

## Antianaerobic Activity of a Novel Fluoroquinolone, WCK 771, Compared to Those of Nine Other Agents

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**Agar dilution MIC methodology was used to compare the activity of WCK 771 with those of ciprofloxacin, levofloxacin, moxifloxacin, gatifloxacin, piperacillin, piperacillin-tazobactam, imipenem, clindamycin, and metronidazole against 350 anaerobes. Overall, the MICs (in micrograms per milliliter) at which 50 and 90%, respectively, of the isolates tested were inhibited were as follows: WCK 771, 0.5 and 2.0; ciprofloxacin, 2.0 and 32.0; levofloxacin, 1.0 and 8.0; gatifloxacin, 0.5 and 4.0; moxifloxacin, 0.5 and 4.0; piperacillin, 2.0 and 64.0; piperacillin-tazobactam,  $\leq$ 0.125 and 8.0; imipenem, 0.125 and 1.0; clindamycin, 0.125 and 16.0; and metronidazole, 1.0 and >16.0.**

Anaerobes are becoming increasingly resistant to  $\beta$ -lactams due to  $\beta$ -lactamase production and other mechanisms. Although  $\beta$ -lactamase production, and concomitant resistance to  $\beta$ -lactams, is the norm among the *Bacteroides fragilis* group, other anaerobic gram-negative bacilli in the genera *Prevotella*, *Porphyromonas*, and *Fusobacterium* have increasingly become  $\beta$ -lactamase positive.  $\beta$ -Lactamase production also has been described for clostridia. Metronidazole resistance in organisms other than non-spore-forming gram-positive bacilli has been described, as has clindamycin resistance in anaerobic gram-negative bacilli (1–3).

Quinolones such as ciprofloxacin, ofloxacin, fleroxacin, pefloxacin, enoxacin, and lomefloxacin are inactive or marginally active against anaerobes. Newer quinolones with increased antianaerobic activity include (i) those with slightly increased activity against aerobic gram-positive and some nonfermentative gram-negative bacteria (sparfloxacin, grepafloxacin, and levofloxacin) and (ii) those with significantly improved anti-anaerobic activity (garenoxacin, clinafloxacin, and sitafloxacin) are the most active, followed by trovafloxacin, moxifloxacin, and gatifloxacin (5–9, 11, 12, 18, 20). Development and/or marketing of many of the latter quinolones has been discontinued.

During the past few years, several reports on quinolone-resistant anaerobic strains with defined quinolone resistance mechanisms (efflux or type II topoisomerase mutations) have been published (4, 14, 15, 17). Plasmid-mediated complementation of *gyrA* and *gyrB* in quinolone-resistant *B. fragilis* has also been described (16). Additionally Golan and coworkers (10) have recently described the emergence of fluoroquinolone resistance among *Bacteroides* species. Increased use of quinolones against mixed aerobic and anaerobic infections will probably lead to an increased incidence of these strains, but this hypothesis will need validation by future in vitro surveys.

WCK 771 (Fig. 1), an experimental fluoroquinolone, is the hydrate of the arginine salt of *S*-(-)-nadifloxacin and has ex-

panded gram-positive and -negative activity. The present study tested the antianaerobic activity of WCK 771 compared to those of ciprofloxacin, levofloxacin, moxifloxacin, gatifloxacin, piperacillin, piperacillin-tazobactam, imipenem, clindamycin, and metronidazole against 350 anaerobes. All anaerobes were clinical strains isolated during the past 4 years, identified by standard procedures (19), and kept frozen in double-strength skim milk (dehydrated skim milk; Difco Laboratories, Detroit, Mich.) at  $-70^{\circ}\text{C}$  until use. Prior to testing, strains were subcultured twice onto enriched brucella agar plates supplemented with hemin and vitamin  $\text{K}_1$  (13). WCK 771 susceptibility powder was provided by Wockhardt Research Center, Aurangabad, India. MICs were based upon the weight of the fluoroquinolone moiety. Other drugs were obtained from their manufacturers.  $\beta$ -Lactamase testing was by the nitrocefin disk method (Cefinase; BBL Microbiology Systems, Cockeysville, Md.). Agar dilution susceptibility testing was according to the latest method recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (13), using brucella agar supplemented with hemin, vitamin  $\text{K}_1$ , and 5% sterile defibrinated sheep blood. Tazobactam was added to piperacillin at a fixed concentration of 4.0  $\mu\text{g}/\text{ml}$ . All anaerobe quality control gram-negative and -positive strains recommended by NCCLS were included with each run; in every case, the results (where available) were in range. No studies on efflux or type II topoisomerase mutations were performed with quinolone-resistant strains.

