ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 1988, p. 1450–1455
0066-4804/88/091450-06$02.00/0

Vol. 32, No. 9

In Vitro Activities of PD 117,596 and Reference Antibiotics against 448 Clinical Bacterial Strains

RAYMOND P. SMITH,* ALDONA L. BALTCH, MARK C. HAMMER, AND JOSEPH V. CONROY

Division of Infectious Diseases, Department of Medicine, Veterans Administration Medical Center and Albany Medical College, Albany, New York 12208

Received 26 February 1988/Accepted 7 June 1988

The in vitro activity of PD 117,596, a new fluoroquinolone antibiotic, was tested against 448 bacterial isolates (15 genera) by agar dilution (inoculum, 10^4 CFU per spot). The activity of PD 117,596 was compared with that of 15 antibiotics against 327 gram-negative strains and with that of 8 other antibiotics against 121 gram-positive strains. PD 117,596 demonstrated the best activity against *Klebsiella* spp., *Enterobacter* spp., *Acinetobacter* spp., *Serratia marcescens*, and *Branhamella catarrhalis* (MICs for 90% of the isolates [MIC_{90}s], 0.008 to 0.25 μg/ml). PD 117,596 (MIC_{90}, 0.25 μg/ml) was at least twofold more active than ciprofloxacin against *Pseudomonas aeruginosa* and *Pseudomonas* spp. PD 117,596 and ciprofloxacin were similar in activity against *Escherichia coli*, *Proteus mirabilis*, *Haemophilus influenzae*, *H. parainfluenzae*, *Neisseria gonorrhoeae*, *Legionella pneumophila*, and *Campylobacter jejuni* (MIC_{90}, 0.002 to 0.125 μg/ml). PD 117,596 was more active than ciprofloxacin against streptococcal groups A, B, C, and G, *S. pneumoniae*, and enterococci (MIC_{90}s, 0.06 to 0.125 μg/ml). Against *Staphylococcus aureus*, including methicillin-resistant isolates, PD 117,596 (MIC_{90}s, 0.03 to 0.06 μg/ml) was 4- to 16-fold more active than ciprofloxacin and was most active against *Corynebacterium* spp. PD 117,596 appears to be the most active fluoroquinolone to date, with excellent activity against gram-positive bacteria and enhanced activity against gram-negative aerobic-facultative bacteria.

PD 117,596 is a recently synthesized, orally administered bactericidal antibiotic of the fluoroquinolone class (8). The structural formulas of PD 117,596 and nalidixic acid are shown in Fig. 1. The addition of the fluorine atom at the 8 position improves both in vivo and in vitro antibacterial activity against gram-positive cocci. The substitution of a 3-amino pyrrolidine side chain for the piperazine moiety of other active agents also improves gram-positive activity and maintains the high tissue absorption associated with the piperazine group. A cyclopropyl group at position 1 contributes to activity against gram-negative bacilli (8). The currently studied quinolone compounds are known to be active against many gram-negative microorganisms (1–7, 9). Their activity against gram-positive bacteria varies considerably, a factor which may limit their use in empiric therapy. Since PD 117,596 has been demonstrated to have marked activity against some gram-positive cocci as well as improved activity against a small number of gram-negative organisms including *Pseudomonas aeruginosa* (8), we evaluated its activity against a wide variety of clinical bacterial isolates.

We studied the in vitro activity of PD 117,596 against 327 gram-negative and 121 gram-positive aerobic clinical bacterial isolates, and we compared its inhibitory activity with that of ciprofloxacin, CI 934, and 13 other reference antibacterial agents.

Bacterial isolates. A total of 448 facultative and aerobic clinical bacterial isolates were obtained from the Veterans Administration Medical Center, Albany Medical Center Hospital, and the Bacteriology Laboratory of the Wadsworth Laboratories for Research of the New York State Health Department, Albany. The organisms tested and the number of strains of each species are listed in Table 1. Control strains included *Escherichia coli* ATCC 25922, *P. aeruginosa* ATCC 27853, and *Streptococcus faecalis* ATCC 29212.

