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In Vitro and In Vivo Antibacterial Activities of Levofloxacin (*l*-Ofloxacin), an Optically Active Ofloxacin

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The antibacterial activity of levofloxacin was compared with those of ofloxacin, ciprofloxacin, and other antibiotics. In general, levofloxacin was equally active or up to fourfold more active than ofloxacin against all 801 organisms tested. Levofloxacin was 64-fold more active than ciprofloxacin against *Streptococcus pneumoniae* and 2- to 4-fold more active than ciprofloxacin against *Staphylococcus aureus*, *Xanthomonas maltophilia*, and *Bacteroides fragilis*. Levofloxacin was two- to eightfold more active than ciprofloxacin against coagulase-negative staphylococci and *Acinetobacter* spp., although these improvements in potency may not be clinically relevant. Levofloxacin inhibited 90% of streptococci when it was used at concentrations of 1 to 2 μg/ml. Levofloxacin was two- to fourfold less active than ciprofloxacin against most members of the family *Enterobacteriaceae*, such as *Escherichia coli*; *Klebsiella pneumoniae*; *Citrobacter*, *Proteus*, *Providencia*, *Salmonella*, and *Yersinia* spp.; and *Pseudomonas aeruginosa*. Both compounds were equally active against *Pseudomonas cepacia*. The in vitro DNA gyrase inhibitory activity of levofloxacin was as potent as that of ciprofloxacin, with a 50% inhibitory concentration of 0.65 μg/ml against an *E. coli* enzyme. In vivo, oral treatment with levofloxacin was as efficacious or more efficacious than that with ciprofloxacin in systemic as well as pyelonephritis infections in mice. Levofloxacin achieved higher concentrations in the serum and tissue of mice than did ciprofloxacin. This study presents some potential advantages of the pure L isomer of ofloxacin over ciprofloxacin and other quinolones.

During the past decade, there has been continued interest in improving the antibacterial activities of fluorinated quinolones such as norfloxacin (5), ofloxacin (10), ciprofloxacin (12), and fleroxacin (4). Ofloxacin (9, 11) exists as two optically active isomers because of the asymmetric center at C-3 of the oxazine ring, and levofloxacin (*l*-ofloxacin) is the more active of the two isomers (3).

In this report, we describe the in vitro and in vivo antibacterial activities of levofloxacin compared with those of other antibiotics. Levofloxacin was synthesized at Daiichi Seiyaku Co., Ltd., Tokyo, Japan. All other antibiotics were obtained from their respective manufacturers. Organisms were fresh clinical isolates obtained from clinical laboratories throughout the continental United States between 1990 and 1991. MICs and MBCs were determined in Mueller-Hinton agar by the procedures of the National Committee for Clinical Laboratory Standards (7, 8) by using a final inoculum of 10^4 CFU per spot. GC agar (BBL Microbiology Systems, Cockeysville, Md.) was supplemented with lysed sheep blood and IsoVitaleX (BBL Microbiology Systems, Cockeysville, Md.) for *Neisseria*, *Haemophilis*, and *Branhamella* species. The inhibitory activities of levofloxacin and other quinolones against *Escherichia coli* DNA gyrase in vitro were compared by an established method by using pBR322 DNA as the substrate (1).

The therapeutic effects of levofloxacin were determined against acute systemic and localized infections in mice. For systemic infections, female mice (CF-1; weight, 20 ± 2 g) were challenged with one 100% lethal dose (LD_{100}) by intraperitoneal injection of bacteria. Treatment was administered orally 1 and 3 h after infection. The 50% effective dose (ED_{50}) was calculated on day 7 after infection. In another study, mice were challenged with 100× the LD_{50}, and treatment was one dose given intravenously 1 h after infection.

The efficacies of levofloxacin in pyelonephritis and pneumococcal lower respiratory tract infections (LRTIs) in mice were also determined and compared with those of ciprofloxacin. Pyelonephritis was established with *Staphylococcus aureus* by a previously described method (2). Treatment was oral, starting 1 and 4 h after infection, and was continued twice daily for a total of 4 days. Twenty-four hours after the last treatment, kidneys were excised, weighed, and homogenized, and viable bacterial counts were quantitated. LRTIs were established after nasal instillation of 2×10^7 CFU of *Streptococcus pneumoniae* into anesthetized mice. Oral treatment consisted of two doses given 24 h after infection. Twenty-four hours after treatment, the lungs were excised, weighed, and homogenized, and viable counts were quantitated. Concentrations of levofloxacin and ciprofloxacin in serum and tissue were assayed by an agar well diffusion method with *E. coli* OC 160 as the indicator organism.