Among the anaerobic gram-negative bacilli tested, 49 of 54 (90.7%) of *B. fragilis* group strains, 56 of 104 (53.8%) of *Pre-*

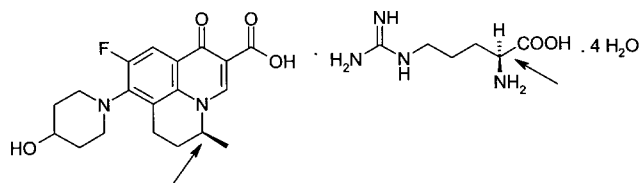


FIG. 1. Chemical structure of WCK 771. Arrows show chiral structure.

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TABLE 1. MICs of agents

Organism (no. of β-lactamase-positive strains/no. tested) and drug	MIC (μg/ml) <sup>a</sup>			Organism (no. of β-lactamase-positive strains/no. tested) and drug	MIC (μg/ml) <sup>a</sup>		
	MIC	50%	90%		MIC	50%	90%
<i>Bacteroides fragilis</i> (11/11)				<i>Prevotella bivia</i> (26/42)			
WCK 771	1->32	1	16	WCK 771	0.25->32	1	1
Ciprofloxacin	2->32	4	>32	Ciprofloxacin	8->32	16	8
Levofloxacin	1->32	2	32	Levofloxacin	2->32	4	8
Gatifloxacin	0.5->32	0.5	16	Gatifloxacin	1->32	4	4
Moxifloxacin	0.5->32	0.5	8	Moxifloxacin	2->32	4	4
Piperacillin	2->128	16	>128	Piperacillin	1-128	4	32
Piperacillin-tazobactam	0.5-4	2	2	Piperacillin-tazobactam	≤0.125	≤0.125	≤0.125
Imipenem	0.06-2	0.25	2	Imipenem	0.03-0.25	0.03	0.06
Metronidazole	0.25-1	1	1	Metronidazole	0.5-8	2	4
Clindamycin	0.125-2	2	2	Clindamycin	≤0.016->32	0.03	0.06
<i>Bacteroides thetaiotaomicron</i> (11/11)				<i>Prevotella corporis</i> (4/12)			
WCK 771	1-8	1	2	WCK 771	0.06-1	0.125	0.25
Ciprofloxacin	16->32	16	>32	Ciprofloxacin	0.5-2	1	1
Levofloxacin	4->32	4	8	Levofloxacin	0.5-1	1	1
Gatifloxacin	1-32	2	4	Gatifloxacin	0.25-0.5	0.25	0.5
Moxifloxacin	1-16	2	2	Moxifloxacin	0.5-1	0.5	1
Piperacillin	16-64	64	64	Piperacillin	≤0.125-32	1	16
Piperacillin-tazobactam	4-16	16	16	Piperacillin-tazobactam	≤0.125	≤0.125	≤0.125
Imipenem	0.125-0.5	0.5	0.5	Imipenem	0.016-0.06	0.03	0.06
Metronidazole	0.5-1	1	1	Metronidazole	≤0.125-1	0.25	0.5
Clindamycin	0.125->32	4	>32	Clindamycin	≤0.016-32	≤0.016	≤0.016
<i>Bacteroides distasonis</i> (6/11)				<i>Prevotella intermedia</i> (6/10)			
WCK 771	1-2	2	2	WCK 771	0.06-1	0.125	0.125
Ciprofloxacin	4-16	4	8	Ciprofloxacin	0.5-8	1	1
Levofloxacin	1-4	2	2	Levofloxacin	0.5-8	0.5	1
Gatifloxacin	0.5-2	1	2	Gatifloxacin	0.25-2	0.25	0.5
Moxifloxacin	0.25-1	0.5	1	Moxifloxacin	0.25-8	0.5	0.5
Piperacillin	4->128	64	>128	Piperacillin	≤0.125-16	2	8
Piperacillin-tazobactam	4-16	4	4	Piperacillin-tazobactam	≤0.125	≤0.125	≤0.125