Antibacterial agents. Antibiotic standards and sources from which each was obtained were as follows: PD 117,596, CI 934, and chloramphenicol from Warner-Lambert Co., Pharmaceutical Research Division, Ann Arbor, Mich.; ciprofloxacin from Miles Laboratories, Inc., Elkhart, Ind.; aztreonam from E. R. Squibb & Sons, Princeton, N.J.; piperacillin from Lederle Laboratories, Pearl River, N.Y.; cephalothin and vancomycin from Eli Lilly & Co., Indianapolis, Ind.; oxacillin and amikacin from Bristol-Myers Laboratories, Wallingford, Conn.; clindamycin and erythromycin from The Upjohn Co., Kalamazoo, Mich.; imipenem from Merck Sharp & Dohme, Rahway, N.J.; trimethoprim-sulfamethoxazole from Sigma Chemical Co., St. Louis, Mo.

Susceptibility testing. Antibiotic susceptibilities were determined by the agar dilution technique (11) with double dilutions of antibiotic and a Steers replicator (10). Bacteria from overnight agar cultures (48 h of growth was used for *Legionella pneumophila*) were suspended in 0.9% NaCl to a final concentration of 10^7 CFU/ml. The replicating device delivered 10^4 CFU per spot to the surface of antibiotic-containing agar plates. All prepared plates were used within 24 to 48 h. The following agar and incubation conditions were used: for members of the family *Enterobacteriaceae*, *Pseudomonas* spp., *S. aureus*, and coagulase-negative staphylococci, Mueller-Hinton agar (MHA), in air, 37°C, 18 h; for *Corynebacterium* spp. and all streptococci, MHA with

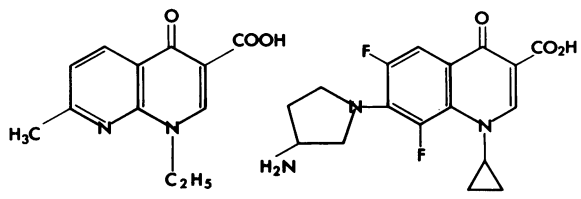

FIG. 1. Chemical structures of nalidixic acid (left) and PD 117,596 (right).

* Corresponding author.

