Comparative Activity of Ciprofloxacin, Ofloxacin, Sparfloxacin, Temafloxacin, CI-960, CI-990, and WIN 57273 against Anaerobic Bacteria

ELLIE J. C. GOLDSTEIN^{1,2*} AND DIANE M. CITRON¹

R. M. Alden Research Laboratory, Santa Monica Hospital Medical Center, Santa Monica, California 90404,¹ and University of California at Los Angeles School of Medicine, Los Angeles, California 90073²

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The in vitro activities of seven fluoroquinolones against 290 anaerobes were determined by agar dilution. CI-960 and WIN 57273 inhibited >95% of the strains at $\leq 2 \mu g/ml$. CI-990 required $\leq 16 \mu g/ml$. Clustering around 2 to 4 $\mu g/ml$ was noted for *Bacteroides fragilis* group organisms with CI-990, sparfloxacin, and temafloxacin. Temafloxacin and sparfloxacin inhibited most strains at $\leq 2 \mu g/ml$. B. fragilis was more susceptible to all quinolones than were the other B. fragilis group strains.

The activity of fluoroquinolones against anaerobic bacteria has been reported to be moderate to poor (2, 3, 5–9, 11, 13, 15, 16, 18, 19). Consequently, industry has attempted to synthesize new compounds with improved antianaerobic activity (5). We evaluated the activities of seven fluoroquinolone compounds against 290 recent clinical anaerobic isolates and three American Type Culture Collection (ATCC) strains.

The anaerobic bacteria studied (Table 1) were 1990 isolates from two primary-care community hospitals and were identified by standard criteria (4, 10, 17). Standard powders were kindly supplied as follows: ciprofloxacin, Miles Laboratories, West Haven, Conn.; ofloxacin, R. W. Johnson Pharmaceutical Research Institute, Raritan, N.J.; sparfloxacin (AT-4140, RP 64206, and PD 131501), CI-960 (PD 127391 and AM 1091) [7-(3-amino-1-pyrrolidinyl)-8-chloro-1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-3-quinolinecarboxylic acid], and CI-990 (PD 131,628) [(S)-7-(3-amino-1-pyrrolidinyl)-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid]. Parke-Davis Pharmaceutical Research Division of Warner Lambert Co., Ann Arbor, Mich.; temafloxacin, Abbott Laboratories, North Chicago, Ill.; and WIN 57273 [1-cyclopropyl-7-(2,6-dimethyl-4-pyridinyl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolonecarboxylic acid], Sterling Winthrop Co., Rensselaer, N.Y. Isolate susceptibility was determined by the Wadsworth agar dilution method in accordance with National Committee for Clinical Laboratory Standards guidelines (14, 17). Plates were inoculated with a Steers replicator (Craft Machine Inc., Chester, Pa.) to give a final inoculum of 10⁵ CFU per spot. Bacteroides fragilis ATCC 25285, Bacteroides thetaiotaomicron ATCC 29741, and Eubaterium lentum ATCC 43055 were included as controls.

The results are shown in Tables 1 and 2. All Bacteroides ureolyticus, Clostridium perfringens, Bilophila wadsworthia (three strains), Fusobacterium nucleatum, Fusobacterium necrophorum, Eubacterium species (four strains), and Propionibacterium species strains were inhibited by $\leq 2 \mu g$ of all of the agents tested per ml. CI-960 and WIN 57273 were active at $\leq 2 \mu g/ml$ against >95% of all of the strains tested. For one strain each of Bacteroides caccae, Clostridium ramosum, and Prevotella melaninogenica, the MIC of CI- 960 was >4 μ g/ml. One strain each of *Clostridium limosum*

CI-990 was active against all peptostreptococci and 87% of *B. fragilis* species at $\leq 2 \mu g/ml$, but 28% of other *B. fragilis* group species required >4 $\mu g/ml$ for inhibition. Clustering around a concentration of 2 to 4 $\mu g/ml$ was found. MICs against *F. varium* and *F. ulcerans* were higher, with clustering around 2 to 4 $\mu g/ml$, resulting in 69% resistance. Ninety-two percent of *P. bivia* isolates were resistant (MIC, >4 $\mu g/ml$) to CI-990.

B. fragilis species were generally more susceptible to all of the agents tested than were other members of the B. fragilis group. F. varium was the most resistant of the fusobacteria, P. bivia was the most resistant Prevotella species, and Clostridium clostridiiforme was the most resistant Clostridium species tested. Clustering around the proposed breakpoints was noted for the B. fragilis group with CI-990, sparfloxacin, and temafloxacin. Lactobacilli and Veillonella species (five strains of each) showed various susceptibilities.

In 1988, Phillips and King (16) compared the activities of the 4-quinolones and noted that difloxacin, A-56620, ciprofloxacin, ofloxacin, enoxacin, norfloxacin, pefloxacin, CI-934, and nalidixic acid had modest anaerobic activity. Our study showed that two new quinolones, CI-960 and WIN 57272, were the most active, and almost all of the 290

and Fusobacterium gonidiaformans and two of P. melaninogenica were resistant to WIN 57273. Temafloxacin was active against 91% of B. fragilis strains, but several strains of Bacteroides distasonis, Bacteroides thetaiotaomicron, Bacteroides vulgatus, and Bacteroides uniformis were resistant to >4 μ g/ml. For many non-*perfringens Clostridium* species, non-spore-forming gram-positive bacilli, and Fusobacterium varium, Fusobacterium mortiferum, and Fusobacterium ulcerans strains, the temafloxacin MICs were >4 μ g/ml. Of the B. fragilis species and B. fragilis group species, the sparfloxacin MIC for 13 and 16%, respectively, was >4 μ g/ml. For only 17% of Prevotella bivia strains and 57% of P. melaninogenica strains, the sparfloxacin MICs were $\leq 4 \mu g/ml$. The MICs for all strains of F. varium and F. ulcerans were >4µg/ml. While all C. perfringens isolates were susceptible to $\leq 0.5 \ \mu g$ of sparfloxacin per ml, the other clostridia were more resistant, with MICs for 90% of the strains tested (MIC₉₀s) of 8 and 32 μ g/ml. Sparfloxacin was less active against P. bivia, F. varium, F. ulcerans, and P. melaninogenica, often requiring 8 to 16 µg/ml for inhibition.

