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In Vitro Activity of Gemifloxacin (SB 265805) against Anaerobes

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Gemifloxacin mesylate (SB 265805), a new fluoronaphthyridone, was tested against 359 recent clinical anaerobic isolates by the National Committee for Clinical Laboratory Standards reference agar dilution method with supplemented brucella blood agar and an inoculum of 10^5 CFU/spot. Comparative antimicrobials tested included trovafloxacin, levofloxacin, grepafloxacin, sparfloxacin, sitafloxacin (DU-6859a), penicillin G, amoxicillin clavulanate, imipenem, cefoxitin, clindamycin, and metronidazole. The MIC_{50} and MIC_{90} (MICs at which 50 and 90% of the isolates were inhibited) of gemifloxacin against various organisms (with the number of strains tested in parentheses) were as follows (in micrograms per milliliter): for *Bacteroides fragilis* (28), 0.5 and 2; for *Bacteroides thetaiotaomicron* (24), 1 and 16; for *Bacteroides caccae* (12), 1 and 16; for *Bacteroides distasonis* (12), 8 and >16; for *Bacteroides ovatus* (12), 4 and >16; for *Bacteroides stercoris* (12), 0.5 and 0.5; for *Bacteroides uniformis* (12), 1 and 4; for *Bacteroides vulgatus* (11), 4 and 4; for *Clostridium clostridioforme* (15), 0.5 and 0.5; for *Clostridium difficile* (15), 1 and >16; for *Clostridium innocuum* (13), 0.125 and 2; for *Clostridium perfringens* (13), 0.06 and 0.06; for *Clostridium ramosum* (14), 0.25 and 8; for *Fusobacterium nucleatum* (12), 0.125 and 0.25; for *Fusobacterium necrophorum* (11), 0.25 and 0.5; for *Fusobacterium varium* (13), 0.5 and 1; for *Fusobacterium* spp. (12), 1 and 2; for *Peptostreptococcus anaerobius* (13), 0.06 and 0.06; for *Peptostreptococcus asaccharolyticus* (13), 0.125 and 0.125; for *Peptostreptococcus magnus* (14), 0.03 and 0.03; for *Peptostreptococcus micros* (12), 0.06 and 0.06; for *Peptostreptococcus prevotii* (14), 0.06 and 0.25; for *Porphyromonas asaccharolytica* (11), 0.125 and 0.125; for *Prevotella bivia* (10), 8 and 16; for *Prevotella buccae* (10), 2 and 2; for *Prevotella intermedia* (10), 0.5 and 0.5; and for *Prevotella melaninogenica* (11), 1 and 1. Gemifloxacin mesylate (SB 265805) was 1 to 4 dilutions more active than trovafloxacin against fusobacteria and peptostreptococci, and the two drugs were equivalent against clostridia and *P. asaccharolytica*. Gemifloxacin was equivalent to sitafloxacin (DU 6859a) against peptostreptococci, *C. perfringens*, and *C. ramosum*, and sitafloxacin was 2 to 3 dilutions more active against fusobacteria. Sparfloxacin, grepafloxacin, and levofloxacin were generally less active than gemifloxacin against all anaerobes.

Gemifloxacin mesylate (also called SB 265805 or LB20304), (*R*,*S*)-7-(3-aminomethyl-4-*syn*-methoxyimino-1-pyrrolidinyl)-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid methanesulfonate, is a new fluoronaphthyridone with a broad spectrum of antimicrobial activity and enhanced activity against gram-positive aerobes (1, 3, 6). It is a racemic mixture (specific rotation = 0.0) with equipotent enantiomers (6a). Reports of several studies using a limited number of genera and strains have noted that it has potential activity against anaerobic bacteria, both gram positive and gram negative (1, 4). In order to further evaluate gemifloxacin's potential therapeutic utility against infections caused by anaerobic bacteria, we studied its in vitro activity against 359 recent clinical anaerobic isolates.

MATERIALS AND METHODS

The 359 anaerobic strains used had been isolated recently (from 1995 through 1998) from humans with clinical infections and identified by standard criteria (2, 7). The control strains *Bacteroides fragilis* ATCC 25285 and *Bacteroides thetaiotaomicron* ATCC 29741 were also included on each set of plates tested. Quality control was assured when limits approved by the National Committee for Clinical Laboratory Standards (NCCLS), were recorded for the various established compounds for *B. fragilis* ATCC 25285 and *B. thetaiotaomicron* ATCC 29741. *Fusobacterium necrogenes* ATCC 25556 was included for comparative purposes. The numbers and species of isolates tested are given in Table 1.