TABLE 1. In vitro activity of PD 117,596 and reference antibacterial agents

Organism (no. of isolates tested)	Test agent	MIC (μg/ml)		
		50%	90%	Range
Acinetobacter calcoaceticus subsp. *anitratus* (14)	PD 117,596	0.03	0.125	≤0.008–0.5
	CI 934	1.0	4.0	0.06–8.0
	Imipenem	0.125	0.5	0.125–0.5
	Ciprofloxacin	0.25	1.0	0.06–4
	Aztreonam	16.0–32.0	32.0	4.0–64.0
	Piperacillin	8.0	32.0	4.0–32.0
	Amikacin	1.0	4.0	0.5–16
	Cephalothin	256–>256	>256.0	256.0–>256
Branhamella catarrhalis (10)	PD 117,596	≤0.004–0.008	0.008	≤0.004–0.008
	CI 934	0.06–0.125	0.125	0.06–0.125
	Imipenem	0.008	0.008	0.008–0.06
	Ciprofloxacin	0.015	0.015	0.015
	Aztreonam	0.5	0.5	0.5–1
	Ampicillin	0.125–1	1–2	0.015–2
	Trimethoprim-sulfamethoxazole	0.25	0.25	0.25
	Chloramphenicol	0.5	1	1
Campylobacter jejuni (16)	PD 117,596	0.008–0.015	0.06	0.008–0.06
	CI 934	1	2	0.03–4
	Imipenem	0.015–0.06	0.25	0.015–16
	Ciprofloxacin	0.125–0.25	0.25	0.06–0.5
	Trimethoprim-sulfamethoxazole	4–32	32	1–64
	Rifampin	64–>64	>64	32–>64
	Ampicillin	2–8	32	0.125–128
	Erythromycin	0.25	2	0.125–4
Escherichia coli (13)	PD 117,596	≤0.008	≤0.008	≤0.008
	CI 934	0.125	0.125	0.125–0.25
	Imipenem	0.125	0.125	0.06–0.25
	Ciprofloxacin	≤0.008	≤0.008	≤0.008–0.015
	Aztreonam	≤0.06	≤0.06	≤0.06–0.125
	Piperacillin	0.5	1.0	0.125–64
	Amikacin	1.0	2.0	0.5–4.0
	Cephalothin	4.0–8.0	8.0	0.5–16
Enterobacter spp. (13)[a]	PD 117,596	≤0.008	≤0.008	≤0.008–0.06
	CI 934	0.125	0.5	0.125–1
	Imipenem	0.5	2.0	0.25–16
	Ciprofloxacin	≤0.008	0.06	≤0.008–0.125
	Aztreonam	≤0.06	≤0.06	≤0.06
	Piperacillin	0.5–1	1.0	0.5–8
	Amikacin	0.5–1	1.0	0.5–2
	Cephalothin	256	>256	128.0–>256
Haemophilus influenzae, β-lactamase negative (27)	PD 117,596	≤0.004	≤0.004	≤0.004–0.008
	CI 934	0.03	0.06	0.03–0.125
	Imipenem	1.0	2.0	0.06–4
	Ciprofloxacin	≤0.004	0.008	≤0.004–0.015
	Aztreonam	0.06	0.125	0.008–0.25
	Ampicillin	0.25	0.5	0.125–2
	Trimethoprim-sulfamethoxazole	0.25	2.0	0.008–2
	Chloramphenicol	0.5	0.5–1	0.125–1
H. influenzae, β-lactamase positive (24)	PD 117,596	≤0.004	0.008	≤0.004–0.06
	CI 934	0.03	0.125	0.03–0.25
	Imipenem	1.0–2.0	4.0	0.5–8.0
	Ciprofloxacin	≤0.004	0.008	≤0.004–0.008
	Aztreonam	0.03	0.06	0.015–0.125
	Ampicillin	16.0–32.0	>32.0	0.5–>32
	Trimethoprim-sulfamethoxazole	0.25	0.5	0.015–4
	Chloramphenicol	0.5	1.0	0.5–1
Haemophilus parainfluenzae (20)	PD 117,596	≤0.004	0.008	≤0.004–0.008
	CI 934	0.06–0.125	0.25	0.06–0.25
	Imipenem	0.25–0.5	4	0.25–>16