The overall in vitro activity of levofloxacin compared with those of the reference compounds is summarized in Table 1. Levofloxacin, in general, was equally active or up to fourfold more active than ofloxacin against all of the organisms tested. Levofloxacin was the most active compound tested against *S. aureus*, including methicillin-resistant strains. All

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TABLE 1. Comparative in vitro activities of levofloxacin

Organism (no. of isolates)	Antimicrobial agent	MIC (μg/ml)		
		Range	50%	90%
Staphylococcus aureus, methicillin resistant (46)	Levofloxacin	0.25–32.0	0.5	0.5
	Ofloxacin	0.5–32.0	1.0	2.0
	Ciprofloxacin	0.12–64.0	0.5	2.0
	Norfloxacin	0.5–>128.0	2.0	4.0
Staphylococcus aureus, methicillin susceptible (63)	Levofloxacin	0.12–16.0	0.25	0.5
	Ofloxacin	0.25–32.0	0.5	2.0
	Ciprofloxacin	0.25–64.0	0.5	2.0
	Norfloxacin	0.5–>128.0	2.0	4.0
	Methicillin	2.0–8.0	4.0	8.0
	Vancomycin	1.0–4.0	2.0	2.0
Coagulase-negative staphylococci, methicillin resistant (22)	Levofloxacin	0.25–16.0	0.25	8.0
	Ofloxacin	0.5–16.0	0.5	16.0
	Ciprofloxacin	0.25–64.0	0.5	16.0
	Norfloxacin	0.5–>128.0	2.0	128.0
	Methicillin	32.0–>128.0	>128.0	>128.0
	Vancomycin	2.0–4.0	4.0	4.0
Coagulase-negative staphylococci, methicillin susceptible (18)	Levofloxacin	0.12–16.0	0.25	8.0
	Ofloxacin	0.25–32.0	0.5	16.0
	Ciprofloxacin	0.12–128.0	0.5	64.0
	Norfloxacin	0.5–>128.0	2.0	128.0
	Methicillin	1.0–8.0	4.0	8.0
	Vancomycin	1.0–4.0	2.0	4.0
Group A streptococci (28)	Levofloxacin	0.5–2.0	0.5	2.0
	Ofloxacin	1.0–4.0	1.0	4.0
	Ciprofloxacin	0.25–4.0	0.5	2.0
	Norfloxacin	1.0–32.0	4.0	8.0
	Enoxacin	4.0–32.0	16.0	32.0
	Ampicillin	0.015–0.03	0.03	0.03
Group B/C streptococci (23)	Levofloxacin	0.5–1.0	0.5	1.0
	Ofloxacin	1.0–2.0	2.0	2.0
	Ciprofloxacin	1.0–2.0	2.0	2.0
	Norfloxacin	4.0–16.0	4.0	16.0
	Enoxacin	8.0–32.0	32.0	32.0
	Ampicillin	0.03–0.5	0.25	0.5
Enterococcus faecalis (22)	Levofloxacin	0.25–4.0	1.0	2.0
	Ofloxacin	0.5–8.0	2.0	8.0
	Ciprofloxacin	1.0–4.0	2.0	4.0
	Norfloxacin	4.0–16.0	8.0	16.0
	Enoxacin	4.0–128.0	8.0	32.0
	Ampicillin	0.5–64.0	1.0	32.0
Streptococcus pneumoniae (19)	Levofloxacin	1.0–2.0	1.0	2.0
	Ofloxacin	2.0–4.0	2.0	2.0
	Ciprofloxacin	0.03–4.0	1.0	4.0
	Norfloxacin	2.0–16.0	8.0	16.0
	Enoxacin	8.0–32.0	8.0	16.0
	Ampicillin	0.03–0.5	0.06	0.06
Escherichia coli (90)	Levofloxacin	≤0.008–0.25	0.06	0.06
	Ofloxacin	≤0.008–0.25	0.12	0.12
	Ciprofloxacin	≤0.008–0.06	0.03	0.03
	Norfloxacin	0.015–0.25	0.12	0.12
	Ceftazidime	0.06–8.0	0.25	1.0