Imipenem	0.5-1	1	1	Imipenem	≤0.008-0.125	0.03	0.03
Metronidazole	0.5-1	1	1	Metronidazole	0.25-0.5	0.25	0.5
Clindamycin	0.03->32	8	16	Clindamycin	≤0.016->32	≤0.016	≤0.016
<i>Bacteroides vulgatus</i> (10/10)				<i>Prevotella melaninogenica</i> (9/10)			
WCK 771	0.25-16	0.5	16	WCK 771	0.125-8	0.125	8
Ciprofloxacin	16->32	16	32	Ciprofloxacin	1-16	2	8
Levofloxacin	1->32	2	>32	Levofloxacin	1-32	1	16
Gatifloxacin	0.5-16	0.5	16	Gatifloxacin	0.25-16	1	16
Moxifloxacin	0.25-16	0.5	16	Moxifloxacin	0.5-16	1	16
Piperacillin	8->128	16	>128	Piperacillin	0.5-64	4	64
Piperacillin-tazobactam	0.25->32	4	8	Piperacillin-tazobactam	≤0.125	≤0.125	≤0.125
Imipenem	0.25-2	1	1	Imipenem	≤0.008-0.125	0.016	0.125
Metronidazole	0.25-2	1	2	Metronidazole	0.25-0.5	0.25	0.5
Clindamycin	≤0.016->32	0.03	0.5	Clindamycin	≤0.016-0.03	≤0.016	≤0.016
Miscellaneous <i>Bacteroides</i> (11/11) <sup>b</sup>				<i>Prevotella buccae</i> (2/11)			
WCK 771	1-8	2	4	WCK 771	0.125-0.5	0.25	0.5
Ciprofloxacin	8->32	8	>32	Ciprofloxacin	1-4	2	4
Levofloxacin	4->32	4	>32	Levofloxacin	0.5-1	1	1
Gatifloxacin	1-16	2	16	Gatifloxacin	0.25-0.5	0.25	0.5
Moxifloxacin	1-16	1	8	Moxifloxacin	0.25-0.5	0.5	0.5
Piperacillin	16->128	128	>128	Piperacillin	1-8	2	4
Piperacillin-tazobactam	1-8	2	8	Piperacillin-tazobactam	≤0.016	≤0.125	≤0.125
Imipenem	0.125-1	0.5	0.5	Imipenem	0.03-0.06	0.06	0.06
Metronidazole	0.25-2	1	2	Metronidazole	0.5-2	1	2
Clindamycin	0.5->32	4	>32	Clindamycin	≤0.016-0.03	≤0.016	≤0.016
<i>Bacteroides fragilis</i> group (49/54)				Miscellaneous <i>Prevotella</i> and <i>Porphyromonas</i> (9/19) <sup>c</sup>			
WCK 771	0.25->32	1	8	WCK 771	0.03-1	0.125	0.5
Ciprofloxacin	2->32	16	>32	Ciprofloxacin	0.5-4	1	2
Levofloxacin	1->32	4	32	Levofloxacin	0.125-8	1	1
Gatifloxacin	0.5->32	1	16	Gatifloxacin	0.06-2	0.25	0.5
Moxifloxacin	0.25->32	1	8	Moxifloxacin	0.125-1	0.5	1
Piperacillin	2->128	32	>128	Piperacillin	≤0.125-128	8	128
Piperacillin-tazobactam	0.25->32	4	16	Piperacillin-tazobactam	≤0.125-8	≤0.125	≤0.125
Imipenem	0.06-2	0.5	1	Imipenem	≤0.008-0.25	0.03	0.125
Metronidazole	0.25-2	1	1	Metronidazole	≤0.125-4	0.5	4
Clindamycin	≤0.016->32	2	>32	Clindamycin	≤0.016->32	≤0.016	0.06