^{*} Corresponding author.

TABLE 1. Comparative activities of ciprofloxacin, off	loxacin, sparfloxacin,	temafloxacin,	CI-960, CI-99	0, and WIN 57273	against 290
clinica	al isolates of anaerobi	c bacteria			

and antimicrobial agent Range $59\%^{4}$ $99\%^{4}$ Conex 1 Conex 2 Conex 3 Actimoryces sp. (5) ⁷ Ciprofloxacin -0.06-16 8 20 20 40 Ofloxacin 0.125-3 8 20 20 40 Ofloxacin 0.125-3 8 20 20 40 Tennafloxacin -C008-3 4 20 20 100 100 CL990 -0.015-1 0.5 100 100 100 100 CL990 -0.025-0.5 0.25 100 0 0 0 Optication 83128 8 30 40 90 0 Offorxetin 0.125-32 2 4 80 90 90 90 100 100 100 Termafloxacin 0.125-32 2 4 10 50 90 90 100 100 100 100 100 100 100 100 100 100 100<	Organism (no. of isolates tested) and antimicrobial agent	MIC (µg/ml)			% of isolates susceptible at ^a :		
		Range	50% ^b	90% ^b	Concn 1	Concn 2	Concn 3
$\begin{array}{c} Cprofixacin & -1 & -1 & -2 & -4 & -4 & -2 & -2 & -4 & -4 & -4$	Actinomyces sp. $(5)^c$						
$\begin{array}{cccccc} 0.025-8 & 8 & 20 & 40 & 80 \\ Sparftoxacin & <0.03-4 & 4 & 20 & 20 & 100 \\ Tematoxacin & <0.03-8 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 4 & 20 & 20 & 100 \\ C1-90 & <0.03-4 & 0.25 & 100 & 100 \\ C1-90 & 0.03-8 & 0.125 & 22 & 0 & 0 & 0 \\ Ofloxacin & 0.125-32 & 2 & 4 & 30 & 80 & 90 \\ Tematoxacin & 0.125-42 & 2 & 4 & 30 & 80 & 90 \\ Tematoxacin & 0.125-42 & 2 & 4 & 10 & 50 & 90 \\ C1-90 & 0.03-8 & 0.125 & 0.25 & 100 & 100 & 100 \\ C1-90 & 0.04-8 & 0.125 & 0.25 & 100 & 100 & 100 \\ Decteroides distasonis (12) & & & & & & & & \\ C1-90 & 0.06-4 & 0.25 & 0.5 & 100 & 100 & 100 \\ Decteroides distasonis (12) & & & & & & & & & \\ C1-90 & 0.06-4 & 0.25 & 1 & 92 & 100 & 100 & 100 \\ C1-90 & 0.06-2 & 0.125 & 1 & 92 & 100 & 100 \\ C1-90 & 0.06-2 & 0.125 & 1 & 92 & 100 & 100 \\ C1-90 & 0.06-2 & 0.125 & 1 & 92 & 100 & 100 \\ C1-90 & 0.06-2 & 0.125 & 1 & 92 & 100 & 100 \\ Decteroides finglis (23) & & & & & & & & & & & & \\ C1-900 & 0.06-2 & 0.125 & 1 & 92 & 100 & 100 & 100 \\ Decteroides finglis (23) & & & & & & & & & & & & & & & & & & \\ C1-900 & 0.06-2 & 0.125 & 0.5 & 100 & 100 & 100 \\ Decteroides finglis (23) & & & & & & & & & & & & & & & & & & &$	Ciprofloxacin	< 0.06-16	8		20	20	40
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Ofloxacin	0.125-8	8		20	40	80
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Sparfloxacin	<0.03-4	4		20	20	100
$\begin{array}{cccc} C1-90 & <0.015-1 & 0.5 & 100 & 100 & 100 \\ CC-90 & <0.03-4 & 4 & 20 & 20 & 1000 \\ WIN 57273 & <0.015-0.5 & 0.25 & 100 & 100 & 100 \\ \hline \\ Bacteroides caccae (10) & & & & & & & & & & & & & & & & & & &$	Temafloxacin	<0.03-8	4		20	80	100
$\begin{array}{ccccc} \dot{C}_{1} = \dot{90} & \dot{c}_{0} & c$	CI-960	< 0.015-1	0.5		100	100	100
WIN 57273 $< 0.015 - 0.5$ 0.25 100 100 100 Bacteroides caccae (10)	CI-990	< 0.03-4	4		20	20	100
Bacteroides caccae (10) Bacteroides caccae (10) 0<	WIN 57273	<0.015-0.5	0.25		100	100	100