Standard laboratory powders were supplied as follows: gemifloxacin and amoxicillin clavulanate by SmithKline Beecham, Philadelphia, Pa.; trovafloxacin by Pfizer Inc., New York, N.Y.; levofloxacin by R. W. Johnson Pharmaceutical Research Institute, Raritan, N.J.; grepafloxacin by Glaxo-Wellcome Inc., Research Triangle Park, N.C.; sparfloxacin by Rhone-Poulenc Rorer, Collegeville, Pa.; sitafloxacin by Daichi Pharmaceuticals, Tokyo, Japan; cefoxitin and imipenem by Merck & Co., West Point, Pa.; clindamycin by Pharmacia Upjohn Co., Kalamazoo, Mich.; metronidazole by Searle Research & Development, Skokie, Ill.; and penicillin G by Sigma Chemical Co., St. Louis, Mo.

Frozen cultures were transferred twice on brucella agar supplemented with hemin, vitamin K_1, and 5% sheep blood. Susceptibility testing was performed according to NCCLS standards (5). Brucella agar supplemented with hemin, vitamin K_1, and 5% laked sheep blood was the basal medium. Antimicrobial agents were reconstituted according to the manufacturers' instructions. Serial twofold dilutions of various concentrations of antimicrobial agents were prepared on the day of the test and added to the test agar medium.

The agar plates were inoculated with a Steers replicator (Craft Machine Inc., Chester, Pa.). The inoculum used was 10^5 CFU per spot. Plates were incubated in an anaerobic chamber for 48 h at 37°C prior to examination. The MIC was defined as the lowest concentration of an agent that yielded either no growth or a marked change in the appearance of growth compared to that on the growth control plate.

RESULTS AND DISCUSSION

The comparative activities of gemifloxacin and the other agents tested are presented in Table 1. Our comparison of compounds was conducted on a MIC basis, since breakpoints have not yet been established for all of the compounds.

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TABLE 1. In vitro activity of gemifloxacin (SB 265805) compared to those of 11 other antimicrobial agents against 359 recently isolated clinical anaerobic bacterial strains