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TABLE 1—Continued

Organism (no. of β-lactamase-positive strains/no. tested) and drug	MIC (μg/ml) <sup>a</sup>			Organism (no. of β-lactamase-positive strains/no. tested) and drug	MIC (μg/ml) <sup>a</sup>		
	MIC	50%	90%		MIC	50%	90%
<i>Prevotella</i> and <i>Porphyromonas</i> (56/104)				Peptostreptococci (0/27) <sup>d</sup>			
WCK 771	0.03->32	0.25	1	WCK 771	0.03-4	0.5	1
Ciprofloxacin	0.5->32	2	32	Ciprofloxacin	0.25-16	1	4
Levofloxacin	0.125->32	1	8	Levofloxacin	0.25-16	2	4
Gatifloxacin	0.06->32	0.5	4	Gatifloxacin	0.125-8	0.5	1
Moxifloxacin	0.125->32	1	4	Moxifloxacin	0.125-4	0.25	0.5
Piperacillin	≤0.125-128	4	64	Piperacillin	≤0.125-2	≤0.125	0.25
Piperacillin-tazobactam	≤0.125-8	≤0.125	≤0.125	Piperacillin-tazobactam	≤0.125-2	≤0.125	0.25
Imipenem	≤0.008-0.25	0.03	0.125	Imipenem	0.016-0.5	0.06	0.125
Metronidazole	≤0.125-8	1	4	Metronidazole	≤0.125-4	0.5	2
Clindamycin	≤0.016->32	≤0.016	0.06	Clindamycin	≤0.016-8	0.125	1
<i>Fusobacterium nucleatum</i> (0/12)				Propionibacteria (0/20)			
WCK 771	0.125-0.5	0.25	0.25	WCK 771	0.125-1	0.125	0.125
Ciprofloxacin	2-4	2	4	Ciprofloxacin	0.5-1	1	1
Levofloxacin	0.5-2	1	2	Levofloxacin	0.25-0.5	0.5	0.5
Gatifloxacin	0.25-0.5	0.25	0.5	Gatifloxacin	0.25	0.25	0.25
Moxifloxacin	0.125-0.25	0.25	0.25	Moxifloxacin	0.25-0.5	0.25	0.25
Piperacillin	≤0.125	≤0.125	≤0.125	Piperacillin	0.5-2	1	2
Piperacillin-tazobactam	≤0.125	≤0.125	≤0.125	Piperacillin-tazobactam	≤0.125-2	0.25	1
Imipenem	≤0.008-0.06	0.03	0.06	Imipenem	0.016-0.06	0.03	0.06
Metronidazole	≤0.125-0.5	≤0.125	0.25	Metronidazole	>16	>16	>16
Clindamycin	≤0.016-0.06	0.06	0.06	Clindamycin	0.03-0.25	0.06	0.125
<i>Fusobacterium necrophorum</i> (0/12)				<i>Lactobacillus</i> (0/12)			
WCK 771	0.25-1	1	1	WCK 771	1-32	2	16
Ciprofloxacin	1-4	2	2	Ciprofloxacin	1->32	2	>32
Levofloxacin	1-4	2	2	Levofloxacin	1->32	2	>32
Gatifloxacin	0.25-1	0.5	1	Gatifloxacin	0.25-16	0.5	8
Moxifloxacin	0.25-2	1	2	Moxifloxacin	0.25-8	0.5	8
Piperacillin	≤0.125-2	≤0.125	≤0.125	Piperacillin	1-2	2	2
Piperacillin-tazobactam	≤0.125-1	≤0.125	≤0.125	Piperacillin-tazobactam	1-2	2	2
Imipenem	≤0.008-1	0.016	0.06	Imipenem	0.25-4	1	2
Metronidazole	≤0.125-0.25	≤0.125	0.25	Metronidazole	16->16	>16	>16
Clindamycin	≤0.016-0.125	0.06	0.06	Clindamycin	0.125-4	0.5	4
<i>Fusobacterium mortiferum</i> (2/11)				<i>Eubacterium lentum</i> (0/11)			
WCK 771	0.125-0.5	0.125	0.25	WCK 771	0.25-0.5	0.5	0.5
Ciprofloxacin	0.5-4	2	2	Ciprofloxacin	0.5-1	0.5	1
Levofloxacin	1-2	1	2	Levofloxacin	0.5	0.5	0.5
Gatifloxacin	0.25-1	0.5	0.5	Gatifloxacin	0.25	0.25	0.25
Moxifloxacin	0.5-1	0.5	1	Moxifloxacin	0.125-0.25	0.25	0.25
Piperacillin	0.25->128	0.5	>128	Piperacillin	16-32	16	16
Piperacillin-tazobactam	≤0.125-1	0.25	1	Piperacillin-tazobactam	16	16	16
Imipenem	0.25-1	0.25	1	Imipenem	0.5	0.5	0.5
Metronidazole	0.25-0.5	0.25	0.5	Metronidazole	0.25-1	0.5	1
Clindamycin	0.06-0.5	0.125	0.125	Clindamycin	0.125->32	0.125	0.25
<i>Fusobacterium varium</i> (0/12)				Other gram-positive non-spore-forming bacilli (0/15) <sup>e</sup>			
WCK 771	4->32	8	16	WCK 771	0.25-2	1	2
Ciprofloxacin	4->32	8	16	Ciprofloxacin	0.5-32	4	16
Levofloxacin	4->32	4	8	Levofloxacin	1-8	4	4
Gatifloxacin	2->32	4	4	Gatifloxacin	0.25-2	1	2
Moxifloxacin	2->32	4	8	Moxifloxacin	0.25-2	2	2
Piperacillin	4-32	8	32	Piperacillin	≤0.125-4	0.5	2
Piperacillin-tazobactam	2-16	8	8	Piperacillin-tazobactam	≤0.125-2	0.5	2
Imipenem	0.5-2	1	2	Imipenem	0.016-0.5	0.125	0.25
Metronidazole	≤0.125-1	≤0.125	0.5	Metronidazole	0.5->16	>16	>16
Clindamycin	2->32	32	>32	Clindamycin	≤0.016->32	0.03	>32
<i>Fusobacterium</i> (2/47)				<i>Clostridium perfringens</i> (0/25)			
WCK 771	0.125->32	0.5	8	WCK 771	0.03-0.25	0.06	0.25
Ciprofloxacin	0.5->32	2	8	Ciprofloxacin	0.25-1	0.5	1
Levofloxacin	0.5->32	2	4	Levofloxacin	0.25-2	0.5	1
Gatifloxacin	0.25->32	0.5	4	Gatifloxacin	0.25-1	0.5	0.5
Moxifloxacin	0.125->32	1	4	Moxifloxacin	0.25-1	0.5	0.5
Piperacillin	≤0.125->128	0.25	16	Piperacillin	≤0.125-1	0.5	1
Piperacillin-tazobactam	≤0.125-16	≤0.125	8	Piperacillin-tazobactam	≤0.125-1	0.25	0.5
Imipenem	≤0.008-2	0.25	1	Imipenem	0.06-0.5	0.125	0.25
Metronidazole	≤0.125-1	≤0.125	0.25	Metronidazole	0.5-2	1	1
Clindamycin	≤0.016->32	0.06	32	Clindamycin	0.03-2	0.5	2