$\begin{array}{c} Ciprofloxacin & 8 -> 128 & 16 & 32 & 0 & 0 & 0 \\ Oboxacin & 1 -> 128 & 8 & 8 & 10 & 40 & 90 \\ Sparfloxacin & 0.125 - 32 & 2 & 4 & 30 & 80 & 90 \\ CI -960 & 0.03 - 8 & 0.125 & 0.25 & 90 & 90 & 90 \\ CI -960 & 1 -32 & 2 & 4 & 10 & 50 & 90 \\ WIN 57273 & 0.06 - 4 & 0.25 & 0.5 & 100 & 100 & 100 \\ \hline Bacteroides distasonis (12) & & & & & & & & \\ Ciprofloxacin & 2 - 64 & 2 & 16 & 58 & 83 & 83 \\ Oboxacin & 2 - 64 & 2 & 16 & 50 & 75 & 92 \\ CI -960 & 0.06 - 2 & 0.125 & 1 & 92 & 100 & 100 \\ CI -990 & 2 - 32 & 2 & 16 & 50 & 75 & 92 \\ Temafloxacin & 2 - 32 & 2 & 16 & 0 & 50 & 83 \\ VIN 57273 & 0.25 - 1 & 0.5 & 100 & 100 & 100 \\ CI -990 & 2 - 32 & 2 & 16 & 0 & 50 & 83 \\ WIN 57273 & 0.25 - 1 & 0.5 & 100 & 100 & 100 \\ CI -990 & 2 - 32 & 2 & 16 & 0 & 50 & 83 \\ WIN 57273 & 0.25 - 128 & 4 & 8 & 0 & 9 & 67 & 91 \\ Sparfloxacin & 2 - 516 & 1 & 4 & 61 & 87 & 91 \\ Cipofloxacin & 2 - 516 & 1 & 4 & 61 & 87 & 91 \\ Cipofloxacin & 0 - 5 - 16 & 1 & 4 & 61 & 87 & 91 \\ Sparfloxacin & 0 - 5 - 16 & 1 & 4 & 61 & 87 & 91 \\ Cipofloxacin & 2 - 54 & 2 & 8 & 78 & 60 & 100 & 100 \\ CI -990 & 1 - 16 & 2 & 4 & 43 & 87 & 91 \\ Sparfloxacin & 0 - 5 - 16 & 1 & 4 & 61 & 87 & 91 \\ Cipofloxacin & 0 - 5 - 16 & 1 & 4 & 61 & 87 & 91 \\ Cipofloxacin & 0 - 5 - 16 & 1 & 4 & 61 & 87 & 91 \\ WIN 57273 & 0.125 - 2 & 0.25 & 0.5 & 100 & 100 & 100 \\ Bacteroides voatus (10) & & & & & & \\ Cipofloxacin & 8 - 16 & 16 & 0 & 0 & 0 & 0 \\ Oboxacin & 8 - 16 & 16 & 16 & 0 & 0 & 0 & 0 \\ Oboxacin & 0 - 2 - 4 & 4 & 4 & 4 & 0 & 40 & 900 \\ WIN 57273 & 0.25 - 1 & 0 - 5 & 1 & 100 & 100 & 100 \\ Temafloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Sparfloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Sparfloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 12 & 82 & 82 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 58 & 33 & 92 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 58 & 33 & 92 \\ Cipofloxacin & 0 - 5 - 16 & 2 & 8 & 58 & 33 &$	Bacteroides caccae (10)						
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Ciprofloxacin	8->128	16	32	0	0	0
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Ofloxacin	1->128	8	8	10	40	90
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Sparfloxacin	0.125-32	2	4	30	80	90
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Temafloxacin	0.25-64	2	4	80	90	90
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CI-960	0.03_8	0 125	0.25	90	90	90
Win 5773 $0.06-4$ 0.25 0.5 100 100 Bacteroides distasonis (12) $0.06-4$ 0.25 0.5 100 100 Bacteroides distasonis (12) $2-64$ 2 16 58 83 83 Sparfloxacin $2-64$ 2 16 50 75 92 Ciprofloxacin $2-32$ 2 16 0 50 83 83 WIN 57273 $0.25-1$ 0.5 0.5 100 100 100 Bacteroides fragilis (23) C C 8 8 9 67 Ofloxacin $2-512$ 4 8 0 9 67 Ofloxacin $2-512$ 4 8 0 9 67 Ofloxacin $2-512$ 4 8 0 9 67 Ciprofloxacin $0.5-16$ 1 4 61 61 60 00 <t< td=""><td>CL-900</td><td>1_32</td><td>2</td><td>4</td><td>10</td><td>50</td><td>90</td></t<>	CL-900	1_32	2	4	10	50	90
Bacteroides distasonis (12) -Ciprofloxacin 2-64 4 32 0 8 58 Ofloxacin 1-16 2 4 33 75 92 Temafloxacin 1-16 2 4 33 75 92 Cl-960 0.06-2 0.125 1 92 100 100 Cl-960 0.23-2 2 16 0 50 83 WIN 57273 0.25-1 0.5 0.5 100 100 100 Bacteroides fragilis (23) - - 8 78 87 91 Sparfloxacin 2->128 4 8 78 91 91 Cl-960 0.06-2 0.125 0.5 96 100 100 Cl-960 0.16-2 2 4 43 87 91 WIN 57273 0.125-2 0.25 0.5 100 100 100 Bacteroides ovatus (10) Ciprofloxacin 8-16 16	WIN 57273	0.06-4	0.25	0.5	100	100	100
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Bacteroides distasonis (12)						
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Ciprofloxacin	2–64	4	32	0	8	58
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Ofloxacin	2-64	2	16	58	83	83