Organism (no. of isolates) and agent	MIC		
	Range	50%	90%
Bacteroides fragilis (28)			
Gemifloxacin	0.5–2	0.5	2
Trovafloxacin	0.125–4	0.25	0.5
Sitafloxacin	0.06–0.25	0.06	0.25
Grepafloxacin	1–16	2	4
Levofloxacin	1–>16	1	4
Sparfloxacin	0.5–16	1	2
Penicillin G	0.5–>64	16	>64
Amoxicillin clavulanate	0.25–32	0.5	8
Cefoxitin	2–128	8	32
Imipenem	0.03–>32	0.125	2
Metronidazole	0.5–>16	2	2
Clindamycin	≤0.06–>128	1	>128
Bacteroides thetaiotaomicron (24)			
Gemifloxacin	0.5–>16	1	16
Trovafloxacin	0.25–4	0.5	4
Sitafloxacin	0.06–16	0.25	2
Grepafloxacin	2–>16	2	>16
Levofloxacin	2–>16	4	>16
Sparfloxacin	2–>16	2	>16
Penicillin G	4–>64	32	>64
Amoxicillin clavulanate	0.5–16	1	4
Cefoxitin	4–128	32	64
Imipenem	0.125–8	0.25	1
Metronidazole	0.5–4	2	2
Clindamycin	≤0.06–>128	16	>128
Bacteroides caccae (12)			
Gemifloxacin	0.5–16	1	16
Trovafloxacin	0.125–4	0.5	2
Sitafloxacin	0.06–2	0.125	2
Grepafloxacin	2–>16	4	8
Levofloxacin	1–>16	4	>16
Sparfloxacin	0.5–>16	2	16
Penicillin G	8–64	8	32
Amoxicillin clavulanate	0.25–8	0.25	2
Cefoxitin	8–32	16	16
Imipenem	0.03–0.5	0.06	0.25
Metronidazole	1–8	2	4
Clindamycin	0.25–>128	2	>128
Bacteroides distasonis (12)			
Gemifloxacin	0.5–>16	8	>16
Trovafloxacin	0.125–4	0.5	2
Sitafloxacin	0.06–4	0.5	2
Grepafloxacin	1–>16	8	>16
Levofloxacin	1–>16	4	16
Sparfloxacin	1–16	4	16
Penicillin G	8–>64	16	>64
Amoxicillin clavulanate	0.25–8	2	8
Cefoxitin	8–128	16	32
Imipenem	0.03–1	0.25	0.5
Metronidazole	1–8	4	4
Clindamycin	0.125–>128	2	>128
Bacteroides ovatus (12)			
Gemifloxacin	0.5–>16	4	>16
Trovafloxacin	0.5–8	1	4
Sitafloxacin	0.125–>16	0.5	4
Grepafloxacin	2–>16	8	>16
Levofloxacin	4–>16	4	>16
Sparfloxacin	1–>16	2	16
Penicillin G	16–>64	32	>64
Amoxicillin clavulanate	0.5–8	0.5	2
Cefoxitin	16–>128	32	128
Imipenem	0.125–1	0.25	0.5
Metronidazole	1–4	2	2
Clindamycin	1–>128	2	>128
Bacteroides stercoris (12)			
Gemifloxacin	0.25–8	0.5	0.5
Trovafloxacin	0.25–1	0.25	0.5
Sitafloxacin	0.06–1	0.06	0.125
Grepafloxacin	2–8	2	2
Levofloxacin	1–8	1	2
Sparfloxacin	0.5–2	1	2
Penicillin G	2–>64	8	16
Amoxicillin clavulanate	0.25–4	1	2
Cefoxitin	1–32	8	32
Imipenem	≤0.015–0.5	0.125	0.25
Metronidazole	0.25–4	4	4
Clindamycin	≤0.06–>128	2	4
Bacteroides uniformis (12)			
Gemifloxacin	0.125–16	1	4
Trovafloxacin	0.06–4	0.5	4
Sitafloxacin	0.03–4	0.125	4
Grepafloxacin	0.25–>16	4	8
Levofloxacin	≤0.5–>16	4	>16
Sparfloxacin	0.25–>16	2	8
Penicillin G	0.125–>64	16	>64
Amoxicillin clavulanate	0.125–8	0.5	4
Cefoxitin	1–128	8	32
Imipenem	0.06–1	0.25	1
Metronidazole	≤0.06–4	4	4
Clindamycin	≤0.06–>128	0.5	>128
Bacteroides vulgatus (1)			
Gemifloxacin	0.5–16	4	4
Trovafloxacin	0.125–4	0.25	4
Sitafloxacin	0.06–4	0.125	1
Grepafloxacin	2–>16	4	8
Levofloxacin	1–>16	2	>16
Sparfloxacin	0.5–>16	1	16
Penicillin G	1–>64	64	>64
Amoxicillin clavulanate	0.25–8	2	2
Cefoxitin	2–128	16	32
Imipenem	0.03–1	0.25	1
Metronidazole	1–4	2	2
Clindamycin	≤0.06–>128	0.25	>128
Clostridium clostridioforme (15)			
Gemifloxacin	0.125–1	0.5	0.5
Trovafloxacin	0.5–8	4	8
Sitafloxacin	0.125–0.5	0.25	0.25
Grepafloxacin	1–16	8	16
Levofloxacin	8–>16	8	>16
Sparfloxacin	4–>16	8	16
Penicillin G	0.5–>32	2	32
Amoxicillin clavulanate	0.5–4	0.5	4
Cefoxitin	2–16	4	16
Imipenem	0.06–2	1	2
Metronidazole	≤0.06–0.5	0.125	0.5
Clindamycin	0.03–8	0.06	4
Clostridium difficile (15)			
Gemifloxacin	1–>16	1	>16
Trovafloxacin	0.5–>16	1	>16
Sitafloxacin	0.125–1	0.25	1
Grepafloxacin	4–>16	16	16
Levofloxacin	2–>16	4	>16

