

Antimicrobial Activity and Spectrum of LB20304, a Novel Fluoronaphthyridone

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Compound LB20304 is a fluoronaphthyridone carboxylic acid with a novel pyrrolidine substituent. This drug was compared with ciprofloxacin, levofloxacin, ofloxacin, sparfloxacin, and trovafloxacin against over 800 pathogens, most from blood stream infections, by National Committee for Clinical Laboratory Standards reference methods. LB20304 was the most active agent against gram-positive species including strains observed to be resistant to other fluoroquinolones and glycopeptides. The potency of LB20304 (MIC₅₀, 0.03 µg/ml) against the *Enterobacteriaceae* was exceeded only by that of ciprofloxacin (0.015 µg/ml). It has limited activity against gram-negative anaerobes.

Antimicrobial resistance is an increasing clinical problem, particularly among the gram-positive pathogens (12). Contemporary problems include penicillin resistance in *Streptococcus pneumoniae* (6), ampicillin- and glycopeptide-resistant enterococci (3, 12), and oxacillin resistance in staphylococci (11). A number of quinolone compounds (trovafloxacin, clinafloxacin, and DU6859a) with enhanced activity against gram-positive bacteria and which retain good activity against aerobic gram-negative species have been synthesized (1, 2, 9). None of these compounds are available for clinical use at the present time, and it is not apparent which, if any, will have an acceptable pharmacokinetic and safety profile.

LB20304 is a fluoronaphthyridone carboxylic acid with a novel pyrrolidine substituent (11). Previous reports have documented remarkable potency against gram-positive cocci including oxacillin-resistant staphylococci (*Staphylococcus aureus* and *S. epidermidis*) (5, 10). Its activity against aerobic gram-negative bacilli is generally comparable to that of ciprofloxacin (10). It has bactericidal activity against *S. aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* at concentrations at or close to the measured MIC (11). Animal studies suggest that LB20304 may be less epileptogenic than ciprofloxacin (4). Bioavailability after oral administration is 95.3% and 75% in rats and dogs, respectively. LB20304 is effective for therapy of systemic infection in mice when given by the oral route (4). In this study, we have compared the in vitro activity of LB20304 relative to five other quinolone antimicrobials (ciprofloxacin, levofloxacin, ofloxacin, sparfloxacin, and trovafloxacin) using reference susceptibility testing methods (7, 8).

Bacterial strains were more than 800 recent clinical isolates from the collection at the University of Iowa College of Medicine (Iowa City) as outlined in Tables 1 to 3. Strains were selected to include representative examples of contemporary antimicrobial resistance problems, in particular, those that have become more prevalent among the gram-positive cocci.

LB20304 was obtained from Biotech Research Institute (LG Chemical Ltd., Tae Jon, Korea). Ciprofloxacin was provided by Miles Pharmaceuticals (West Haven, Conn.), ofloxacin and levofloxacin by Ortho-McNeil Pharmaceuticals (Raritan, N.J.), sparfloxacin by Rhone-Poulenc Rorer (Collegeville, Pa.), and

trovafloxacin by Pfizer Central Research (Groton, Conn.). Microdilution broth trays were prepared by Prepared Media Laboratories (Tualatin, Oreg.) and stored at -70°C until used. Antimicrobial susceptibility testing was performed by reference methods as recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (7, 8). The susceptibility test medium was Mueller-Hinton broth with added 5% lysed horse blood for susceptibility testing of *S. pneumoniae* and other fastidious species. Anaerobes and pathogenic neisseriae were tested on brucella blood agar and GC agar by the agar dilution method (7, 8), respectively. Quality control of mediums, methods, and antimicrobial agents was performed with *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *S. aureus* ATCC 25923 and 29213, and *Enterococcus faecalis* ATCC 29212. All quality control results were within the published ranges for ciprofloxacin, levofloxacin, and ofloxacin and showed good reproducibility for the investigational compounds.