Continued on following page

TABLE 1—*Continued*

Organism (no. of isolates tested)	Test agent	MIC (μg/ml)		
		50%	90%	Range
	Ciprofloxacin	≤0.004–0.008	0.008	≤0.004–0.015
	Aztreonam	0.008–0.015	0.25	0.008–0.25
	Ampicillin	0.25	32	0.125–>32
	Trimethoprim-sulfamethoxazole	0.25	1–2	0.125–2
	Chloramphenicol	0.25	0.5	0.25–0.5
Klebsiella pneumoniae (15)	PD 117,596	≤0.008	≤0.008	≤0.008–0.015
	CI 934	0.125–0.25	0.25	0.125–0.5
	Imipenem	0.125	0.25–0.5	0.125–0.5
	Ciprofloxacin	0.015	0.03	≤0.008–0.25
	Aztreonam	0.06	0.06	0.06
	Piperacillin	2.0	16.0	1.0–>256
	Amikacin	0.5	1.0	0.5–1.0
	Cephalothin	1.0–2.0	16.0	1.0–64
Klebsiella oxytoca (14)	PD 117,596	≤0.008	≤0.008	≤0.008–0.015
	CI 934	0.06–0.125	1.0	0.06–1.0
	Imipenem	0.125	0.125	0.125–0.25
	Ciprofloxacin	≤0.008	0.06	≤0.008–0.125
	Aztreonam	0.125	64.0	0.06–256
	Piperacillin	4.0	>256.0	0.5–>256
	Amikacin	0.5	1.0	0.5–2.0
	Cephalothin	8.0	>256.0	0.125–>256
Legionella pneumophila (31)	PD 117,596	0.004	0.008	≤0.002–0.008
	CI 934	0.06	0.125	≤0.002–0.125
	Ciprofloxacin	0.008–0.015	0.015	≤0.002–0.015
	Imipenem	0.06–0.25	0.5	≤0.002–1
	Trimethoprim-sulfamethoxazole	0.06–0.125	0.125	≤0.008–0.25
	Erythromycin	0.06	0.125	≤0.008–0.25
	Tetracycline	2.0–4.0	4.0–8.0	0.125–8.0
	Rifampin	≤0.001	≤0.001	≤0.001
Neisseria gonorrhoeae (30)	PD 117,596	≤0.002	≤0.002	≤0.002–0.008
	CI 934	0.004–0.008	0.015	≤0.002–0.015
	Imipenem	0.015	0.06	≤0.002–0.06
	Ciprofloxacin	≤0.002	≤0.002	≤0.002
	Spectinomycin	16–32	32	16–32
	Penicillin G	0.015–0.03	0.03–0.06	≤0.002–0.5
	Ceftriaxone	≤0.002	≤0.002	≤0.002–0.004
	Cefoxitin	0.25	1	0.06–1
Proteus mirabilis (23)	PD 117,596	0.03–0.06	0.125	≤0.008–0.125
	CI 934	1.0–2.0	2.0	0.5–4.0
	Imipenem	2.0	4.0	≤0.008–4
	Ciprofloxacin	0.03	0.125	≤0.008–0.5
	Aztreonam	≤0.03	≤0.03	≤0.03
	Piperacillin	64.0	256.0	0.125–>256
	Amikacin	2.0–4.0	4.0–8.0	2.0–8.0
	Cephalothin	16.0	64.0	8.0–256.0
Pseudomonas aeruginosa (56)	PD 117,596	0.06	0.25	0.03–0.5
	CI 934	4.0	8.0	1.0–>16
	Imipenem	4.0	8.0	1.0–>16
	Ciprofloxacin	0.125–0.25	0.5	0.06–2
	Piperacillin	4.0–8.0	16.0	2.0–256
	Ceftazidime	1.0–2.0	8.0	0.5–256
	Amikacin	8.0	64.0	0.25–256
	Aztreonam	4.0	64.0	2.0–>256
Pseudomonas spp. (8)[b]	PD 117,596	0.06		0.008–0.5
	CI 934	4.0		0.125–8
	Imipenem	4.0		0.03–>16
	Ciprofloxacin	0.125		0.03–4
	Piperacillin	4.0		0.125–256
	Ceftazidime	1.0		1.0–128