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TABLE 1—*Continued*

Organism (no. of isolates) and agent	MIC		
	Range	50%	90%
Sparfloxacin	4–>16	4	>16
Penicillin G	1–4	2	4
Amoxicillin clavulanate	0.5–1	1	1
Cefoxitin	>32	>32	>32
Imipenem	2–16	4	4
Metronidazole	0.125–1	0.5	1
Clindamycin	0.5–>128	4	>128
Clostridium innocuum (13)			
Gemifloxacin	0.06–2	0.125	2
Trovafloxacin	0.125–8	0.25	4
Sitafloxacin	0.125–4	0.125	1
Grepafloxacin	0.5–>16	1	>16
Levofloxacin	1–>16	2	16
Sparfloxacin	0.25–16	0.5	16
Penicillin G	0.25–0.5	0.25	0.5
Amoxicillin clavulanate	0.125–0.5	0.5	0.5
Cefoxitin	8–>32	>32	>32
Imipenem	0.5–2	1	2
Metronidazole	0.25–1	0.5	0.5
Clindamycin	0.25–>128	0.5	>128
Clostridium perfringens (13)			
Gemifloxacin	0.03–0.125	0.06	0.06
Trovafloxacin	0.06–0.25	0.125	0.25
Sitafloxacin	≤0.015–0.125	0.06	0.06
Grepafloxacin	0.06–2	0.25	0.5
Levofloxacin	0.25–1	0.25	1
Sparfloxacin	0.03–0.5	0.125	0.25
Penicillin G	0.03–0.125	0.06	0.125
Amoxicillin clavulanate	≤0.015–0.06	≤0.015	0.06
Cefoxitin	0.25–2	0.5	1
Imipenem	0.03–0.125	0.06	0.06
Metronidazole	0.5–2	1	2
Clindamycin	0.03–4	1	2
Clostridium ramosum (14)			
Gemifloxacin	0.125–8	0.25	8
Trovafloxacin	0.25–16	0.5	8
Sitafloxacin	0.125–8	0.25	4
Grepafloxacin	1–>16	2	>16
Levofloxacin	2–>16	4	>16
Sparfloxacin	0.5–>16	2	>16
Penicillin G	0.06–0.5	0.125	0.5
Amoxicillin clavulanate	0.06–0.25	0.06	0.125
Cefoxitin	4–>32	8	>32
Imipenem	0.125–0.5	0.25	0.25
Metronidazole	1–>16	1	2
Clindamycin	4–8	8	8
Fusobacterium nucleatum (12)			
Gemifloxacin	0.03–0.25	0.125	0.25
Trovafloxacin	0.03–0.5	0.03	0.5
Sitafloxacin	≤0.015–0.06	0.03	0.03
Grepafloxacin	0.25–1	0.5	0.5
Levofloxacin	0.06–1	0.5	0.5
Sparfloxacin	0.25–2	0.5	1
Penicillin G	≤0.015	≤0.015	≤0.015
Amoxicillin clavulanate	≤0.015–0.06	≤0.015	≤0.015
Cefoxitin	≤0.015–0.25	≤0.015	0.06
Imipenem	≤0.015–0.03	≤0.015	0.03
Metronidazole	≤0.06–0.5	0.125	0.25
Clindamycin	≤0.015–0.06	0.03	0.06