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TABLE 1—*Continued*

Organism (no. of isolates)	Antimicrobial agent	MIC (μg/ml)		
		Range	50%	90%
Klebsiella pneumoniae (44)	Levofloxacin	0.03–0.5	0.12	0.25
	Ofloxacin	0.06–2.0	0.12	0.5
	Ciprofloxacin	0.015–0.25	0.06	0.12
	Norfloxacin	0.06–1.0	0.25	0.25
	Ceftazidime	0.06–64.0	0.25	1.0
Enterobacter cloacae (21)	Levofloxacin	0.015–0.5	0.06	0.12
	Ofloxacin	0.03–1.0	0.12	0.25
	Ciprofloxacin	≤0.008–0.12	0.03	0.12
	Norfloxacin	0.03–2.0	0.12	0.25
	Enoxacin	0.03–1.0	0.25	0.5
	Ceftazidime	0.12–>128.0	0.5	128.0
Citrobacter species (13)	Levofloxacin	0.06–0.25	0.06	0.12
	Ofloxacin	0.12–0.5	0.12	0.25
	Ciprofloxacin	0.015–0.06	0.03	0.06
	Norfloxacin	0.06–0.25	0.12	0.25
	Ceftazidime	0.12–0.5	0.25	0.5
Serratia marcescens (24)	Levofloxacin	0.06–4.0	0.25	0.5
	Ofloxacin	0.25–4.0	0.5	1.0
	Ciprofloxacin	0.03–4.0	0.25	0.5
	Norfloxacin	0.12–8.0	0.5	1.0
	Ceftazidime	0.12–8.0	1.0	2.0
Proteus mirabilis (12)	Levofloxacin	0.06–0.25	0.12	0.25
	Ofloxacin	0.12–0.5	0.25	0.5
	Ciprofloxacin	0.06–0.25	0.06	0.12
	Norfloxacin	0.06–1.0	0.25	1.0
	Gentamicin	1.0–4.0	2.0	4.0
Providencia stuartii (17)	Levofloxacin	≤0.008–2.0	0.12	0.25
	Ofloxacin	≤0.008–4.0	0.25	0.5
	Ciprofloxacin	≤0.008–2.0	0.06	0.12
	Norfloxacin	0.015–4.0	0.25	0.25
	Ceftazidime	0.03–1.0	0.12	0.5
Providencia rettgeri (15)	Levofloxacin	0.015–0.5	0.12	0.5
	Ofloxacin	0.03–2.0	0.25	1.0
	Ciprofloxacin	≤0.008–1.0	0.03	0.12
	Norfloxacin	0.06–8.0	0.12	0.5
	Ceftazidime	0.015–2.0	0.06	0.5
Salmonella species (35)	Levofloxacin	0.03–0.12	0.06	0.12
	Ofloxacin	0.06–0.25	0.12	0.12
	Ciprofloxacin	0.015–0.06	0.03	0.03
	Norfloxacin	0.06–0.25	0.12	0.25
	Ceftazidime	0.25–2.0	0.5	1.0
Yersinia enterocolitica (12)	Levofloxacin	0.015–1.0	0.03	0.12
	Ofloxacin	0.03–2.0	0.06	0.25
	Ciprofloxacin	≤0.008–1.0	0.015	0.06
	Norfloxacin	0.03–4.0	0.06	0.25
	Enoxacin	0.03–4.0	0.12	0.5
	Ceftazidime	0.03–32.0	0.12	4.0
Pseudomonas aeruginosa (74)	Levofloxacin	0.25–128.0	1.0	8.0
	Ofloxacin	0.50–128.0	2.0	8.0
	Ciprofloxacin	0.06–64.0	0.25	2.0
	Enoxacin	0.25–128.0	1.0	8.0
Pseudomonas cepacia (17)	Levofloxacin	0.06–8.0	0.25	2.0
	Ofloxacin	0.12–16.0	0.5	4.0
	Ciprofloxacin	0.06–8.0	0.25	2.0
	Norfloxacin	0.25–32.0	4.0	16.0
	Enoxacin	0.25–16.0	2.0	4.0
	Ceftazidime	0.06–>128.0	64.0	>128.0