Continued on following page

TABLE 1—*Continued*

Organism (no. of isolates tested)	Test agent	MIC (μg/ml)		
		50%	90%	Range
	Amikacin	4.0		1.0–>256
	Aztreonam	4.0		0.25–256
Serratia marcescens (13)	PD 117,596	0.015	0.06	0.015–0.125
	CI 934	0.5	4.0	0.5–8
	Imipenem	0.5	1.0	0.25–2
	Ciprofloxacin	0.06	0.125	0.06–2
	Aztreonam	≤0.06	1.0	≤0.06–8
	Piperacillin	2.0–4.0	8.0–256	0.25–>256
	Amikacin	1.0–2.0	16.0	1.0–64
	Cephalothin	>256	>256	>256
Staphylococcus aureus (11)	PD 117,596	0.03	0.06	0.03–0.06
	CI 934	0.06–0.125	0.125	0.06–0.125
	Imipenem	0.015–0.03	0.03	0.015–0.03
	Ciprofloxacin	0.25	0.5	0.125–0.5
	Clindamycin	0.06–0.125	0.125	0.06–1
	Vancomycin	0.5–1	1	0.5–1
	Cephalothin	0.125–0.25	0.5	0.125–0.5
	Oxacillin	0.125	0.25	0.125–0.5
S. aureus, methicillin resistant (14)	PD 117,596	0.015	0.03	0.015–0.03
	CI 934	0.03	0.125	0.03–0.125
	Imipenem	16–>16	>16	0.5–>16
	Ciprofloxacin	0.25	0.5	0.25–0.5
	Clindamycin	>64	>64	>64
	Vancomycin	1.0	1.0	1.0
	Cephalothin	32.0	64.0	4.0–64
	4% NaCl–oxacillin	128.0–>128	>128	64–>128
Staphylococcus epidermidis (14)	PD 117,596	0.03–0.06	0.06	0.03–0.06
	CI 934	0.125	0.125	0.06–0.125
	Imipenem	0.03	0.25	0.015–1
	Ciprofloxacin	0.125–0.25	0.25	0.125–0.5
	Clindamycin	0.06	0.125	0.06–>64
	Vancomycin	0.5–1	2	0.5–4
	Cephalothin	0.125–0.25	0.5	0.125–1
	Oxacillin	0.25	2	0.125–2
Streptococcus spp., group A (20)	PD 117,596	0.06	0.125	0.03–0.25
	CI 934	0.125	0.25	0.06–0.5
	Imipenem	≤0.008	0.06	≤0.008–1
	Ciprofloxacin	0.5	2.0	0.25–4
	Clindamycin	0.03	0.03	0.03–0.06
	Vancomycin	0.5	0.5–1	0.5–2
	Cephalothin	0.03–0.06	0.06–0.125	0.03–1
	Penicillin G	≤0.008	≤0.008	≤0.008–0.25
Streptococcus spp., groups B, C, and G[c]	PD 117,596	0.06	0.125	0.06–0.125
	CI 934	0.125	0.25	0.06–0.25
	Imipenem	≤0.008	0.015	≤0.008–0.015
	Ciprofloxacin	0.5	1	0.25–2
	Vancomycin	0.25–0.5	1	0.25–1
	Cephalothin	0.03	0.06	≤0.015–0.06
	Clindamycin	0.03	0.06	≤0.008–0.06
	Penicillin G	≤0.008	≤0.008	≤0.008–0.015
Streptococcus pneumoniae (29)	PD 117,596	0.06	0.06	≤0.008–0.125
	CI 934	0.125	0.25	0.06–0.5
	Imipenem	≤0.008	0.015	≤0.008–0.015
	Ciprofloxacin	0.5–1	1.0	0.06–4
	Vancomycin	0.06–0.125	0.25	≤0.015–0.5
	Clindamycin	0.015	0.03	≤0.008–0.03
	Cephalothin	0.03	0.06	≤0.015–0.25
	Penicillin G	≤0.008	≤0.008	≤0.008–0.06

Continued on following page

TABLE 1—*Continued*

Organism (no. of isolates tested)	Test agent	MIC (μg/ml)		
		50%	90%	Range
Enterococci (11)	PD 117,596	0.125	0.125–0.25	0.125–0.25
	CI 934	0.125–0.25	0.5	0.125–0.5
	Imipenem	1.0	2.0	1.0–2.0
	Ciprofloxacin	1.0	2.0	1.0–2.0
	Vancomycin	2.0–4.0	4.0	1.0–4.0
	Clindamycin	32.0	>64	4.0–>64
	Cephalothin	16.0–32.0	64	16–64
	Penicillin G	1.0–2.0	4.0	1.0–4.0
Corynebacterium spp. (12)[d]	PD 117,596	0.015	0.06	≤0.008–0.125
	CI 934	0.125–0.25	0.5	0.06–1
	Imipenem	0.03	0.06	≤0.008–>64
	Ciprofloxacin	0.125	1	0.03–1
	Clindamycin	0.25	2	≤0.008–>128
	Penicillin G	0.125	0.25	≤0.015–>128
	Vancomycin	0.125–0.25	0.5	0.125–2
	Cephalothin	0.06	0.125	≤0.008–>128

[a] Seven *E. cloacae*, four *E. aerogenes*, and two *E. agglomerans*.
[b] Two *P. fluorescens*, two *P. maltophilia*, one *P. pseudoalcaligenes*, one *P. stutzeri*, and two unidentified.
[c] Four group B, three group C, and four group G.
[d] Two group JK, two *C. ulcerans*, two *C. pseudodiphtheriticum*, one *C. xerosis*, one *C. pseudotuberculosis*, one *C. haemolyticum*, one *C. renale*, one *C. diphtheriae*, and one unidentified.