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TABLE 1—Continued

Organism (no. of $\beta$ -lactamase-positive strains/no. tested) and drug	MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>			Organism (no. of $\beta$ -lactamase-positive strains/no. tested) and drug	MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>		
	MIC	50%	90%		MIC	50%	90%
<i>Clostridium difficile</i> (0/12)				Piperacillin	$\leq 0.125$ –64	1	16
WCK 771	0.5–4	0.5	1	Piperacillin-tazobactam	$\leq 0.125$ –32	0.25	8
Ciprofloxacin	8–>32	16	16	Imipenem	0.03–1	0.25	0.5
Levofloxacin	4–>32	4	8	Metronidazole	$\leq 0.125$ –4	1	4
Gatifloxacin	1–16	2	2	Clindamycin	0.03–>32	2	16
Moxifloxacin	1–8	1	2	All strains (107/350)			
Piperacillin	8–16	8	16	WCK 771	0.03–>32	0.5	2
Piperacillin-tazobactam	8–32	8	16	Ciprofloxacin	0.25–>32	2	32
Imipenem	4–8	8	8	Levofloxacin	0.125–>32	1	8
Metronidazole	$\leq 0.125$ –0.5	0.25	0.25	Gatifloxacin	0.06–>32	0.5	4
Clindamycin	4–>32	8	>32	Moxifloxacin	0.125–>32	0.5	4
Miscellaneous clostridia (0/23) <sup>f</sup>				Piperacillin	$\leq 0.125$ –>128	2	64
WCK 771	0.03–1	0.125	1	Piperacillin-tazobactam	$\leq 0.125$ –>32	$\leq 0.125$	8
Ciprofloxacin	0.25–8	2	8	Imipenem	$\leq 0.008$ –8	0.125	1
Levofloxacin	0.25–8	1	8	Metronidazole	$\leq 0.125$ –>16	1	>16
Gatifloxacin	0.25–4	0.5	4	Clindamycin	$\leq 0.016$ –>32	0.125	16
Moxifloxacin	0.25–4	0.5	2				