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TABLE—*Continued*

Organism (no. of isolates)	Antimicrobial agent	MIC (μg/ml)		
		Range	50%	90%
Xanthomonas maltophilia (24)	Levofloxacin	0.5–2.0	1.0	2.0
	Ofloxacin	1.0–4.0	2.0	4.0
	Ciprofloxacin	1.0–4.0	2.0	4.0
	Norfloxacin	16.0–32.0	32.0	32.0
	Enoxacin	4.0–16.0	8.0	16.0
	Ceftazidime	8.0–>128.0	64.0	>128.0
Acinetobacter species (24)	Levofloxacin	0.06–16.0	0.12	16.0
	Ofloxacin	0.12–32.0	0.25	32.0
	Ciprofloxacin	0.06–128.0	0.25	128.0
	Norfloxacin	0.12–>128.0	2.0	>128.0
	Ceftazidime	0.25–>128.0	8.0	128.0
Haemophilus influenzae (34)	Levofloxacin	0.015–0.03	0.015	0.015
	Ofloxacin	0.03–0.12	0.06	0.06
	Ciprofloxacin	≤0.008–≤0.008	≤0.008	≤0.008
	Norfloxacin	0.06–0.5	0.12	0.12
	Enoxacin	0.12–0.5	0.25	0.25
	Ampicillin	0.12–>4.0	0.25	>4.0
	Cefaclor	8.0–128.0	8.0	32.0
Neisseria gonorrhoeae (19)	Levofloxacin	≤0.008–0.015	0.015	0.015
	Ofloxacin	0.015–0.06	0.015	0.06
	Ciprofloxacin	≤0.008–≤0.008	≤0.008	≤0.008
	Norfloxacin	0.06–0.12	0.06	0.06
	Enoxacin	0.03–0.12	0.06	0.12
	Ampicillin	0.015–128.0	0.12	0.5
Branhamella catarrhalis (29)	Levofloxacin	0.06–0.06	0.06	0.06
	Ofloxacin	0.06–0.12	0.12	0.12
	Ciprofloxacin	0.015–0.06	0.06	0.06
	Norfloxacin	0.12–0.5	0.25	0.25
	Enoxacin	0.12–0.5	0.25	0.25
	Ampicillin	≤0.008–16.0	≤0.008	0.015
Bacteroides fragilis (39)	Levofloxacin	1.0–8.0	2.0	2.0
	Ofloxacin	2.0–16.0	4.0	8.0
	Ciprofloxacin	4.0–32.0	8.0	8.0
	Clindamycin	0.06–>128.0	1.0	8.0
	Metronidazole	0.5–2.0	1.0	2.0
	Rifampin	0.25–1.0	0.5	0.5
Peptostreptococcus species (11)	Levofloxacin	0.5–8.0	1.0	8.0
	Ofloxacin	1.0–16.0	2.0	16.0
	Ciprofloxacin	0.5–4.0	2.0	4.0
	Clindamycin	0.06–16.0	0.12	1.0
	Metronidazole	0.25–1.0	0.5	1.0
	Rifampin	≤0.008–1.0	≤0.008	1.0
	Penicillin G	0.015–8.0	0.015	4.0
Clostridium species (6)	Levofloxacin	1.0–8.0		
	Ofloxacin	1.0–16.0		
	Ciprofloxacin	1.0–32.0		
	Clindamycin	0.06–32.0		
	Metronidazole	1.0–2.0		
	Rifampin	≤0.008–1.0		
	Penicillin G	0.12–1.0		

quinolones tested, however, had high upper-range values that were above clinically useful concentrations against staphylococci, but the MICs of levofloxacin for 90% of these organisms (MIC_{90}s) were within attainable levels in humans. The MIC_{90} of levofloxacin for *S. aureus* was 0.5 μg/ml. This was fourfold more active than ciprofloxacin. Levofloxacin was eightfold more active than ciprofloxacin against methicillin-susceptible, coagulase-negative staphylococci and twofold more active than ciprofloxacin against methicillin-resistant, coagulase-negative staphylococci. The MIC_{90} of levofloxacin against *S. pneumoniae* was 2.0 μg/ml; this activity was two times greater than that of ciprofloxacin. The MIC of levofloxacin ranged from 1 to 2 μg/ml against other streptococci. Against various species of enteric organisms,