5% sheep blood, in air, 37°C, 20 h; for *Neisseria gonorrhoeae*, *Branhamella catarrhalis*, and *Haemophilus* spp., MHA with 1% chocolatized hemoglobin and 1% IsoVitaleX (BBL Microbiology Systems, Cockeysville, Md.), in air, 24 h; for *Campylobacter jejuni*, MHA with 5% sheep blood, Campy-pak (BBL), 37°C, 48 h; for *L. pneumophila*, buffered yeast extract agar with starch in air, 37°C, 48 h. For testing susceptibilities of methicillin-resistant *Staphylococcus aureus*, 4% NaCl was added to MHA, and the incubation was at 35°C for 24 h. Control strains were utilized for each experimental run. The MIC was defined as the lowest concentration of antibiotic which gave no growth, a single colony, or a barely visible haze. The results are reported as concentrations in micrograms per milliliter that inhibited the growth of 50% of the isolates (MIC_{50}) or 90% of the isolates (MIC_{90}) and the range of MICs.

The in vitro activity of PD 117,596 and other antibacterial agents tested is shown in Table 1. PD 117,596 was uniformly more active than amikacin, the reference aminoglycoside antibiotic in this study, when tested against *Acinetobacter calcoaceticus*, *E. coli*, *Enterobacter* spp., *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *P. aeruginosa*, and *Serratia marcescens*. The MIC_{90} of PD 117,596 ranged from 0.008 to 0.25 μg/ml, and the MIC_{90} of amikacin ranged from 1.0 to 64.0 μg/ml. In comparison with imipenem, PD 117,596 demonstrated markedly enhanced activity against many gram-negative aerobic and facultative species tested. These differences were especially prominent for *E. coli*, *Enterobacter* spp., *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Klebsiella* spp., *P. mirabilis*, and *P. aeruginosa*. PD 117,596 was also generally more active than aztreonam against gram-negative bacilli. As expected, aztreonam (MIC_{90}, 32.0 μg/ml) was much less active than PD 117,596 (MIC_{90}, 0.125 μg/ml) against *A. calcoaceticus*. PD 117,596 was also more active than aztreonam against *Haemophilus* spp., *Klebsiella* spp., and *P. aeruginosa*. In contrast, against *P. mirabilis*, aztreonam (MIC_{90}, <0.03 μg/ml) was more active than PD 117,596 (MIC_{90}, 0.125 μg/ml). PD 117,596 demonstrated superior in vitro activity compared with that of ciprofloxacin against *A. calcoaceticus*, *Enterobacter* spp., *K. oxytoca*, *K. pneumoniae*, and *Serratia marcescens*.

PD 117,596 was at least twofold more active than ciprofloxacin when tested against *P. aeruginosa* and *Pseudomonas* spp. The MIC_{90}s of PD 117,596 and ciprofloxacin against *P. aeruginosa* were 0.25 and 0.5 μg/ml, whereas for *Pseudomonas* spp. the MIC_{90}s were 0.25 and 2.0 μg/ml, respectively. The upper limit of range for the MICs, however, against *P. aeruginosa* was 2.0 μg/ml for ciprofloxacin but only 0.5 μg/ml for PD 117,596.

PD 117,596 was 4- to 16-fold more active than ciprofloxacin against staphylococci, including methicillin-resistant *S. aureus*. The MIC_{90} of PD 117,596 for all *S. aureus* strains, including methicillin-resistant isolates, was 0.06 μg/ml, compared with MIC_{90}s of 0.5 μg/ml for ciprofloxacin and 0.125 μg/ml for CI 934, a quinolone agent known to be highly active against gram-positive cocci.

The MIC_{90} of PD 117,596 for *S. pneumoniae* was 0.06 μg/ml. Only penicillin G and imipenem were more active among the cell-wall-active agents tested. Against streptococcus groups A, B, C and G, PD 117,596 was less active than imipenem, more active than CI 934, and 8- to 16-fold more active than ciprofloxacin. PD 117,596 was the most active agent (MIC_{90}, 0.125 μg/ml) tested against enterococci.

PD 117,596 was the most active agent against *Corynebacterium* spp., including the JK isolates (MIC range, 0.008 to 0.125 μg/ml).