Fusobacterium necrophorum (11)			
Gemifloxacin	0.125–0.5	0.25	0.5
Trovafloxacin	0.125–2	0.5	1
Sitafloxacin	≤0.015–0.06	0.03	0.06
Grepafloxacin	2–8	4	8
Levofloxacin	0.5–4	2	2
Sparfloxacin	0.5–4	1	2
Penicillin G	≤0.015	≤0.015	≤0.015
Amoxicillin clavulanate	≤0.015–0.03	≤0.015	0.03
Cefoxitin	≤0.015–0.06	0.03	0.03
Imipenem	≤0.015	≤0.015	≤0.015
Metronidazole	≤0.06–0.5	0.125	0.5
Clindamycin	≤0.015–0.03	≤0.015	0.03
Fusobacterium varium (13)			
Gemifloxacin	0.125–16	0.5	1
Trovafloxacin	0.5–8	4	4
Sitafloxacin	0.06–8	0.25	0.5
Grepafloxacin	4–>16	16	>16
Levofloxacin	1–>16	8	>16
Sparfloxacin	1–>16	8	16
Penicillin G	0.06–1	0.5	0.5
Amoxicillin clavulanate	0.25–2	1	2
Cefoxitin	0.25–8	4	8
Imipenem	0.06–2	0.5	1
Metronidazole	0.125–2	0.5	2
Clindamycin	0.125–16	4	16
Fusobacterium spp. (12)[a]			
Gemifloxacin	0.125–8	1	2
Trovafloxacin	0.5–4	2	4
Sitafloxacin	0.06–1	0.5	0.5
Grepafloxacin	8–>16	16	>16
Levofloxacin	1–>16	8	>16
Sparfloxacin	1–>16	8	>16
Penicillin G	≤0.015–>32	0.25	1
Amoxicillin clavulanate	0.5–32	1	4
Cefoxitin	1–8	4	8
Imipenem	0.25–1	0.5	1
Metronidazole	0.25–2	0.5	1
Clindamycin	0.06–32	0.125	32
Peptostreptococcus anaerobius (13)			
Gemifloxacin	≤0.015–8	0.06	0.06
Trovafloxacin	≤0.015–8	0.125	0.125
Sitafloxacin	≤0.015–0.5	0.03	0.03
Grepafloxacin	0.25–8	1	1
Levofloxacin	0.25–>16	0.25	0.5
Sparfloxacin	0.125–>16	0.5	1
Penicillin G	≤0.015–16	0.125	8
Amoxicillin clavulanate	≤0.015–16	0.15	16
Cefoxitin	≤0.015–16	0.5	16
Imipenem	≤0.015–1	0.06	1
Metronidazole	0.25–>32	2	4
Clindamycin	≤0.015–1	0.25	0.5
Peptostreptococcus asaccharolyticus (13)			
Gemifloxacin	≤0.015–125	0.125	0.125
Trovafloxacin	0.06–1	0.5	1
Sitafloxacin	≤0.015–0.5	0.125	0.25
Grepafloxacin	0.125–2	0.5	2
Levofloxacin	0.25–8	4	8
Sparfloxacin	0.06–4	0.25	4
Penicillin G	≤0.015–0.125	≤0.015	0.03
Amoxicillin clavulanate	≤0.015–0.06	0.03	0.06
Cefoxitin	0.03–0.125	0.06	0.125
Imipenem	≤0.015	≤0.015	≤0.015
Metronidazole	0.125–2	1	2