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Sparfloyacin	1_16	$\frac{1}{2}$	4	33	75	92
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Temaflovacin	2_32	2	16	50	75	92
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CL 960	0.06.2	0 125	10	92	100	100
C1390 WIN S7273 $0.25-1$ 0.5 0.5 100 100 Bacteroides fragilis (23) $2-5128$ 4 8 0 9 67 Offoxacin $2-5128$ 4 8 0 9 67 Sparfloxacin $0.5-16$ 1 4 61 87 91 Cl-960 $0.06-2$ 0.125 0.5 96 100 100 Bacteroides ovatus (10) C C 2 4 87 91 Clyrofloxacin $8-64$ 16 16 0 0 100 Bacteroides ovatus (10) C C 0 0 0 0 Clyrofloxacin $2-4$ 4 4 0 00 100 Bacteroides thetaiotachicron $0.25-1$ 0.5 1 100 100 100 Clyrofloxacin $2-4$ 4 4 0 40 90 <t< td=""><td>CI 900</td><td>2 32</td><td>2</td><td>16</td><td>0</td><td>50</td><td>83</td></t<>	CI 900	2 32	2	16	0	50	83
Bacteroides fragilis (23) Ciprofloxacin $2 - 5128$ 4 8 0 9 67 Ofloxacin $2-64$ 2 8 78 87 91 Sparfloxacin $0.5-16$ 1 4 61 87 91 Temafloxacin $1-32$ 1 4 87 91 91 C1-960 $0.06-2$ 0.125 0.5 96 100 100 C1-960 $0.125-2$ 0.25 0.5 100 100 100 Bacteroides ovatus (10) Ciprofloxacin $8-64$ 16 16 0 0 0 Ciprofloxacin $2-4$ 4 20 80 1000 100 Temafloxacin 2.4 4 4 0 40 100 100 Cliprofloxacin $0.25-1$ 0.5 1 100 100 100 Cliprofloxacin 2.4 4 4 0 40 90 WIN \$7273	WIN 57273	0.25-1	0.5	0.5	100	100	100
Date robust Ciprofloxacin $2 - > 128$ 480967Ofloxacin $2 - 64$ 28788791Temafloxacin $1 - 32$ 14618791Temafloxacin $1 - 32$ 14879191C1-960 $0.06 - 2$ 0.125 0.5 96100100C1-90 $1 - 16$ 24438791WIN 57273 $0.125 - 2$ 0.25 0.5 100100100Bacteroides ovatus (10)Ciprofloxacin $8 - 64$ 16160040Sparfloxacin $1 - 4$ 242080100Ofloxacin $2 - 4$ 4440100100Ciprofloxacin $1 - 4$ 244040Sparfloxacin $2 - 4$ 44040Sparfloxacin $2 - 4$ 440100Ciprofloxacin $2 - 4$ 44040Ofloxacin $2 - 4$ 44040Ofloxacin $2 - 32$ $2 - 32$ 100 100100Ciprofloxacin $8 - 128$ 1664000Ofloxacin $2 - 32$ $2 - 32$ 59 8_2 82 Ciprofloxacin $2 - 32$ $2 - 32$ 59 8_2 82	Protovoidos fascilis (22)						
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Tematioxacin1-3214879191C1-9600.06-20.1250.596100100C1-9901-1624438791WIN 572730.125-20.250.5100100100Bacteroides ovatus (10)Ciprofloxacin8-641616000Ofloxacin8-1616160040Sparfloxacin1-42440100100Clorofloxacin2-44440100100Clorofloxacin2-44440100100Clorofloxacin2-44404090WIN 572730.25-10.51100100100Ciprofloxacin8-128664000Ciprofloxacin8-128128222Sparfloxacin0.5-1628128282Ciprofloxacin0.5-162812828222Temafloxacin2-32232598.2828281Clorofloxacin2-520.52100100100100Clorofloxacin2-5222100100100Ciprofloxacin2-52281282Ciprofloxacin<	Sparnoxacin	0.5-16	1	4	01	0/	91
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Temafloxacin	1-32	1	4	8/	91	91
C1-990 WIN 572731-16 0.125-22 0.254 0.543 10087 10091 100Bacteroides ovatus (10) Ciprofloxacin8-64 8-1616 	C1-960	0.06-2	0.125	0.5	96	100	100
WIN 57273 $0.125-2$ 0.25 0.5 100 100 100 Bacteroides ovatus (10) Ciprofloxacin $8-64$ 16 16 0 0 0 Sparfloxacin $1-4$ 2 4 20 80 100 Temafloxacin $2-4$ 4 4 40 100 100 Ciprofloxacin $2-4$ 4 4 40 100 100 Ciprofloxacin $2-4$ 4 4 0 40 90 Cl-960 $0.125-0.5$ 0.125 0.25 100 100 100 Bacteroides thetaiotaomicron (17) Ciprofloxacin $8-128$ 16 64 0 0 0 Ciprofloxacin $2-32$ 2 32 59 8.2 82 82 82 Ciprofloxacin $2-32$ 2 32 59 8.2 82 Ciprofloxacin $2-25$	CI-990	1–16	2	4	43	87	91