Results for the non-fastidious aerobic gram-negative bacilli are presented in Table 1. LB20304 is more potent than levofloxacin, ofloxacin, sparfloxacin, or trovafloxacin against most species of *Enterobacteriaceae*. It is approximately one log₂ dilution step less active than ciprofloxacin for most of these species. It is noteworthy that the MICs of all fluoroquinolones, including LB20304, were elevated for strains of those species of *Enterobacteriaceae* (*C. freundii*, *P. rettgeri*, and *P. stuartii*) in which resistance to ciprofloxacin and ofloxacin occurred. Against *Pseudomonas aeruginosa*, LB20304 is equipotent with trovafloxacin, one to two log₂ dilutions less active than ciprofloxacin and more potent than the other fluoroquinolones studied. *Acinetobacter* spp. and *Stenotrophomonas maltophilia* differ from other species of aerobic gram-negative bacilli in that ciprofloxacin is not the most potent of the quinolones studied. The rank order of potency for *Acinetobacter* species was trovafloxacin > LB20304 = sparfloxacin > levofloxacin > ciprofloxacin = ofloxacin. The rank order of activity against *Stenotrophomonas maltophilia* is similar, although against this species, even the most potent of this group of quinolones has only modest activity. As with other fluoroquinolones, LB20304 has limited activity against gram-negative anaerobic bacilli. For *Bacteroides* spp., the LB20304 MICs range from 0.5 to >8 µg/ml and a similar level of activity was observed with a small number of *Prevotella* spp. and *Porphyromonas* spp.

Results for the gram-positive species are summarized in Table 2. LB20304 and trovafloxacin were the most potent com-

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TABLE 1. Antimicrobial activity of LB20304 compared to six other quinolones or naphthyridones tested against 300 aerobic and 25 anaerobic gram-negative bacilli

Organism (no. of isolates tested)	Antimicrobial agent	MIC ($\mu\text{g/ml}$)			% Susceptibility at MIC ($\mu\text{g/ml}$) ^a of:	
		50%	90%	Range	≤ 1	≤ 2
<i>Citrobacter freundii</i> (20)	LB20304	0.03	2	0.015->8	85	95
	Ciprofloxacin	0.015	1	≤ 0.02 ->4	(90)	95
	Levofloxacin	0.06	2	0.015->8	80	(90)
	Ofloxacin	0.12	4	0.03->8	80	(80)
	Sparfloxacin	0.12	8	0.06->8	60	80
	Trovafloxacin	0.06	2	0.015->8	85	90
<i>Citrobacter koseri</i> (10)	LB20304	0.015	0.03	≤ 0.004 -0.03	100	100
	Ciprofloxacin	0.008	0.015	0.008-0.06	(100)	100
	Levofloxacin	0.015	0.06	0.015-0.12	100	(100)
	Ofloxacin	0.06	0.06	0.03-0.12	100	(100)
	Sparfloxacin	0.03	0.12	0.015-0.12	100	100
	Trovafloxacin	0.015	0.03	0.008-0.12	100	100
<i>Escherichia coli</i> (20)	LB20304	0.015	0.015	0.008->8	90	90
	Ciprofloxacin	0.015	0.03	0.008->4	(90)	90
	Levofloxacin	0.03	0.06	0.015->8	90	(90)
	Ofloxacin	0.06	0.12	0.03->8	90	(90)
	Sparfloxacin	0.06	0.06	0.03->8	90	90
	Trovafloxacin	0.015	0.03	0.015->8	90	95
<i>Enterobacter aerogenes</i> (20)	LB20304	0.03	0.12	0.015->8	95	95
	Ciprofloxacin	0.015	1	0.008->4	(90)	90
	Levofloxacin	0.06	0.5	0.03->8	90	(90)
	Ofloxacin	0.12	0.25	0.06->8	90	(90)
	Sparfloxacin	0.12	1	0.06->8	90	90
	Trovafloxacin	0.03	0.25	0.015->8	95	95
<i>Enterobacter cloacae</i> (20)	LB20304	0.03	0.25	0.008->8	90	95
	Ciprofloxacin	0.015	0.12	0.008->4	(90)	90
	Levofloxacin	0.06	0.25	0.03->8	90	(90)
	Ofloxacin	0.12	0.5	0.06->8	90	(90)
	Sparfloxacin	0.12	1	0.03->8	90	90
	Trovafloxacin	0.03	0.5	0.015->8	90	90
<i>Klebsiella oxytoca</i> (10)	LB20304	0.03	0.03	0.015-0.06	100	100
	Ciprofloxacin	0.015	0.03	0.008-0.06	(100)	100
	Levofloxacin	0.06	0.12	0.03-0.25	100	(100)
	Ofloxacin	0.12	0.25	0.06-0.5	100	(100)
	Sparfloxacin	0.12	0.12	0.06-0.25	100	100
	Trovafloxacin	0.03	0.06	0.015-0.12	100	100
<i>Klebsiella pneumoniae</i> (20)	LB20304	0.03	0.12	0.015->8	90	90
	Ciprofloxacin	0.03	0.12	0.008->4	(90)	90
	Levofloxacin	0.06	0.25	0.03->8	90	(90)
	Ofloxacin	0.12	0.5	0.06->8	90	(90)
	Sparfloxacin	0.12	0.5	0.06->8	90	90
	Trovafloxacin	0.06	0.25	0.015->8	90	90
<i>Morganella morgani</i> (10)	LB20304	0.06	0.12	0.015-0.12	100	100
	Ciprofloxacin	0.008	0.015	0.004-0.015	(100)	100
	Levofloxacin	0.03	0.06	0.015-0.12	100	(100)
	Ofloxacin	0.03	0.12	0.03-0.25	100	(100)
	Sparfloxacin	0.25	0.5	0.12-1	100	100
	Trovafloxacin	0.12	0.25	0.03-0.25	100	100
<i>Pantoea agglomerans</i> (10)	LB20304	0.015	0.015	≤ 0.004 -0.03	100	100
	Ciprofloxacin	0.008	0.015	0.008-0.03	(100)	100
	Levofloxacin	0.03	0.06	0.015-0.06	100	(100)
	Ofloxacin	0.06	0.12	0.03-0.12	100	(100)
	Sparfloxacin	0.06	0.06	0.015-0.12	100	100
	Trovafloxacin	0.015	0.03	0.008-0.06	100	100
<i>Proteus mirabilis</i> (20)	LB20304	0.06	0.12	0.03-0.25	100	100
	Ciprofloxacin	0.015	0.03	0.008-0.06	(100)	100