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TABLE 1—*Continued*

Organism (no. of isolates) and agent	MIC		
	Range	50%	90%
Clindamycin	≤0.015–128	0.06	32
Peptostreptococcus magnus (14)			
Gemifloxacin	≤0.015–1	0.03	0.03
Trovafloxacin	0.06–2	0.06	0.25
Sitafloxacin	≤0.015–0.25	≤0.015	0.06
Grepafloxacin	0.06–2	0.125	0.5
Levofloxacin	0.25–4	0.5	4
Sparfloxacin	0.06–4	0.125	0.25
Penicillin G	≤0.015–0.25	0.06	0.125
Amoxicillin clavulanate	0.03–0.25	0.125	0.25
Cefoxitin	0.125–1	0.5	0.5
Imipenem	≤0.015–0.125	0.06	0.06
Metronidazole	0.25–2	0.5	1
Clindamycin	0.06–2	1	2
Peptostreptococcus micros (12)			
Gemifloxacin	0.06–0.125	0.06	0.06
Trovafloxacin	0.06–0.125	0.06	0.06
Sitafloxacin	≤0.015–0.03	≤0.015	0.03
Grepafloxacin	1	1	1
Levofloxacin	0.5–1	0.5	0.5
Sparfloxacin	0.5	0.5	0.5
Penicillin G	≤0.015–0.06	≤0.015	0.03
Amoxicillin clavulanate	0.06–0.5	0.06	0.25
Cefoxitin	0.5–1	0.5	1
Imipenem	≤0.015–0.03	0.03	0.03
Metronidazole	≤0.06–0.5	0.5	0.5
Clindamycin	0.125–1	0.125	0.5
Peptostreptococcus prevotii (14)			
Gemifloxacin	0.03–16	0.06	0.25
Trovafloxacin	0.126–>16	0.25	1
Sitafloxacin	≤0.015–1	0.06	0.5
Grepafloxacin	0.25–>16	0.25	4
Levofloxacin	0.25–>16	2	16
Sparfloxacin	0.06–>16	0.25	4
Penicillin G	≤0.015–0.125	0.03	0.125
Amoxicillin clavulanate	≤0.015–0.125	0.03	0.125
Cefoxitin	0.03–1	0.125	0.5
Imipenem	≤0.015–0.06	≤0.015	0.06
Metronidazole	0.25–>32	0.5	2
Clindamycin	≤0.015–128	0.5	64
Porphyromonas asaccharolytica (11)			
Gemifloxacin	0.06–0.125	0.125	0.125
Trovafloxacin	0.125–0.5	0.25	0.25
Sitafloxacin	≤0.015–0.06	0.03	0.03
Grepafloxacin	0.5–4	2	2
Levofloxacin	0.06–1	0.5	0.5
Sparfloxacin	0.06–1	1	1
Penicillin G	≤0.015–2	≤0.015	1
Amoxicillin clavulanate	≤0.015–0.125	≤0.015	0.125
Cefoxitin	≤0.015–2	0.125	1
Imipenem	≤0.015	≤0.015	≤0.015
Metronidazole	≤0.06–0.5	0.25	0.5
Clindamycin	≤0.015–>126	≤0.015	>128
Prevotella bivia (10)			
Gemifloxacin	8–16	8	16
Trovafloxacin	1–2	2	2
Sitafloxacin	0.125–0.25	0.25	0.25
Grepafloxacin	8–16	16	16
Levofloxacin	2–4	2	4
Sparfloxacin	4–8	4	8
Penicillin G	0.06–32	4	16
Amoxicillin clavulanate	0.06–2	0.25	2
Cefoxitin	0.25–8	1	8
Imipenem	≤0.015–0.06	0.03	0.06
Metronidazole	0.5–8	2	2
Clindamycin	≤0.015–>128	≤0.015	0.03
Prevotella buccae (10)			
Gemifloxacin	0.5–4	2	2
Trovafloxacin	0.125–2	0.5	1
Sitafloxacin	0.03–0.5	0.03	0.06
Grepafloxacin	1–8	4	8
Levofloxacin	0.5–>16	0.5	1
Sparfloxacin	1–>16	1	2
Penicillin G	0.06–>32	16	>32
Amoxicillin clavulanate	0.06–1	0.25	0.5
Cefoxitin	0.5–16	4	8
Imipenem	0.03–0.125	0.06	0.125
Metronidazole	1–8	2	2
Clindamycin	≤0.015–0.25	≤0.015	≤0.015
Prevotella intermedia (10)			
Gemifloxacin	0.06–0.5	0.5	0.5
Trovafloxacin	0.03–0.5	0.5	0.5
Sitafloxacin	≤0.015–0.06	≤0.015	0.03
Grepafloxacin	0.5–2	1	2
Levofloxacin	0.25–1	0.25	0.5
Sparfloxacin	0.25–2	1	1
Penicillin G	≤0.015–>32	0.03	16
Amoxicillin clavulanate	0.03–16	0.06	0.5
Cefoxitin	0.125–32	0.25	2
Imipenem	≤0.015–2	0.03	0.06
Metronidazole	0.5–2	1	2
Clindamycin	≤0.015–0.5	≤0.015	≤0.015
Prevotella melaninogenica (11)			
Gemifloxacin	0.125–16	1	1
Trovafloxacin	0.03–4	1	1
Sitafloxacin	≤0.015–0.5	0.03	0.06
Grepafloxacin	0.125–8	0.25	0.5
Levofloxacin	0.25–8	1	1
Sparfloxacin	0.25–2	2	2
Penicillin G	0.03–16	4	8
Amoxicillin clavulanate	≤0.015–2	0.125	2
Cefoxitin	0.06–2	1	2
Imipenem	≤0.015–0.06	0.03	0.06
Metronidazole	0.25–2	0.5	1
Clindamycin	≤0.015–>128	≤0.015	0.03

[a] Includes *F. mortiferum* (three strains), *F. necrogenes* (four strains), and *F. ulcerans* (five strains).