<sup>a</sup> 50% and 90%, MICs at which 50 and 90% of isolates are inhibited, respectively.

<sup>b</sup> *Bacteroides ovatus*, 7; *Bacteroides uniformis*, 4.

<sup>c</sup> *Prevotella disiens*, 9; *Prevotella oris*, 3; *Prevotella loeschii*, 2; *Prevotella oralis* group, 1; *Prevotella denticola*, 1; *Porphyromonas asaccharolytica*, 2; *Porphyromonas gingivalis*, 1.

<sup>d</sup> *Peptostreptococcus asaccharolyticus*, 2; *Peptostreptococcus magnus*, 6; *Peptostreptococcus micros*, 6; *Peptostreptococcus anaerobius*, 5; *Peptostreptococcus tetradius*, 6; *Peptostreptococcus prevotii*, 2.

<sup>e</sup> *Actinomyces* sp., 6; *Bifidobacterium* sp., 9.

<sup>f</sup> *Clostridium tertium*, 6; *Clostridium bifermentans*, 3; *Clostridium cadaveris*, 3; *Clostridium sordellii*, 4; *Clostridium ramosum*, 3; *Clostridium paraputrificum*, 1; *Clostridium histolyticum*, 1; *Clostridium* sp., 2.

*otella* and *Porphyromonas* strains, and 2 of 47 (4.3%) fusobacteria produced  $\beta$ -lactamase. The results of MIC testing are presented in Table 1. Overall, the MICs (in micrograms per milliliter) at which 50 and 90%, respectively, of the isolates tested were inhibited were as follows: WCK 771, 0.5 and 2.0; ciprofloxacin, 2.0 and 32.0; levofloxacin, 1.0 and 8.0; moxifloxacin, 0.5 and 4.0; gatifloxacin, 0.5 and 4.0; piperacillin, 2.0 and 64.0; piperacillin-tazobactam,  $\leq 0.125$  and 8.0; imipenem, 0.125 and 1.0; clindamycin, 0.125 and 16.0; and metronidazole, 1.0 and >16.0. WCK 771 had MICs which were generally one or two dilutions lower than those of gatifloxacin but similar to those of moxifloxacin against all anaerobe groups.

Although the overall WCK 771 MIC at which 90% of the isolates tested were inhibited was one dilution lower than that of moxifloxacin, for the five groupings of *B. fragilis* group species, moxifloxacin was more active than WCK 771 against two species, inferior against one, and the same against two more. For *Prevotella* species, WCK 771 was more active than moxifloxacin for most species, and there was an even split for fusobacteria. All quinolones tested had high MICs against *Fusobacterium varium* and lactobacilli. Additionally, higher quinolone MICs were observed against *B. fragilis* and *Bacteroides vulgatus* strains than against other members of the *B. fragilis* group. Among *Prevotella* spp., quinolone MICs were higher for *P. melaninogenica* than for other members of this genus. Moxifloxacin was more active than WCK 771 for peptostreptococci, lactobacilli, and *Eubacterium lentum* but was inferior by comparison against clostridia. Because strains for which quinolone MICs were raised were not studied for resistance mechanisms, accurate comparisons with recent publications on this aspect cannot be made. The addition of tazobactam enhanced the activity of piperacillin against  $\beta$ -lactamase-producing anaerobic gram-negative bacilli. Although most strains tested were

susceptible to clindamycin (MICs of  $\leq 2$   $\mu\text{g/ml}$ ), resistance was seen in some gram-negative anaerobic rods, peptostreptococci, anaerobic gram-positive non-spore-forming rods, and clostridia. The only anaerobes resistant to metronidazole were the anaerobic gram-positive bacilli.