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TABLE 1—Continued

Organism (no. of isolates tested)	Antimicrobial agent	MIC ($\mu\text{g/ml}$)			% Susceptibility at MIC ($\mu\text{g/ml}$) ^a of:	
		50%	90%	Range	≤ 1	≤ 2
	Levofloxacin	0.06	0.06	0.03–0.12	100	(100)
	Ofloxacin	0.06	0.25	0.06–0.25	100	(100)
	Sparfloxacin	0.5	1	0.12–1	100	100
	Trovafloxacin	0.12	0.25	0.03–0.25	100	100
<i>Proteus vulgaris</i> (10)	LB20304	0.03	0.12	0.03–0.5	100	100
	Ciprofloxacin	0.015	0.015	0.008–0.06	(100)	100
	Levofloxacin	0.03	0.06	0.03–0.12	100	(100)
	Ofloxacin	0.06	0.12	0.03–0.25	100	(100)
	Sparfloxacin	0.25	1	0.12–8	90	90
	Trovafloxacin	0.12	0.25	0.06–1	100	100
<i>Providencia rettgeri</i> (10)	LB20304	0.06	8	0.015–>8	80	80
	Ciprofloxacin	0.015	>4	0.008–>4	(80)	80
	Levofloxacin	0.06	8	0.06–>8	80	(80)
	Ofloxacin	0.25	>8	0.12–>8	80	(80)
	Sparfloxacin	0.25	>8	0.12–>8	80	80
	Trovafloxacin	0.03	8	0.03–>8	80	80
<i>Providencia stuartii</i> (10)	LB20304	0.25	>8	0.015–>8	60	60
	Ciprofloxacin	0.12	>4	0.015–>4	(60)	60
	Levofloxacin	0.25	>8	0.06–>8	60	(60)
	Ofloxacin	0.5	>8	0.12–>8	60	(60)
	Sparfloxacin	1	>8	0.12–>8	60	60
	Trovafloxacin	0.25	>8	0.03–>8	60	60
<i>Salmonella enteritidis</i> (10)	LB20304	0.015	0.015	0.008–0.015	100	100
	Ciprofloxacin	0.015	0.015	0.008–0.015	(100)	100
	Levofloxacin	0.03	0.06	0.03–0.06	100	(100)
	Ofloxacin	0.06	0.12	0.06–0.12	100	(100)
	Sparfloxacin	0.06	0.06	0.03–0.12	100	100
	Trovafloxacin	0.03	0.03	0.015–0.06	100	100
<i>Serratia marcescens</i> (20)	LB20304	0.25	0.25	0.12–>8	90	90
	Ciprofloxacin	0.06	0.12	0.06–>4	(90)	90
	Levofloxacin	0.12	0.25	0.12–>8	90	(90)
	Ofloxacin	0.25	0.5	0.25–>8	90	(90)
	Sparfloxacin	1	2	0.5–>8	60	90
	Trovafloxacin	0.25	1	0.12–>8	90	90
<i>Shigella</i> spp. (10)	LB20304	≤ 0.004	0.008	≤ 0.004 –0.015	100	100
	Ciprofloxacin	0.004	0.015	0.004–0.015	(100)	100
	Levofloxacin	0.015	0.03	0.015–0.06	100	(100)
	Ofloxacin	0.03	0.06	0.03–0.06	100	(100)
	Sparfloxacin	0.03	0.03	0.015–0.06	100	100
	Trovafloxacin	0.008	0.015	≤ 0.004 –0.015	100	100
<i>Yersinia enterocolitica</i> (10)	LB20304	0.008	0.015	≤ 0.004 –0.03	100	100
	Ciprofloxacin	0.015	0.03	0.008–0.25	(100)	100
	Levofloxacin	0.03	0.06	0.03–0.5	100	(100)
	Ofloxacin	0.06	0.12	0.06–1	100	(100)
	Sparfloxacin	0.03	0.12	0.015–0.12	100	100
	Trovafloxacin	0.015	0.03	0.008–0.25	100	100
Other <i>Enterobacteriaceae</i> (10) ^b	LB20304	0.015	0.06	≤ 0.004 –0.12	100	100
	Ciprofloxacin	0.008	0.015	0.008–0.25	(100)	100
	Levofloxacin	0.03	0.06	0.015–0.5	100	(100)
	Ofloxacin	0.06	0.12	0.03–0.5	100	(100)
	Sparfloxacin	0.12	0.25	0.015–0.5	100	100
	Trovafloxacin	0.03	0.12	0.008–0.12	100	100
<i>Acinetobacter</i> spp. (10)	LB20304	0.03	0.06	0.015–0.12	100	100
	Ciprofloxacin	0.12	0.5	0.06–1	(100)	100
	Levofloxacin	0.06	0.25	0.06–0.5	100	(100)
	Ofloxacin	0.12	0.5	0.12–1	100	(100)
	Sparfloxacin	0.03	0.12	0.03–0.25	100	100