TABLE 2. Efficacies of levofloxacin, ciprofloxacin, or norfloxacin in systemic infections in mice

Organism	Compound	MIC (μg/ml)	Inoculum (CFU/mouse)	ED_{50} (mg/kg)
Escherichia coli OC 40	Levofloxacin	0.06	2.6×10^6	0.75 (0.54–1.10)[a]
	Ciprofloxacin	0.03		1.01 (0.73–1.42)
	Norfloxacin	0.12		13.39 (9.62–22.56)
Staphylococcus aureus OC 39, methicillin susceptible	Levofloxacin	0.25	2.4×10^7	4.05 (3.03–5.04)
	Ciprofloxacin	0.5		13.89 (10.09–22.40)
	Norfloxacin	2.0		>20
Pseudomonas aeruginosa OC 34	Levofloxacin	0.5	2.6×10^4	3.1 (1.8–4.5)
	Ciprofloxacin	0.12		4.7 (3.4–6.6)
	Norfloxacin	0.5		13.1 (8.8–21.5)
Klebsiella pneumoniae OC 41	Levofloxacin	0.12	2.9×10^5	0.44 (0.32–0.60)
	Ciprofloxacin	0.06		0.73 (0.52–1.04)
	Norfloxacin	0.12		3.97 (2.79–5.97)

[a] Values in parentheses are 95% confidence limits.

levofloxacin inhibited 90% of the isolates at 0.5 μg/ml or less and was two- to fourfold more active than norfloxacin but two- to fourfold less active than ciprofloxacin. Against *Pseudomonas aeruginosa*, levofloxacin inhibited 90% of the isolates at 8 μg/ml; its activity was inferior to that of ciprofloxacin and equal to that of enoxacin. The MIC_{90} of levofloxacin against *Xanthomonas maltophilia* was superior to that of ciprofloxacin. Levofloxacin and ciprofloxacin were equally active against *Branhamella catarrhalis*. Both *Neisseria gonorrhoeae* and *B. catarrhalis* were highly susceptible to levofloxacin, which inhibited 90% of the isolates at a concentration of less than or equal to 0.06 μg/ml. Levofloxacin was fourfold more active than ciprofloxacin against *Bacteroides fragilis* and *Clostridium* species. On the basis of the *E. coli* DNA gyrase inhibitory activity, levofloxacin at a concentration of 0.65 μg/ml inhibited 50% of the DNA supercoiling activity (data not shown), which was comparable to the inhibitory activity of ciprofloxacin. As with other quinolones, the addition of Mg^{2+} and Ca^{2+} had minimal effects on the MICs and MBCs of levofloxacin, and its activity decreased four- to eightfold under acidic conditions at pH 5.5 or in human urine (data not shown).

The in vivo oral efficacy of levofloxacin compared with those of the other quinolones tested is given in Table 2. Levofloxacin was very effective in protecting mice in this model of systemic infections with *E. coli*, *S. aureus*, *P. aeruginosa*, and *Klebsiella pneumoniae*. Levofloxacin was as potent as ciprofloxacin and was 15 times more potent than norfloxacin against an *E. coli* infection. Levofloxacin was three times more potent than ciprofloxacin against an *S. aureus* infection, whereas norfloxacin was ineffective. Levofloxacin was also about one and one-half times more potent than ciprofloxacin against *P. aeruginosa* and *K. pneumoniae* infections. When given in intravenous doses (Table 3), levofloxacin was more potent than ofloxacin, which was consistent with the in vitro data that were obtained.