WCK 771 is a new experimental fluoroquinolone with expanded activity against pneumococci and staphylococci (M. V. Patel, S. V. Gupte, S. K. Agarwal, D. J. Upadhyay, K. Sreenivas, Y. Chugh, N. Shetty, R. K. Beri, N. J. De Souza, and N. Khorakiwala, Abstr. 41st Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-539, 2001; G. A. Pankuch, M. Jacobs, H. Khorakiwala, N. De Souza, M. Patel, and P. C. Appelbaum, Abstr. 41st Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-541, 2001; M. R. Jacobs, S. Bajaksouzian, A. Windau, M. V. Patel, N. de Souza, H. Khorakiwala, and P. C. Appelbaum, Abstr. 41st Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-542, 2001). Of all quinolones tested in our study, WCK 771 had the lowest overall MICs for all strains tested; no previous data on this have been previously available, to our knowledge. The MICs of ciprofloxacin, levofloxacin, gatifloxacin, and moxifloxacin are similar to those reported previously by us and other workers, while the MICs of non-quinolone agents also reflect previous findings, with low MICs of piperacillin-tazobactam and imipenem against  $\beta$ -lactamase-positive and -negative strains and good activity of clindamycin (except against a few gram-negative and -positive rods and clostridia) and metronidazole (except against gram-positive non-spore-forming rods). The few strains for which quinolone MICs were consistently high were predominantly *F. varium*, a rare human pathogen which is more resistant to fluoroquinolones and other antimicrobials than are other fusobacteria (5–7, 9, 11, 12, 18). The strains studied were isolated during the

past 4 years, and we did not observe the increase in quinolone resistance described by Golan and coworkers (10).

The results of this first published in vitro anaerobe study suggest a potential place for WCK 771, with MICs similar to those of moxifloxacin, in treatment of anaerobic and mixed infections where strains of the *B. fragilis* group do not play a major role (e.g., infections of the respiratory tract, skin, and soft tissue), provided that a breakpoint of  $<4.0 \mu\text{g/ml}$  can be achieved. Pharmacokinetic-pharmacodynamic and experimental animal studies are necessary to further delineate the clinical role of these new quinolones in therapy of anaerobic infections.