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TABLE 1—Continued

Organism (no. of isolates tested)	Antimicrobial agent	MIC ($\mu\text{g/ml}$)			% Susceptibility at MIC ($\mu\text{g/ml}$) ^a of:	
		50%	90%	Range	≤ 1	≤ 2
	Trovafloracin	0.015	0.03	0.008–0.12	100	100
<i>Pseudomonas aeruginosa</i> (30)	LB20304	0.25	2	0.12–2	87	100
	Ciprofloxacin	0.12	0.5	0.06–1	(100)	100
	Levofloxacin	0.5	2	0.25–4	73	(90)
	Ofloxacin	1	4	0.5–8	73	(77)
	Sparfloxacin	1	8	0.5–8	63	73
	Trovafloracin	0.25	2	0.12–2	83	100
<i>Stenotrophomonas maltophilia</i> (10)	LB20304	0.5	4	0.25–8	60	70
	Ciprofloxacin	2	>4	1–>4	(40)	50
	Levofloxacin	0.5	4	0.5–8	50	(60)
	Ofloxacin	1	8	0.5–>8	50	(50)
	Sparfloxacin	0.5	8	0.25–>8	60	70
	Trovafloracin	0.5	2	0.06–8	70	90
<i>Bacteroides fragilis</i> gr. (28) ^c	LB20304	1	8	0.5–>8	54	82
Other anaerobic bacilli (7) ^d	LB20304	8		0.5–>8	29	43

^a Percent susceptibility results in parentheses relate to the NCCLS (1995) breakpoints for ciprofloxacin ($\leq 1 \mu\text{g/ml}$), levofloxacin ($\leq 2 \mu\text{g/ml}$), and ofloxacin ($\leq 2 \mu\text{g/ml}$) (8).

^b Includes *Enterobacter sakazakii*, *Enterobacter taylorae*, *Hafnia alvei*, *Klebsiella ozaenae*, *Salmonella typhi*, and *Serratia liquefaciens*.

^c Includes *B. fragilis* (20 strains), *B. ovatus* (two strains), *B. thetaiotaomicron* (four strains), *B. vulgatus* (two strains).

