 and haemin.
Results: The MIC_{50} and MIC_{90} values (µg/ml) are listed in the Table.
Conclusions: FIN has promising activity against several pathogenic species of the *B. fragilis* group and is slightly more active than MOX against the obligately anaerobic bacteria tested here. Further work will be directed towards investigating the anti-anaerobic activity of finafloxacin under acidic conditions.

Introduction

Finafloxacin (FIN; Fig. 1) is a novel fluoroquinolone belonging to a 8-cyano subclass and exhibits enhanced activity at slightly acidic pH. FIN exhibited superior activity to comparator fluoroquinolones in a wide range of rodent infection models. With the present study the activity of FIN against 83 recently isolated strains of obligately anaerobic bacteria including reference strains was tested and compared to various other antimicrobials.

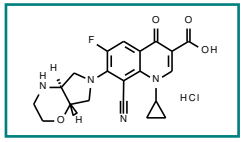

Figure 1 Finafloxacin HCl

Methods

Bacterial Strains
83 obligately anaerobes including reference strains were taken from the culture collection from the Institute for Medical Microbiology and Epidemiology of Infectious Diseases, University of Leipzig, Germany. The strains were collected from clinical specimens at the Institute and from national and international studies and obtained in part from other laboratories. The following strains were used: *Bacteroides fragilis* group (n=62): *B. caccae* (5); *B. distasonis* (10); *B. eggerhtii* (4); *B. fragilis* (6); *B. merdae* (3); *B. ovatus* (7), *B. stercoris* (6); *B. thetaiotaomicron* (7); *B. uniformis* (5); *B. vulgatus* (9) and *Clostridium difficile* (n=21).

Antimicrobial Agents
Antimicrobial agents were obtained as laboratory powders of known potency: FIN from MerLion Pharmaceuticals GmbH, Berlin, Germany; metronidazole (MET) and clindamycin (CLI) from Sigma Chemical Co., St. Louis, USA; moxifloxacin (MOX) and ciprofloxacin (CIP) from Bayer Vital GmbH, Leverkusen, Germany; levofloxacin (LEV) from Aventis Pharma Frankfurt/M., Germany; imipenem (IMP) from MSD Sharp & Dohme GmbH, Haar, Germany; and piperacillin/tazobactam (PIT) from Sigma Chemical Co. and Otsuka Chemical Co. Ltd., Osaka, Japan, respectively.

Broth microdilution MIC determinations
Tests were performed according to the recommendations of the Deutsches Institut für Normung (DIN) and standard DIN 58940-83. The bacterial inocula were prepared by suspending growth from 48 hour cultures grown on supplemented Columbia blood agar in Wilkins-Chalgren broth supplemented with vitamin K_1 and haemin. After semi-automated inoculation (Dynatech MIC-2000-inoculator, Dynatech Laboratories, Inc., Chantilly, USA) resulting in a final dilution of approximately 1.0×10^5 CFU/well (1.0×10^6 CFU/ml), plates were incubated for 48 h at 37°C in an anaerobic chamber. The MIC was defined as the lowest antibiotic concentration that inhibited visible growth.
In addition, pH of broth containing FIN was determined in part before and after incubation.

Results and Discussion

Antimicrobial Agent	*B. fragilis* group (n=62)		*C. difficile* (n=21)	
	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
FIN	0.5	2	1	16
MOX	1	2	8	16
LEV	2	8	32	>64
CIP	16	16	8	32
CLI	1	8	4	>64
IMP	0.25	1	2	4
PIT	0.5	4	0.5	2
MET	0.5	1	0.125	0.125

Table 1: MIC_{50}/MIC_{90} (µg/ml) of antimicrobials against anaerobes

Results and Discussion

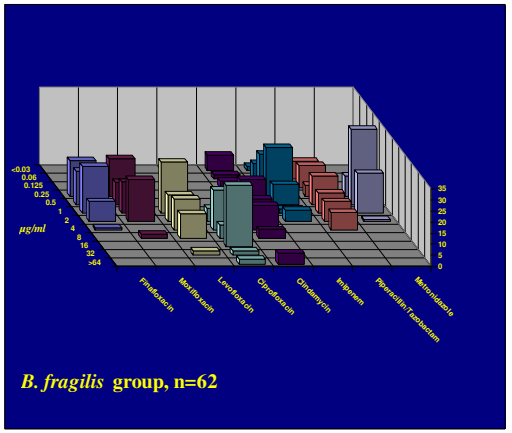

Figure 2

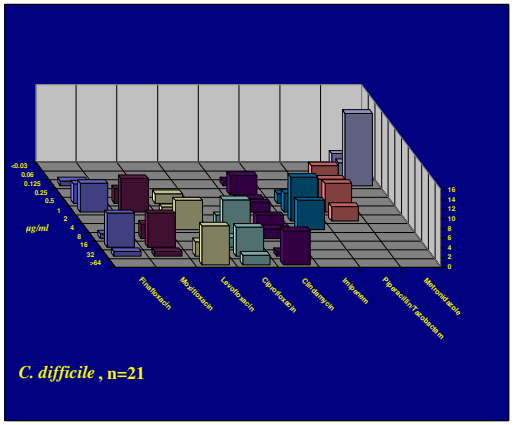

Figure 3

The Figures 2 and 3 show the scatter histograms of MIC values obtained for FIN and the seven other antimicrobial agents against 83 obligately anaerobic bacteria included in this study.

pH was approx. 7.2 before incubation and 5.0 to 7.5 after 48 h of incubation depending on the strains tested and the growth of the bacteria.

The MIC values of the *C. difficile* strains and group 3 and 4 quinolones (Figure 3) seem to display a bimodal distribution indicating that some strains are significantly less susceptible to these quinolones.

Overall, FIN was particularly active against strains of the *B. fragilis* group (Figure 2) and *C. difficile strains* (Figure 3), where it was equal to or more active than MOX and more active than LEV and CIP.

Conclusions

FIN has promising activity against a number of pathogenic species of the *B. fragilis* group and some *C. difficile* strains and is slightly more active than MOX against the obligately anaerobic bacteria tested here.
Further work will be directed towards investigating the anti-anaerobic activity of finafloxacin under acidic conditions and against additional obligately anaerobic bacteria.

Literature

DIN, Deutsches Institut für Normung e.V. Medizinische Mikrobiologie und Immunologie: Diagnostische Verfahren. Berlin, Wien, Zürich: Beuth Verlag, 2004.