Cormicon and Jones (1), using brucella blood agar, tested a limited number of *B. fragilis* group species strains and noted that the MIC of gemifloxacin at which 90% of the isolates were inhibited (MIC_{90}) was 8 μg/ml but did not identify differences among the various species. Our study found marked differences in the activity of gemifloxacin against the various species belonging to the *B. fragilis* group. Gemifloxacin was active against *B. fragilis* at ≤2 μg/ml and was more active than grepafloxacin and levofloxacin (MIC_{90}s, 4 μg/ml). Similar results were reported by Marco et al. (4), who also used brucella agar supplemented with 5% sheep blood and an inoculum of 10^5 CFU/ml. They tested 35 strains of *B. fragilis* and reported a

MIC range of 0.5 to 8 μg/ml and a MIC_{90} of 1 μg/ml for gemifloxacin and a MIC_{90} of 0.5 μg/ml (range, ≤0.25 to 4 μg/ml) for trovafloxacin. They did not, however, report results for other individual member species of the *B. fragilis* group. In our study, sitafloxacin was generally four times more active (MIC_{90}, 0.25 μg/ml) than gemifloxacin, and trovafloxacin (MIC range, 0.125 to 4 μg/ml; MIC_{90}, 0.5 μg/ml) was twice as active. For almost all *Bacteroides distasonis* and *Bacteroides ovatus* strains, the MIC of gemifloxacin was >2 μg/ml. For all but one *Bacteroides stercoris* strain, the MIC of gemifloxacin was ≤0.5 μg/ml. *B. thetaiotaomicron* and *Bacteroides caccae* strains had a biphasic distribution of susceptibility to gemifloxacin, which had a MIC_{50} of 1 μg/ml but a MIC_{90} of 16 μg/ml. *Bacteroides uniformis* and *Bacteroides vulgatus* showed marked strain variation in relation to gemifloxacin.

All *Prevotella intermedia* strains and all but one strain of *Prevotella melaninogenica* were susceptible to ≤0.5 and ≤1 μg of gemifloxacin/ml, respectively. Generally, ≥2 μg/ml was required for inhibition of *Prevotella buccae* and ≥8 μg/ml for that of *Prevotella bivia*. The only species of *Porphyromonas* that we tested was *Porphyromonas asaccharolytica*, all strains of which were inhibited by ≤0.125 μg of gemifloxacin/ml.

Gemifloxacin showed generally good activity against gram-positive anaerobic bacteria. The respective MIC_{90}s of gemifloxacin, trovafloxacin, and sitafloxacin against the various clostridia were as follows: for *Clostridium clostridioforme*, 0.5, 8, and 0.25 μg/ml; for *Clostridium difficile*, >16, >16, and 1 μg/ml; for *Clostridium innocuum*, 2, 4, and 1 μg/ml; for *Clostridium perfringens*, 0.06, 0.25, and 0.06 μg/ml; and for *Clostridium ramosum*, 8, 8, and 4 μg/ml. Marco et al. (4) noted that gemifloxacin and trovafloxacin had MIC_{90}s of 1 μg/ml against a mélange of clostridial species. They also noted that sparfloxacin was much less active, with a MIC_{90} of 8 μg/ml. In our study, gemifloxacin was 1 to 2 dilutions more active than trovafloxacin against fusobacteria and peptostreptococci (*Peptostreptococcus anaerobius*, *Peptostreptococcus asaccharolyticus*, *Peptostreptococcus magnus*, *Peptostreptococcus micros*, and *Peptostreptococcus prevotii*) and was equivalent to trovafloxacin in activity against *P. asaccharolytica* and clostridia. Gemifloxacin was equivalent to sitafloxacin against peptostreptococci, *C. perfringens*, and *C. ramosum* and was 2 to 3 dilutions less active against fusobacteria. Sparfloxacin, grepafloxacin, and levofloxacin were generally less active than gemifloxacin against all anaerobes. Marco et al. (4) reported that gemifloxacin and trovafloxacin each had a MIC_{90} of 2 μg/ml against a combined group of 18 strains of peptostreptococci and a MIC_{90} of 4 μg/ml against fusobacteria. Because the study by Marco et al. (4) used 119 strains of anaerobes of various genera but did not report data on individual species other than *B. fragilis*, it is difficult to draw comparisons with our results, which found such marked variation among species.

Gemifloxacin had selectively potent activity against the various anaerobic species tested, with generally improved activity against gram-positive anaerobes and fusobacteria. It showed moderate but variable activity against gram-negative anaerobes. The advantage of this selective anaerobic activity may become evident if gemifloxacin is proven to have clinical efficacy in situations such as dental, head and neck, and pleuropulmonary infections, where gram-positive anaerobes, fusobacteria, and some *Prevotella* and *Porphyromonas* species predominate, while minimizing disturbance of the normal enteric flora.

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