Bacteroides ovatus (10)Ciprofloxacin8–641616000Ofloxacin8–161616000Sparfloxacin1–4242080100Temafloxacin2–44440100100Cl-9600.125–0.50.1250.25100100100Cl-9902–84404090WIN 572730.25–10.51100100100Bacteroides thetaiotaomicron (17)Ciprofloxacin8–1281664000Ofloxacin2–32232598282Ciprofloxacin2–32232598282Ci-9600.125–20.25282100100Ciprofloxacin2–648160825Ofloxacin2–84483367100Sparfloxacin2–648160825Ofloxacin2–648160825Ofloxacin2–84483367100Sparfloxacin0.5–1628588392Ci-9600.06–20.250.592100100Ciprofloxacin0.5–1628588392Ci-9600.06–20.250.592100100 <td>WIN 57273</td> <td>0.125–2</td> <td>0.25</td> <td>0.5</td> <td>100</td> <td>100</td> <td>100</td>	WIN 57273	0.125–2	0.25	0.5	100	100	100
$\begin{array}{ccc} Ciprofloxacin & 8-64 & 16 & 16 & 0 & 0 & 0 \\ Ofloxacin & 8-16 & 16 & 16 & 0 & 0 & 40 \\ Sparfloxacin & 1-4 & 2 & 4 & 20 & 80 & 100 \\ Temafloxacin & 2-4 & 4 & 4 & 40 & 100 & 100 \\ CI-960 & 0.125-0.5 & 0.125 & 0.25 & 100 & 100 & 100 \\ CI-990 & 2-8 & 4 & 4 & 0 & 40 & 90 \\ WIN 57273 & 0.25-1 & 0.5 & 1 & 100 & 100 & 100 \\ \hline Bacteroides thetaiotaomicron (17) & & & & & \\ Ciprofloxacin & 8-128 & 16 & 64 & 0 & 0 & 0 \\ Ofloxacin & 4-128 & 8 & 128 & 0 & 12 & 82 \\ Sparfloxacin & 0.5-16 & 2 & 8 & 12 & 82 & 82 \\ Temafloxacin & 2-32 & 2 & 32 & 59 & 8.2 & 82 \\ CI-960 & 0.125-2 & 0.25 & 2 & 82 & 100 & 100 \\ CI-990 & 1-16 & 2 & 16 & 6 & 76 & 82 \\ WIN 57273 & 0.25-2 & 0.5 & 2 & 100 & 100 & 100 \\ \hline Bacteroides uniformis (12) & & & & \\ Ciprofloxacin & 2-8 & 4 & 8 & 16 & 0 & 8 & 25 \\ Ofloxacin & 2-8 & 4 & 8 & 33 & 67 & 92 \\ Temafloxacin & 0.5-16 & 2 & 8 & 58 & 83 & 92 \\ CI-960 & 0.125-2 & 0.5 & 2 & 100 & 100 & 100 \\ Factorides uniformis (12) & & & & \\ Ciprofloxacin & 2-64 & 8 & 16 & 0 & 8 & 25 \\ Ofloxacin & 2-8 & 4 & 8 & 33 & 67 & 92 \\ Temafloxacin & 0.5-16 & 2 & 8 & 58 & 83 & 92 \\ CI-960 & 0.06-2 & 0.25 & 0.5 & 92 & 100 & 100 \\ Sparfloxacin & 0.5-16 & 2 & 8 & 58 & 83 & 92 \\ CI-960 & 0.06-2 & 0.25 & 0.5 & 100 & 100 & 100 \\ Sparfloxacin & 0.5-16 & 2 & 8 & 58 & 83 & 92 \\ CI-960 & 0.06-2 & 0.25 & 0.5 & 100 & 100 & 100 \\ \end{array}$	Bacteroides ovatus (10)	2 (1		• /	0	0	0
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Ciprofloxacin	8-64	16	16	0	0	0
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Ofloxacin	8–16	16	16	0	0	40
Temafloxacin2-444440100100C1-9600.125-0.50.1250.25100100100WIN 572730.25-10.51100100100Bacteroides thetaiotaomicron (17)Ciprofloxacin8-1281664000Ofloxacin4-128812801282Sparfloxacin0.5-1628128282Temafloxacin2-32232598282Cl-9600.125-20.25282100100Cle9901-1621667682WIN 572730.25-20.52100100100Bacteroides uniformis (12)Ciprofloxacin2-648160825Ofloxacin2-8483367100Bacteroides uniformis (12)10.5-824336792Temafloxacin0.5-1628588392Cl-9600.06-20.250.592100100Cl-9901-848173383WIN 572730.06-0.50.250.5100100	Sparfloxacin	1–4	2	4	20	80	100
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Temafloxacin	2–4	4	4	40	100	100
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CI-960	0.125-0.5	0.125	0.25	100	100	100
WIN 57273 $0.25-1$ 0.5 1 100 100 100 Bacteroides thetaiotaomicron (17)Ciprofloxacin $8-128$ 16 64 0 0 0 Ofloxacin $4-128$ 8 128 0 12 82 Sparfloxacin $0.5-16$ 2 8 12 82 82 Ci-960 $0.125-2$ 2.32 2 32 59 8_4 82 Ci-960 $0.125-2$ 0.25 2 82 100 100 Ci-960 $0.125-2$ 0.25 2 82 100 100 Bacteroides uniformis (12)Ciprofloxacin $2-64$ 8 16 0 8 25 Ofloxacin $2-8$ 4 8 33 67 100 Sparfloxacin $0.5-16$ 2 8 58 83 92 Ciprofloxacin $0.5-16$ 2 8 58 83 92 Ci-960 $0.06-2$ 0.25 0.5 100 100 100 Ci-960 $0.06-25$ 0.25 0.5 100 100	CI-990	2–8	4	4	0	40	90