^d Includes *Prevotella* spp. (five strains) and two *Porphyromonas* spp.

pounds tested against staphylococci with LB20304 exhibiting a two-fold greater activity. The activity of all of the study compounds was reduced against oxacillin-resistant strains as compared with the oxacillin-susceptible *S. aureus* and *Staphylococcus haemolyticus* strains. Among strains of *S. epidermidis*, the difference in the potency of LB20304 and other quinolone antimicrobials against oxacillin-susceptible and oxacillin-resistant strains was less marked. Although the MIC_{90s} were higher for the oxacillin-resistant strains, the MIC_{50s} were comparable for the two groups. LB20304 demonstrated remarkable activity against both penicillin-susceptible and penicillin-resistant strains of *S. pneumoniae* (MIC₉₀, 0.015 $\mu\text{g/ml}$) and against all other streptococci (MIC_{90s}, 0.015 to 0.03 $\mu\text{g/ml}$). It is the most potent of the study compounds against the enterococci, although as with the other quinolones, it was much less active against strains with the VanA and VanB glycopeptide resistance phenotypes than against vancomycin-susceptible enterococci (Table 2). LB20304 was generally four- to eight-fold more active than trovafloracin against the streptococci and equally potent to four-fold more active versus the enterococci (strain variation was identified). LB20304 was more potent than the comparator quinolones against *B. cereus*; however, none of the six study antimicrobials show significant activity against most strains of *Corynebacterium jeikeium*. LB20304 has potential useful activity against strains of gram-positive anaerobes, *Clostridium* spp. and *Peptostreptococcus* spp.

The results of LB20304 tested against the more fastidious gram-negative species are found in Table 3. All strains of *Haemophilus influenzae*, *Moraxella catarrhalis*, *N. gonorrhoeae*, and *Neisseria* spp. were inhibited by concentrations of LB20304 less than 0.015 $\mu\text{g/ml}$. The overall rank order of potency against these organisms favored LB20304 > trovafloracin > ciprofloxacin = sparfloxacin > levofloxacin > ofloxacin. However, at potential breakpoint concentrations (≤ 1 or $\leq 2 \mu\text{g/ml}$) all compounds were 100% effective.

The in vitro activity of LB20304 against those strains studied

which were resistant to ciprofloxacin or ceftazidime was assessed (data not shown). It is notable that 50% (at $\leq 1 \mu\text{g/ml}$) to 66% (at $\leq 2 \mu\text{g/ml}$) of ciprofloxacin-resistant bacteria were inhibited by LB20304, although the LB20304 MIC for ciprofloxacin-resistant strains was higher compared to ciprofloxacin-susceptible strains of the same species. Likewise, 75% to 85% of ceftazidime-resistant strains are potentially inhibited by LB20304.

LB20304 is a promising addition to the current series of investigational quinolone or naphthyridone antimicrobials. It showed enhanced activity against gram-positive pathogens while retaining an activity most similar to that of ciprofloxacin against aerobic gram-negative species. The potency of LB20304 against strains of a number of species which exhibit important contemporary antimicrobial resistance indicates the potential role for this agent in therapy of infections for which the currently marketed quinolone antimicrobials have a limited role. The activity of LB20304 against *S. pneumoniae* in addition to the common gram-negative respiratory tract pathogens *H. influenzae* and *M. catarrhalis* suggests a potential role in therapy of respiratory tract infections, particularly as penicillin resistance in *S. pneumoniae* becomes more widespread.

The limited activity of LB20304 against gram-negative anaerobic species is a feature which distinguishes it from trovafloracin, the agent with which it is otherwise most similar in potency and spectrum. It seems unlikely that LB20304 could be used as a single agent in situations in which activity against anaerobic species is required; however in many other circumstances the absence of significant activity against gram-negative anaerobic species may be advantageous in limiting the degree of disturbance of the normal colonic flora. This study confirms and extends previous in vitro activity results of this compound reported by the manufacturer (4, 5, 10). Further studies are needed to determine approximate susceptibility breakpoints, human toxicity, pharmacodynamics, and clinical potential.

TABLE 2. Antimicrobial activity of LB20304 compared to six other quinolones or naphthyridones tested against 403 aerobic and 20 anaerobic gram-positive organisms