We studied the in vitro activity of PD 117,596 against a large number of clinical bacterial pathogens, some of them highly resistant to the currently available antimicrobial agents. Generally, PD 117,596 was more active than imipenem, aztreonam, and amikacin against all gram-negative isolates tested. The activity of PD 117,596 was 2- to 16-fold greater than those of these three antimicrobial agents. Furthermore, PD 117,596 was the most active drug tested against *L. pneumophila*, resistant strains of *P. aeruginosa*, and *Pseudomonas* spp. Although the activity of PD 117,596 was similar to or better than that of ciprofloxacin, the most impressive data were those for *P. aeruginosa* and *Pseudo-*

monas spp. PD 117,596 was twofold more active than ciprofloxacin for these bacterial isolates.

PD 117,596 was among the most active compounds against the gram-positive organisms tested (*S. aureus* [including methicillin-resistant strains], *Staphylococcus epidermidis*, *Corynebacterium* spp., and all streptococcal groups including enterococci). For some staphylococci and streptococci the activity of PD 117,596 was similar to that of penicillin G, imipenem, and cephalothin. In a comparison with CI 934, the most active quinolone against gram-positive bacteria to date (2, 6, 9), PD 117,596 was two- to fourfold more active.

In summary, PD 117,596 has excellent activity against gram-negative and gram-positive facultative bacterial pathogens. Its use in the treatment of human infections will depend on the pharmacokinetic properties, side effects, and in vivo effectiveness observed in experimental infections.

This work was supported by the Warner-Lambert Co., Pharmaceutical Research Division, and by the Medical Research Service of the Veterans Administration.

We are grateful for the secretarial assistance of Judith Dean and Paula Hinners.

LITERATURE CITED

1. **Chin, N. X., and H. C. Neu.** 1984. Ciprofloxacin, a quinolone carboxylic acid compound active against aerobic and anaerobic bacteria. Antimicrob. Agents Chemother. **25**:319–326.
2. **Cohen, M. A., T. J. Griffin, P. A. Bien, C. L. Heifetz, and J. M. Domagala.** 1985. In vitro activity of CI-934, a quinolone carboxylic acid active against gram-positive and negative bacteria. Antimicrob. Agents Chemother. **28**:766–772.
3. **Eliopoulos, G. M., A. Gardella, and R. C. Moellering.** 1984. The in vitro activity of ciprofloxacin, a new carboxyquinolone antimicrobial agent. Antimicrob. Agents Chemother. **25**:331–335.
4. **Hooper, D. C., and J. S. Wolfson.** 1985. The fluoroquinolones pharmacology, clinical use and toxicities in humans. Antimicrob. Agents Chemother. **28**:716–721.
5. **King, A., K. Shannon, and I. Phillips.** 1985. The in-vitro activity of enoxacin and ofloxacin compared with that of ciprofloxacin. J. Antimicrob. Chemother. **15**:551–558.
6. **Mandell, W., and H. C. Neu.** 1986. In vitro activity of CI-934, a new quinolone, compared with that of other quinolones and other antimicrobial agents. Antimicrob. Agents Chemother. **29**: 852–857.
7. **Reeves, D. S., M. J. Bywater, H. A. Halt, and L. O. White.** 1984. In-vitro studies with ciprofloxacin. J. Antimicrob. Chemother. **14**:333–346.
8. **Sanchez, J. P., J. M. Domagala, S. E. Hagen, C. L. Heiftez, M. P. Hutt, J. B. Nichols, and A. K. Trehan.** 1988. Quinolone antibacterial agents. Synthesis and structure-activity relationships of 8-substituted quinoline- and 1,8-naphthyridine-3-carboxylic acids. J. Med. Chem. **31**:983–991.
9. **Smith, R. P., A. L. Baltch, M. C. Hammer, and J. V. Conroy.** 1985. In-vitro activity of CI-934 and other antimicrobial agents against Gram-positive and Gram-negative bacteria. Clin. Ther. **9**:106–114.
10. **Steers, E., E. L. Foltz, B. S. Graves, and J. Riders.** 1959. An inocula-replicating apparatus for routine testing for bacterial susceptibility to antibiotics. Antibiotics **9**:307–311.
11. **Washington, J. A., II, and V. C. Sutter.** 1980. Dilution susceptibility tests: agar and macro-broth dilution procedures, p. 453–458. *In* E. H. Lennette, A. Balows, W. J. Hausler, Jr., and P. J. Truant (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.