Bacteroides thetaiotaomicron (17)Ciprofloxacin $\$-128$ 1664000Ofloxacin $4-128$ 812801282Sparfloxacin $0.5-16$ 28128282Temafloxacin $2-32$ 232598282C1-960 $0.125-2$ 0.255 282100100C1-990 $1-16$ 21667682WIN 57273 $0.25-2$ 0.5 2100100100Bacteroides uniformis (12)Ciprofloxacin $2-64$ 8160825Ofloxacin $2-8$ 483367100Sparfloxacin $0.5-8$ 24336792Temafloxacin $0.5-16$ 28588392C1-960 $0.06-2$ 0.25 0.5 92100100VIN 57273 $0.06-0.5$ 0.25 0.5 100100	WIN 57273	0.25–1	0.5	1	100	100	100
Ciprofloxacin $8-128$ 1664000Ofloxacin $4-128$ 8 128 01282Sparfloxacin $0.5-16$ 28128282Temafloxacin $2-32$ 232598282CI-960 $0.125-2$ 0.25 282100100CI-990 $1-16$ 21667682WIN 57273 $0.25-2$ 0.5 2100100100Bacteroides uniformis (12)Ciprofloxacin $2-64$ 8160825Ofloxacin $2-8$ 483367100Sparfloxacin $0.5-8$ 24336792Temafloxacin $0.5-16$ 28588392CI-960 $0.06-2$ 0.25 0.5 92100100UP90 $1-8$ 48173383WIN 57273 $0.06-0.5$ 0.25 0.5 100100	Bacteroides thetaiotaomicron (17)						
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Ciprofloxacin	8–128	16	64	0	0	0
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Ofloxacin	4–128	8	128	0	12	82
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Sparfloxacin	0.5–16	2	8	12	82	82
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Temafloxacin	2–32	2	32	59	82	82
CI-990 WIN 572731-16 0.25-2216 06 7682 0.00Bacteroides uniformis (12)Ciprofloxacin2-6481608 25 0floxacin25 00Sparfloxacin2-8483367100Sparfloxacin0.5-824336792Temafloxacin0.5-1628588392CI-9600.06-20.250.592100100CI-9901-848173383WIN 572730.06-0.50.250.5100100100	CI-960	0.125-2	0.25	2	82	100	100
WIN 572730.25–20.52100100Bacteroides uniformis (12)Ciprofloxacin2–648160825Ofloxacin2–8483367100Sparfloxacin0.5–824336792Temafloxacin0.5–1628588392CI-9600.06–20.250.592100100CI-9901–848173383WIN 572730.06–0.50.250.5100100100	CI-990	1–16	2	16	6	76	82
Bacteroides uniformis (12) Ciprofloxacin 2–64 8 16 0 8 25 Ofloxacin 2–8 4 8 33 67 100 Sparfloxacin 0.5–8 2 4 33 67 92 Temafloxacin 0.5–16 2 8 58 83 92 CI-960 0.06–2 0.25 0.5 92 100 100 CI-990 1–8 4 8 17 33 83 WIN 57273 0.06–0.5 0.25 0.5 100 100 100	WIN 57273	0.25–2	0.5	2	100	100	100
Ciprofloxacin2-648160825Ofloxacin2-8483367100Sparfloxacin0.5-824336792Temafloxacin0.5-1628588392CI-9600.06-20.250.592100100CI-9901-848173383WIN 572730.06-0.50.250.5100100100	Bacteroides uniformis (12)						
Ofioxacin2-8483367100Sparfloxacin0.5-824336792Temafloxacin0.5-1628588392CI-9600.06-20.250.592100100CI-9901-848173383WIN 572730.06-0.50.250.5100100100	Ciprofloxacin	2-64	8	16	0	8	25
Sparfloxacin0.5-824336792Temafloxacin0.5-1628588392CI-9600.06-20.250.592100100CI-9901-848173383WIN 572730.06-0.50.250.5100100100	Ofloxacin	2–8	4	8	33	67	100
Temafloxacin0.5–1628588392CI-9600.06–20.250.592100100CI-9901–848173383WIN 572730.06–0.50.250.5100100100	Sparfloxacin	0.5-8	2	4	33	67	92
CI-9600.06-20.250.592100100CI-9901-848173383WIN 572730.06-0.50.250.5100100100	Temafloxacin	0.5-16	2	8	58	83	92
CI-990 1-8 4 8 17 33 83 WIN 57273 0.06-0.5 0.25 0.5 100 100 100	CI-960	0.06-2	0.25	0.5	92	100	100
WIN 57273 0.06–0.5 0.25 0.5 100 100 100	CI-990	1-8	4	8	17	33	83
	WIN 57273	0.06-0.5	0.25	0.5	100	100	100