In an LRTI model (Table 4), levofloxacin at oral doses of 20 and 40 mg/kg of body weight reduced the number of *S. pneumoniae* cells in lungs from control levels of 8.1 log units to 6.4 and 5.5 log units, respectively ($P < 0.05$). Compared with the control, ciprofloxacin at the same doses was ineffective. In a pyelonephritis model in mice infected with *S. aureus* (Fig. 1), levofloxacin at doses of 3.125 to 25 mg/kg

TABLE 3. Comparative in vivo activities of levofloxacin

Organism	Compound	MIC (μg/ml)	Inoculum (CFU/mouse)[a]	ED_{50} (mg/kg)[b]
Staphylococcus aureus OC667, methicillin resistant	Levofloxacin	0.25	1.8×10^8	9.4 (6.5–15.2)
	Ofloxacin	0.5		11.6 (6.7–26.5)
Staphylococcus aureus OC 39, methicillin susceptible	Levofloxacin	0.25	1.0×10^7	3.7 (2.7–5.0)
	Ofloxacin	0.5		4.9 (2.5–6.5)
Pseudomonas aeruginosa OC 43	Levofloxacin	0.5	1.7×10^7	6.2 (4.7–7.9)
	Ofloxacin	0.5		11.6 (8.8–13.7)

[a] Inocula were 100 times the LD_{50}.
[b] Treatment consisted of one intravenous dose given 1 h postchallenge.

TABLE 4. In vivo efficacies of single doses of levofloxacin or ciprofloxacin in pneumococcal LRTIs in mice

Antibiotic	Oral dose (mg/kg)	Log CFU/g of lung (mean ± SD)
Control	0	8.12 ± 0.33
Levofloxacin[a]	10	7.93 ± 0.38
	20	6.39 ± 2.31[b]
	40	5.47 ± 2.47[b]
Ciprofloxacin	10	8.11 ± 0.48
	20	8.54 ± 0.47
	40	7.51 ± 1.02

[a] The MICs of levofloxacin and ciprofloxacin against *S. pneumoniae* were 1 μg/ml.
[b] $P < 0.05$; the data were ranked and an analysis of variance (F test) was applied to the ranked data (10 mice per dose).

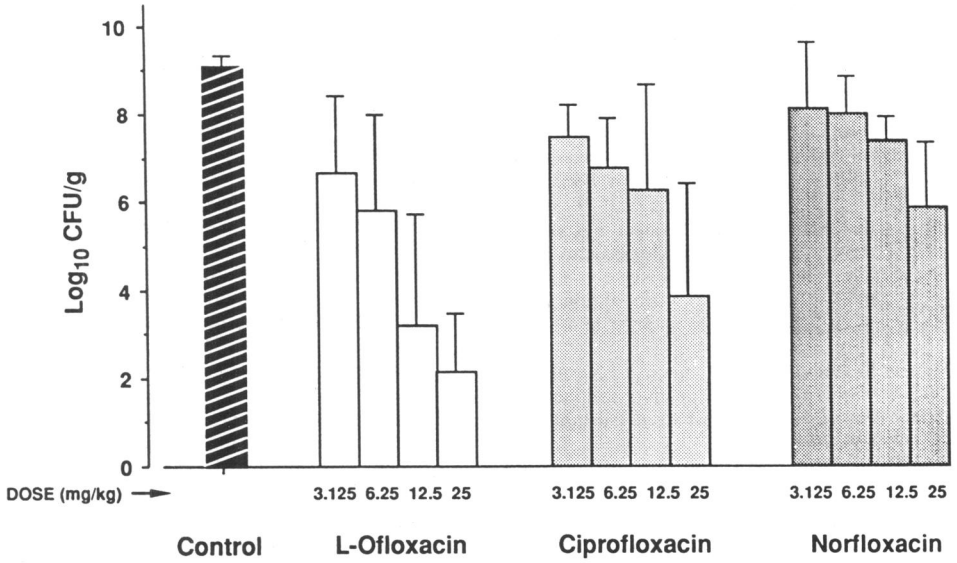

FIG. 1. Therapeutic efficacies of levofloxacin in *S. aureus* pyelonephritis in mice. The lines above the bars are standard deviations.

reduced the viable cell counts by 2.5 to 7 log units, respectively, compared with the counts in the vehicle-treated controls ($P < 0.05$). Ciprofloxacin at the same doses reduced the viable cell counts by 1.7 to 5.3 log units, and norfloxacin reduced the viable cell counts by only 1 to 3.3 log units. The calculated ED_{50}s for this infection were 9.2, 21.3, and 35.9 mg/kg for levofloxacin, ciprofloxacin, and norfloxacin, respectively.