Organism (no. of isolates tested)	Antimicrobial agent	MIC ($\mu\text{g/ml}$)			% Susceptibility at MIC ($\mu\text{g/ml}$) ^a of:		
		50%	90%	Range	≤ 1	≤ 2	
<i>Staphylococcus aureus</i>							
Oxacillin susceptible (100)	LB20304	0.015	0.03	$\leq 0.004-1$	100	100	
	Ciprofloxacin	0.25	0.5	0.06->4	(95)	98	
	Levofloxacin	0.12	0.25	0.06-4	98	(98)	
	Ofloxacin	0.25	0.5	0.12-8	98	(98)	
	Sparfloxacin	0.12	0.12	0.06->8	98	98	
	Trovafoxacin	0.015	0.03	$\leq 0.004-1$	100	100	
	Oxacillin resistant (50)	LB20304	1	2	0.008->8	78	92
		Ciprofloxacin	>4	>4	0.25->4	(28)	30
		Levofloxacin	4	>8	0.12->8	36	(40)
		Ofloxacin	8	>8	0.25->8	30	(36)
Sparfloxacin		8	>8	0.06->8	36	42	
Trovafoxacin	0.5	4	0.015->8	78	86		
<i>Staphylococcus epidermidis</i>							
Oxacillin susceptible (23)	LB20304	0.015	0.015	$\leq 0.004-0.015$	100	100	
	Ciprofloxacin	0.25	0.25	0.06-0.25	(100)	100	
	Levofloxacin	0.12	0.25	0.06-0.25	100	(100)	
	Ofloxacin	0.25	0.5	0.12-0.5	100	(100)	
	Sparfloxacin	0.12	0.25	0.06-0.25	100	100	
	Trovafoxacin	0.03	0.03	0.015-0.6	100	100	
	Oxacillin resistant (27)	LB20304	0.008	0.25	$\leq 0.004-1$	100	100
		Ciprofloxacin	0.25	4	0.12->4	(78)	89
		Levofloxacin	0.12	2	0.06-4	81	(93)
		Ofloxacin	0.25	4	0.12->8	78	(89)
Sparfloxacin		0.25	8	0.06-8	81	81	
Trovafoxacin	0.03	0.5	0.015-2	96	100		
<i>Staphylococcus haemolyticus</i>							
Oxacillin susceptible (7)	LB20304	0.008		0.008	100	100	
	Ciprofloxacin	0.12		0.12-0.5	(100)	100	
	Levofloxacin	0.12		0.06-0.25	100	(100)	
	Ofloxacin	0.25		0.12-0.5	100	(100)	
	Sparfloxacin	0.03		0.015-0.06	100	100	
	Trovafoxacin	0.015		0.015-0.03	100	100	
	Oxacillin resistant (13)	LB20304	1	4	0.5-4	77	85
		Ciprofloxacin	>4	>4	1->4	(0)	0
		Levofloxacin	>8	>8	8->8	0	(8)
		Ofloxacin	>8	>8	8->8	0	(0)
Sparfloxacin		>8	>8	8->8	0	0	
Trovafoxacin	2	>8	1->8	8	77		
Coagulase-negative staphylococci (20)							
Oxacillin susceptible (20)	LB20304	0.015	0.015	$\leq 0.004-0.5$	100	100	
	Ciprofloxacin	0.12	0.5	0.06->4	(95)	95	
	Levofloxacin	0.25	0.5	0.03-4	95	(95)	
	Ofloxacin	0.25	1	0.06-8	95	(95)	
	Sparfloxacin	0.25	0.5	0.015-8	95	95	
	Trovafoxacin	0.03	0.06	$\leq 0.004-2$	95	100	
<i>Streptococcus pneumoniae</i>							
Penicillin susceptible (17)	LB20304	0.015	0.015	$\leq 0.004-0.03$	100	100	
	Ciprofloxacin	1	1	0.5-4	(93)	93	
	Levofloxacin	1	1	0.5-1	100	(100)	
	Ofloxacin	2	2	1-4	53	(94)	
	Sparfloxacin	0.12	0.25	0.12-0.5	100	100	
	Trovafoxacin	0.06	0.12	0.06-0.25	100	100	
	Penicillin resistant (13)	LB20304	0.008	0.015	$\leq 0.004-0.03$	100	100
		Ciprofloxacin	1	1	0.25-4	(93)	93
		Levofloxacin	0.5	1	0.5-1	100	(100)
		Ofloxacin	1	2	1-2	77	(100)
Sparfloxacin		0.12	0.25	0.06-0.25	100	100	
Trovafoxacin	0.06	0.12	0.03-0.12	100	100		
Beta-hemolytic <i>Streptococcus</i> spp.							
Group A (20)	LB20304	0.015	0.015	$\leq 0.004-0.03$	100	100	
	Ciprofloxacin	0.25	0.5	0.12-2	(95)	100	