Continued on following page

Organism (no. of isolates tested) and antimicrobial agent	 MIC (µg/ml)			% of isolates susceptible at ^a :		
	Range	50% ^b	90% ^b	Concn 1	Concn 2	Concn 3
Bacteroides vulgatus (12)						
Ciprofloxacin	4-128	16	64	0	0	8
Ofloxacin	1–16	2	16	67	75	92
Sparfloxacin	0.5-2	1	2	75	100	100
Temafloxacin	0.5-8	0.5	2	92	92	100
CI-960	0.06-1	0.06	05	100	100	100
CI-990	2-16	2	16	0	50	75
WIN 57273	0.03-0.5	0 .06	0.125	100	100	100
Bacteroides ureolyticus group (11) ^d						
Ciprofloxacin	<0.06-0.25	< 0.06	0.25	100	100	100
Ofloxacin	< 0.06–1	0.125	0.5	100	100	100
Sparfloxacin	< 0.015-1	0.06	0.5	100	100	100
Temafloxacin	<0.015-2	0.125	1	100	100	100
	< 0.015 - 2	<0.125	0.06	100	100	100
CI-900		<0.015 0.02	0.00	100	100	100
WIN 57273	<0.015-0.125 <0.015-0.5	0.03	0.125	100	100	100
Other Clostridium spp (23)e						
Ciprofloxacin	0 5-32	2	16	22	52	70
Offerencia	0.5 32	2	16	18	61	83
Snorflowedin	0.3-32	4	10	20	70	92
Sparnoxacin	0.25-10	2	0	50	/0	03
Temanoxacin	0.25-16	2	10	/4	85	8/
CI-960	0.03-1	0.25	0.5	100	100	100
CI-990	0.25-16	1	4	61	74	95
WIN 57273	≤0.015-8	0.125	0.5	96	96	100
Clostridium perfringens (12)						
Ciprofloxacin	0.25-0.5	0.5	0.5	100	100	100
Ofloxacin	0.5–1	0.5	0.5	100	100	100
Sparfloxacin	0.125-0.5	0.25	0.5	100	100	100
Temafloxacin	0.125-0.5	0.25	0.5	100	100	100
CI-960	0.06-0.125	0.06	0.125	100	100	100
CI-990	0.125-0.25	0.125	0.25	100	100	100
WIN 57273	≤0.015-0.06	≤0.015	0.03	100	100	100
Clostridium ramosum-C. innocuum- C. clostridiiforme group (15)						
Ciprofloxacin	1->128	8	64	7	7	20
Ofloxacin	$1 \rightarrow 128$	16	128	7	7	47
Sparfloyacin	0.25-32	4	32	20	33	53
Temeflowacin	0.25-52	4	32	40	53	60
CL 060	0.125 9	4	32	40	02	00
CI-900	0.125-6	0.5	22	07	93 60	93 67
WIN 57273	<0.06–64 0.06–2	0.25	2	100	100	100
Other Eucobacterium ann (20)						
Cincef avoir	0 5 16	2	0	25	00	00
Cipronoxacin	0.5-10	2	0	33	90 00	
Onoxacin	0.5-64	2	10	85 25	90	90
Spartloxacin	0.5-8	2	8	35	85	90
Temafloxacin	0.125-8	0.5	8	75	90	100
CI-960	0.03-0.5	0.06	0.5	100	100	100
CI-990	0.25-8	1	4	85	90	95
WIN 57273	0.03-1	0.06	1	100	100	100
Fusobacterium varium-F. ulcerans- F. gonidiaformans group (14)						
Ciprofloxacin	2_32	8	16	Ο	7	7
Oflovacin	2-32	8	16	ž	7	50
Sportforrooin	2-120	16	16	/ 0	, 0	
Spariioxaciii Temefleweeiz	4-32	10	10	U 7	7	/ ∠A
CL 0(0	2-32	0.5	10	· /	/	100
CI-900	0.125-2	0.5	1 A	93 7	100	100
CI-990	2-8	4	4	1	29	93
WIN 57273	0.125 - 32	2	2	93	93	93

TABLE 1-Continued

Continued on following page

TABLE 1-Continued

Organism (no. of isolates tested) and antimicrobial agent	MIC (μg/ml)			% of isolates susceptible at ^a :		
	Range	50% ^b	90% ^b	Concn 1	Concn 2	Concn 3
Peptostreptococcus sp. (22) ^g						
Ciprofloxacin	0.125-8	1	4	59	86	91
Ofloxacin	0.125-16	0.5	8	59	86	91
Sparfloxacin	0.06-4	0.25	1	91	91	100
Temafloxacin	0.06-2	0.25	2	100	100	100
CI-960	< 0.015-0.5	0.03	ō 5	100	100	100
CI-990	0.03-2	0.05	2	86	100	100
WIN 57273	≤0.015-0.25	0.03	0.125	100	100	100
Prevotella bivia (12)						
Ciprofloxacin	4-16	16	16	0	0	8
Ofloxacin	2_8	8	8	17	25	100
Sparfloxacin	2-16	4	16	1	17	58
Temafloxacin	2_10	4	4	25	92	100
CI-960	0 25 0 5	0.25	0.5	100	100	100
CI 900	0.25-0.5	0.25	0.5	100	100	100
WIN 57273	0.25-0.5	0.5	0.5	100	100	100
Pigmented Porphyromonas- Prevotella spp. (17) ^h						
Ciprofloxacin	<0.06-64	1	16	62	81	86
Ofloxacin	0.2564	ī	16	76	86	90
Sparfloxacin	< 0.03-32	2	16	33	86	90
Temafloxacin	< 0.03-64	1	16	86	90	90
CI-960	0.03_4	0.06	0 25	95	95	100
CI-990	< 0.03-8	1	2	67	95	95
WIN 57273	0.06–16	0.25	0.5	90	90	95
Other, nonpigmented <i>Prevotella</i> spp. (14) ⁱ						
Ciprofloxacin	1-4	2	2	21	93	100
Ofloxacin	1-2	2	$\frac{1}{2}$	100	100	100
Sparfloxacin	1-2	2	$\frac{2}{2}$	20	100	100
Temafloxacin	1-2	1	$\tilde{2}$	100	100	100
CI-960	0.03 0.125	0.03	0.06	100	100	100
CI-990	0.05-0.125	1	1	03	100	100
WIN 57273	0.125-0.5	0.25	0.5	100	100	100
Propionibacterium sp $(11)^{\checkmark}$						
Ciprofloxacin	0.25_1	0.25	0.5	100	100	100
Oflovacin	0.25-0.5	0.25	0.5	100	100	100
Sparfloyacin	0.06-0.25	0.25	0.25	100	100	100
Temaflovacin	0.125 0.25	0.25	0.25	100	100	100
CL060	0.125-0.25	0.23	0.25	100	100	100
CI-000	0.05-0.00	0.05	0.00	100	100	100
WIN 57273		0.5	0.5	100	100	100
WIIN 57275	<0.013-0.03	0.05	0.05	100	100	100

^a Concentrations 1, 2, and 3, respectively, were 1, 2, and 4 µg/ml for ciprofloxacin, sparfloxacin, CI-960, and CI-990 and 2, 4, and 8 µg/ml for ofloxacin, ^b 50% and 90%, concentrations of antimicrobial agents required to inhibit 50 and 90% of the strains, respectively.