After a single oral administration of 20 mg/kg, levofloxacin achieved significantly higher concentrations in the sera and kidneys of mice than did ciprofloxacin (Table 5 and Fig. 2). Absorption of levofloxacin was rapid, with a peak level in serum of 2.5 μg/ml observed within 30 min; in comparison, the peak level of ciprofloxacin in serum was 0.5 μg/ml. For levofloxacin, the level remained above 1 μg/ml for 60 min; these concentrations are inhibitory against most pathogens.

Our results indicate that levofloxacin is a broad-spectrum antibacterial agent and is effective in treating mice given lethal infections with different clinical pathogens. In vitro, it is more active than ciprofloxacin against *S. aureus*, including methicillin-resistant *S. aureus*, *X. maltophilia*, and *B. fragilis*. Levofloxacin, with an MIC_{90} of 2 μg/ml, is two times more active than ciprofloxacin against *S. pneumoniae*. The in vitro DNA gyrase inhibitory activity of levofloxacin was as potent to that of ciprofloxacin, with a 50% inhibitory concentration of 0.65 μg/ml against an *E. coli* enzyme (data not shown). In vivo mouse protection studies indicated that levofloxacin is as active or is more active than ciprofloxacin against selected gram-negative organisms and is three times more potent than ciprofloxacin against *S. aureus*. In localized infection models such as pyelonephritis caused by *S. aureus* and LRTIs caused by *S. pneumoniae* in mice, levofloxacin was more efficacious than ciprofloxacin. These data suggest that levofloxacin exhibits more potent in vivo efficacy than ciprofloxacin, possibly because of its higher levels in serum and greater tissue penetration.

TABLE 5. Concentrations of levofloxacin and ciprofloxacin in kidneys after a single oral administration of 20 mg/kg in mice[a]

Time (min)	Concn (μg/g [mean ± SD])	
	Levofloxacin	Ciprofloxacin
15	4.55 ± 1.60	0.59 ± 0.11
30	3.59 ± 0.65	0.52 ± 0.07
60	1.55 ± 0.29	0.27 ± 0.15
120	0.48 ± 0.21	0.24 ± 0.23
180	0.59 ± 0.27	0.03 ± 0.02

[a] Ten mice were tested at each time interval.

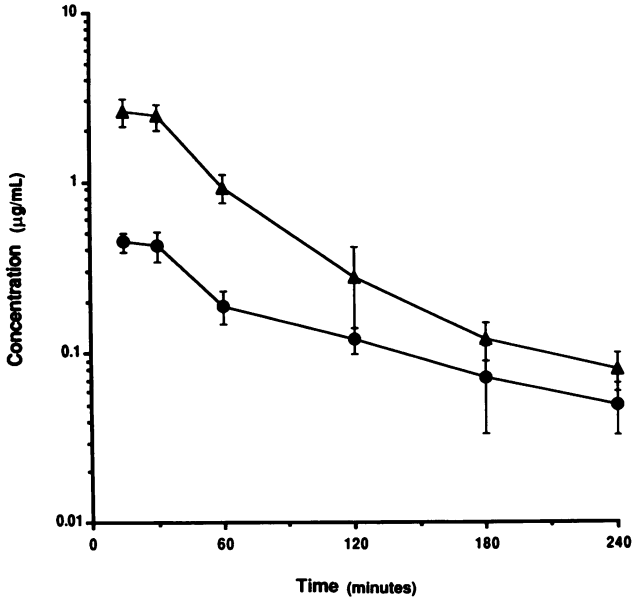

FIG. 2. Concentrations (mean ± standard deviation) of levofloxacin (▲) and ciprofloxacin (●) in serum after a single 20-mg/kg oral dose in mice.

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ERRATUM

In Vitro and In Vivo Antibacterial Activities of Levofloxacin (*l*-Ofloxacin), an Optically Active Ofloxacin

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Volume 36, no. 4, p. 860, line 3 of the abstract: "64-fold" should read "twofold."