Continued on following page

TABLE 2—Continued

Organism (no. of isolates tested)	Antimicrobial agent	MIC ($\mu\text{g/ml}$)			% Susceptibility at MIC ($\mu\text{g/ml}$) ^a of:		
		50%	90%	Range	≤ 1	≤ 2	
Group B (20)	Levofloxacin	0.5	0.5	0.25–1	100	(100)	
	Ofloxacin	1	1	0.5–2	95	(100)	
	Sparfloxacin	0.25	0.5	0.06–0.5	100	100	
	Trovaflaxacin	0.06	0.12	0.015–0.25	100	100	
	LB20304	0.015	0.03	0.008–0.06	100	100	
	Ciprofloxacin	0.5	1	0.25–1	(100)	100	
	Levofloxacin	0.5	1	0.5–1	100	(100)	
	Ofloxacin	1	2	1–2	85	(100)	
	Sparfloxacin	0.25	0.25	0.12–0.5	100	100	
	Trovaflaxacin	0.12	0.12	0.06–0.25	100	100	
Group C (10)	LB20304	0.008	0.015	≤ 0.004 –0.015	100	100	
	Ciprofloxacin	0.25	0.5	0.12–0.5	(100)	100	
	Levofloxacin	0.25	0.5	0.25–0.5	100	(100)	
	Ofloxacin	1	1	0.25–1	100	(100)	
	Sparfloxacin	0.12	0.25	0.06–0.5	100	100	
	Trovaflaxacin	0.06	0.06	0.015–0.06	100	100	
	LB20304	0.08	0.015	≤ 0.004 –0.015	100	100	
	Ciprofloxacin	0.12	0.5	0.12–0.5	(100)	100	
	Levofloxacin	0.25	0.5	0.12–0.5	100	(100)	
	Ofloxacin	0.5	1	0.5–1	100	(100)	
Group G (10)	Sparfloxacin	0.12	0.25	0.03–0.25	100	100	
	Trovaflaxacin	0.03	0.06	0.015–0.06	100	100	
	<i>Enterococcus</i> spp.						
	Vancomycin susceptible (25)	LB20304	0.12	4	0.03–4	64	84
		Ciprofloxacin	2	>4	0.5–>4	(44)	56
		Levofloxacin	2	>8	0.5–>8	36	(68)
		Ofloxacin	4	>8	1–>8	4	(44)
		Sparfloxacin	2	>8	1–>8	32	80
		Trovaflaxacin	0.5	4	0.5–8	60	80
	<i>vanA</i> (6)	LB20304	2	1	1–8	7	50
Ciprofloxacin		>4		2–>4	(0)	33	
Levofloxacin		4		2–>8	0	(33)	
Ofloxacin		>8		4–>8	0	(0)	
Sparfloxacin		4		2–>8	0	33	
Trovaflaxacin		4		2–>8	0	33	
<i>vanB</i> (10)		LB20304	2	>8	1–>8	20	40
		Ciprofloxacin	>4	>4	0.5–>4	(10)	30
		Levofloxacin	>8	>8	0.5–>8	10	(10)
		Ofloxacin	>8	>8	1–>8	10	(10)
	Sparfloxacin	>8	>8	0.5–>8	10	30	
	Trovaflaxacin	8	>8	0.06–>8	10	30	
	<i>vanC</i> (15)	LB20304	0.12	0.25	0.03–1	100	100
		Ciprofloxacin	1	2	1–4	(60)	93
		Levofloxacin	2	2	1–4	27	(93)
		Ofloxacin	2	4	2–8	0	(53)
Sparfloxacin		1	2	0.5–4	60	93	
Trovaflaxacin		0.25	0.5	0.12–1	100	100	
<i>Bacillus cereus</i> (7)		LB20304	≤ 0.004		≤ 0.004 –0.008	100	100
		Ciprofloxacin	0.03		0.015–0.12	(100)	100
		Levofloxacin	0.06		0.03–0.06	100	(100)
		Ofloxacin	0.12		0.06–0.12	100	(100)
	Sparfloxacin	0.015		0.015–0.03	100	100	
	Trovaflaxacin	0.008		≤ 0.004 –0.015	100	100	
<i>Corynebacterium jeikeium</i> (10)	LB20304	4	4	0.004–8	10	20	
	Ciprofloxacin	>4	>4	0.12–>4	(10)	10	
	Levofloxacin	8	>8	0.12–>8	10	(10)	
	Ofloxacin	>8	>8	0.5–>8	10	(10)	
	Sparfloxacin	>8	>8	0.004–>8	10	10	
	Trovaflaxacin	8	>8	0.06–>8	10	20	
<i>Clostridium</i> spp. (10)	LB20304	0.12	2	0.12–2	80	100	
<i>Peptostreptococcus</i> spp. (10)	LB20304	0.25	2	0.03–2	80	100	

^a Percent susceptibility results in parentheses relate to the NCCLS (1995) breakpoints for ciprofloxacin (≤ 1 $\mu\text{g/ml}$), levofloxacin (≤ 2 $\mu\text{g/ml}$), and ofloxacin (≤ 2 $\mu\text{g/ml}$) (8).