^c One *A. israelii*, one *Actinomyces* VPI group 1, two *A. meyerii* and one *A. odontolyticus* isolate. ^d Three *B. gracilis*, six *B. ureolyticus*, and two *Wolinella recta* isolates.

^e Four C. bifermentans, three C. butyricum, one C. cadaveris, three C. difficile, one C. limosum, three C. paraputrificum, two C. sordelii, three C. subterminale, one C. symbiosum, and two C. tertium isolates.

^f Six F. mortiferum, ten F. necrophorum, four F. nucleatum isolates.

⁸ Four P. anaerobius, five P. asaccharolyticus, four P. micros, four P. magnus, and five P. prevotii isolates.

^h Two P. asaccharolytica, two P. gingivalis, six P. intermedia, and seven P. melaninogenica isolates.

¹ Seven P. buccae and seven P. oralis isolates.

^j Five P. acnes, three P. avidum, and three P. granulosum isolates.

isolates from the 12 genera and 52 species tested were susceptible to $\leq 2 \mu g/ml$. As reported previously (8, 16, 19), ciprofloxacin had relatively poor activity.

King et al. (12) tested CI-960 (PD 127391) and found that "differences in susceptibility between the Bact. fragilis group were minimal but Bact. ovatus and Bact. uniformis were the least sensitive." We noted that all of the B. fragilis group species were very susceptible to CI-960 but B. thetaiotaomicron, for which the MIC₉₀ was 2 µg/ml, was the least susceptible. In accord with others studies (6, 11), most of our isolates were also very susceptible to WIN 57273, but we encountered resistance in four strains (P. melaninogenica,

TABLE 2.	MICs obtained for ATCC control strains on
	supplemented brucella agar

	MIC range (mode; µg/ml)					
Drug	B. fragilis ATCC 25285	B. thetaiotaomicron ATCC 29741	E. lentum ATCC 43055			
Ciprofloxacin	2-2 (2)	16-16	0.5-2 (1)			
Ofloxacin	1-2(2)	8-8	1-1(1)			
CI-960	0.06-0.06 (0.06)	0.25-0.25	0.03-0.06 (0.06)			
CI-990	1-1 (1)	2–2	0.5-0.5 (0.5)			
Sparfloxacin	1-2(1)	2–2	1-1 (1)			
Temafloxacin	0.5 - 1(0.5)	2-4	0.5-1 (0.5)			
WIN 57273	0.25-0.25 (0.25)	0.25-0.25	0.06-0.25 (0.125)			

C. limosum, and F. gonidiaformans), and several other strains, including isolates of B. caccae, B. distasonis, B. fragilis, B. thetaiotaomicron, F. varium, F. ulcerans, and Veillonella species, required up to $2 \mu g/ml$ for inhibition.

Studies of the efficacy of sparfloxacin against anaerobes have used diverse methods and inocula (1, 3, 13, 18). By using an agar dilution method, brucella blood agar, and a 10^5 CFU inoculum, we showed slightly different results with species variation among B. fragilis group isolates. We also noted clustering at concentrations of 2 to 4 μ g/ml for B. fragilis but not the other B. fragilis group species. Sparfloxacin had MIC₉₀s of 4 µg/ml for B. fragilis, B. caccae, B. distasonis, and B. ovatus but 2 µg/ml for B. vulgatus and 8 µg/ml for B. thetaiotaomicron. Temafloxacin and CI-990 were similar in their spectra of activity against anaerobic bacteria. CI-990 was more active than temafloxacin against the B. ureolyticus group, some clostridia, some fusobacteria, lactobacilli, and pigmented Prevotella-Porphyromonas species, while temafloxacin was more active against B. vulgatus and P. bivia. Our temafloxacin data for B. fragilis (MIC₉₀, 4 µg/ml) and C. perfringens (MIC₉₀, 0.5 µg/ml) were the same as those of Hardy et al. (9), who used Wilkins-Chalgren agar. Comparatively, our strains of peptostreptococci were more susceptible (MIC₉₀, 0.25 versus 2 μ g/ml) but we could not compare their "other *Bacteroides* species" group owing to lack of species identification data. Cohen et al. (5) recently tested PD 131628, the active metabolite of the prodrug L-ananyl aminde, PD 131112 (CI-990), against 41 anaerobic bacteria by using a broth microdilution method and showed it to be active at $\leq 4 \mu g/ml$ against *B. fragilis* group species. Our data showed that the CI-990 MIC₉₀ was 4 μ g/ml for B. fragilis, B. caccae, and B. ovatus strains but B. distasonis, B. thetaiotaomicron, and B. vulgatus strains were more resistant (MIC₉₀, 16 µg/ml).

Isolates included strains variously susceptible to clindamycin, cefoxitin, and piperacillin. No relationship between resistance to those agents and resistance to the fluoroquinolones was noted. One *B. fragilis* strain resistant to imipenem (MIC, >128 μ g/ml) and all beta-lactams was susceptible to all quinolones except ciprofloxacin. For strains for which the MIC of any fluoroquinolone was increased, the MICs of the others were quantitatively similarly increased.

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