#### REFERENCES

1. Appelbaum, P. C., A. Philippon, M. R. Jacobs, S. K. Spangler, and L. Gutmann. 1990. Characterization of  $\beta$ -lactamases from non-*Bacteroides fragilis* group *Bacteroides* spp. belonging to seven species and their role in  $\beta$ -lactam resistance. *Antimicrob. Agents Chemother.* **34**:2169–2176.
2. Appelbaum, P. C., S. K. Spangler, and M. R. Jacobs. 1990.  $\beta$ -Lactamase production and susceptibilities to amoxicillin, amoxicillin-clavulanate, ticarcillin, ticarcillin-clavulanate, cefoxitin, imipenem, and metronidazole of 320 non-*Bacteroides fragilis* *Bacteroides* and 129 fusobacteria from 28 U.S. centers. *Antimicrob. Agents Chemother.* **34**:1546–1550.
3. Appelbaum, P. C., S. K. Spangler, G. A. Pankuch, A. Philippon, M. R. Jacobs, R. Shiman, E. J. C. Goldstein, and D. Citron. 1994. Characterization of a  $\beta$ -lactamase from *Clostridium clostridioforme*. *J. Antimicrob. Chemother.* **33**:33–40.
4. Bachoual, R., L. Dubreuil, C.-J. Soussy, and J. Tankovic. 2000. Roles of *gyrA* mutations in resistance of clinical isolates and in vitro mutants of *Bacteroides fragilis* to the new fluoroquinolone trovafloxacin. *Antimicrob. Agents Chemother.* **44**:1842–1845.
5. Barry, A. L., and P. C. Fuchs. 1991. In vitro activities of sparfloxacin, tosufloxacin, ciprofloxacin, and feroxacin. *Antimicrob. Agents Chemother.* **35**:955–960.
6. Barry, A. L., P. C. Fuchs, D. M. Citron, S. D. Allen, and H. M. Wexler. 1993. Methods for testing the susceptibility of anaerobic bacteria to two fluoroquinolone compounds, PD 131628 and clinafloxacin. *J. Antimicrob. Chemother.* **31**:893–900.
7. Bauernfeind, A. 1993. Comparative in vitro activities of the new quinolone, Bay y3118, and ciprofloxacin, sparfloxacin, tosufloxacin, CI-960 and CI-990. *J. Antimicrob. Chemother.* **31**:505–522.
8. Bauernfeind, A. 1997. Comparison of the antibacterial activities of the quinolones Bay 12–8039, gatifloxacin (AM 1155), trovafloxacin, clinafloxacin, levofloxacin and ciprofloxacin. *J. Antimicrob. Chemother.* **40**:639–651.
9. Ednie, L. M., M. R. Jacobs, and P. C. Appelbaum. 1998. Activities of gatifloxacin compared to those of seven other agents against anaerobic organisms. *Antimicrob. Agents Chemother.* **42**:2459–2462.
10. Golan, Y., L. A. McDermott, N. V. Jacobus, E. J. C. Goldstein, S. Finegold, L. J. Harrell, D. W. Hecht, S. G. Jenkins, C. Pierson, R. Venezia, J. Rihs, P. Iannini, S. L. Gorbach, and D. R. Snyderman. 2003. Emergence of fluoroquinolone resistance among *Bacteroides* species. *J. Antimicrob. Chemother.* **52**:208–213.
11. Goldstein, E. J. C., and D. M. Citron. 1992. Comparative activity of ciprofloxacin, ofloxacin, sparfloxacin, temafloxacin, CI-960, CI-990, and Win 57273 against anaerobic bacteria. *Antimicrob. Agents Chemother.* **36**:1158–1162.
12. Hoellman, D. B., L. M. Kelly, M. R. Jacobs, and P. C. Appelbaum. 2001. Comparative antianaerobic activity of BMS 284756. *Antimicrob. Agents Chemother.* **45**:589–592.
13. National Committee for Clinical Laboratory Standards. 2004. Methods for antimicrobial susceptibility testing of anaerobic bacteria, 5th ed. Approved standard. NCCLS publication M11-A6. National Committee for Clinical Laboratory Standards, Wayne, Pa.
14. Oh, H., and C. Edlund. 2003. Mechanisms of quinolone resistance in anaerobic bacteria. *Clin. Microbiol. Infect.* **9**:512–517.
15. Oh, H., N. El Amin, T. Davies, P. C. Appelbaum, and C. Edlund. 2001. *GyrA* mutations associated with quinolone-resistance in *Bacteroides fragilis* group strains. *Antimicrob. Agents Chemother.* **45**:1977–1981.
16. Peterson, M. L., J. C. Rotschafer, and L. J. V. Piddock. 2003. Plasmid-mediated complementation of *gyrA* and *gyrB* in fluoroquinolone-resistant *Bacteroides fragilis*. *J. Antimicrob. Chemother.* **52**:481–484.
17. Ricci, V., M. L. Peterson, J. C. Rotschafer, H. Wexler, and L. J. V. Piddock. 2004. Role of topoisomerase mutations and efflux in fluoroquinolone resistance of *Bacteroides fragilis* clinical isolates and laboratory mutants. *Antimicrob. Agents Chemother.* **48**:1344–1346.
18. Spangler, S. K., M. R. Jacobs, and P. C. Appelbaum. 1994. Activity of CP 99,219 compared with those of ciprofloxacin, grepafloxacin, metronidazole, cefoxitin, piperacillin, and piperacillin-tazobactam against 489 anaerobes. *Antimicrob. Agents Chemother.* **38**:2471–2476.
19. Summanen, P., E. J. Baron, D. M. Citron, C. A. Strong, H. M. Wexler, and S. M. Finegold. 1993. *Wadsworth anaerobic bacteriology manual*, 5th ed. Star Publishing Co., Belmont, Calif.
20. Wexler, H. M., E. Molitoris, D. Molitoris, and S. M. Finegold. 1996. In vitro activities of trovafloxacin against 557 strains of anaerobic bacteria. *Antimicrob. Agents Chemother.* **40**:2232–2235.