TABLE 3. Antimicrobial activity of LB20304 compared to six other quinolones or naphthyridones tested against 127 fastidious gram-negative respiratory and genital tract pathogens

Organism (no. of isolates tested)	Antimicrobial agent	MIC ($\mu\text{g/ml}$)			% Susceptibility at MIC ($\mu\text{g/ml}$) ^a of:	
		50%	90%	Range	≤ 1	≤ 2
<i>Haemophilus influenzae</i>						
β -Lactamase negative, ampicillin susceptible (20)	LB20304	≤ 0.004	≤ 0.004	≤ 0.004	100	100
	Ciprofloxacin	0.004	0.004	≤ 0.002 –0.008	(100)	100
	Levofloxacin	0.008	0.008	≤ 0.004 –0.015	100	(100)
	Ofloxacin	0.015	0.015	0.008–0.03	100	(100)
	Sparfloxacin	≤ 0.004	≤ 0.004	≤ 0.004 –0.008	100	100
	Trovaflaxacin	≤ 0.004	0.008	≤ 0.004 –0.008	100	100
β -Lactamase positive (20)	LB20304	≤ 0.004	≤ 0.004	≤ 0.004	100	100
	Ciprofloxacin	0.004	0.008	0.002–0.008	(100)	100
	Levofloxacin	0.008	0.008	0.008	100	(100)
	Ofloxacin	0.015	0.015	0.015	100	(100)
	Sparfloxacin	≤ 0.004	≤ 0.004	≤ 0.004	100	100
	Trovaflaxacin	≤ 0.004	0.008	≤ 0.004 –0.008	100	100
β -Lactamase negative, ampicillin resistant (19)	LB20304	≤ 0.004	≤ 0.004	≤ 0.004 –0.015	100	100
	Ciprofloxacin	0.008	0.008	0.004–0.015	(100)	100
	Levofloxacin	0.015	0.015	0.008–0.03	100	(100)
	Ofloxacin	0.015	0.03	0.015–0.03	100	(100)
	Sparfloxacin	≤ 0.004	0.015	≤ 0.004 –0.015	100	100
	Trovaflaxacin	≤ 0.004	0.015	≤ 0.004 –0.015	100	100
<i>Moraxella catarrhalis</i>						
β -Lactamase negative (8)	LB20304	≤ 0.004		≤ 0.004 –0.008	100	100
	Ciprofloxacin	0.015		0.015–0.03	(100)	100
	Levofloxacin	0.03		0.03	100	(100)
	Ofloxacin	0.06		0.06	100	(100)
	Sparfloxacin	0.015		0.015–0.03	100	100
	Trovaflaxacin	0.008		0.008–0.015	100	100
β -Lactamase positive BRO-1 (10)	LB20304	0.015	0.008	≤ 0.004 –0.008	100	100
	Ciprofloxacin	0.015	0.015	0.015	(100)	100
	Levofloxacin	0.03	0.03	0.03	100	(100)
	Ofloxacin	0.06	0.06	0.06	100	(100)
	Sparfloxacin	0.015	0.03	0.015–0.03	100	100
	Trovaflaxacin	0.008	0.008	≤ 0.004 –0.008	100	100
BRO-2 (10)	LB20304	0.008	0.008	≤ 0.004 –0.008	100	100
	Ciprofloxacin	0.015	0.03	0.015–0.03	(100)	100
	Levofloxacin	0.03	0.03	0.03	100	(100)
	Ofloxacin	0.06	0.06	0.06	100	(100)
	Sparfloxacin	0.03	0.03	0.015–0.03	100	100
	Trovaflaxacin	0.008	0.015	0.008–0.015	100	100
<i>Neisseria gonorrhoeae</i>						
β -Lactamase negative, penicillin susceptible (10)	LB20304	0.015	0.015	0.008–0.015	100	100
β -Lactamase positive (20) ^b	LB20304	0.008	0.008	≤ 0.004 –0.03	100	100
β -Lactamase negative, penicillin resistant (10)	LB20304	0.015	0.03	0.015–0.03	100	100

^a Percent susceptibility results in parentheses relate to the NCCLS (1995) breakpoints for ciprofloxacin ($\leq 1 \mu\text{g/ml}$), levofloxacin ($\leq 2 \mu\text{g/ml}$), and ofloxacin ($\leq 2 \mu\text{g/ml}$) (8).

^b Includes *N. meningitidis* (ten strains), *N. sicca* (four strains), *N. flava* (three strains), and *N. subflava* (three strains).

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