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In Vitro Activity of Bay 12-8039, a New 8-Methoxyquinolone, Compared to the Activities of 11 Other Oral Antimicrobial Agents against 390 Aerobic and Anaerobic Bacteria Isolated from Human and Animal Bite Wound Skin and Soft Tissue Infections in Humans

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The in vitro activity of Bay 12-8039, a new oral 8-methoxyquinolone, was compared to the activities of 11 other oral antimicrobial agents (ciprofloxacin, levofloxacin, ofloxacin, sparfloxacin, azithromycin, clarithromycin, amoxicillin clavulanate, penicillin, cefuroxime, cefpodoxime, and doxycycline) against 250 aerobic and 140 anaerobic bacteria recently isolated from animal and human bite wound infections. Bay 12-8039 was active against all aerobic isolates, both gram-positive and gram-negative isolates, at ≤1.0 μg/ml (MICs at which 90% of isolates are inhibited [MIC_{90s} ≤0.25 μg/ml) and was active against most anaerobes at ≤0.5 μg/ml; the exceptions were *Fusobacterium nucleatum* and other *Fusobacterium* species (MIC_{90}s, ≥4.0 μg/ml) and one strain of *Prevotella loeschii* (MICs, 2.0 μg/ml). In comparison, the other quinolones tested had similar in vitro activities against the aerobic strains but were less active against the anaerobes, including peptostreptococci, *Porphyromonas* species, and *Prevotella* species. The fusobacteria were relatively resistant to all the antimicrobial agents tested except penicillin G (one penicillinase-producing strain of *F. nucleatum* was found) and amoxicillin clavulanate.

One of two Americans are bitten by animals or other humans in their lifetimes, and 5 to 25% of these wounds become infected and require antimicrobial therapy (12, 21). Most bite wound infections result from the oral bacterial flora of the biting animal (veterinary isolates in the case of dog and cat bite wound infections in humans) (4, 12, 15, 19, 30). Most of these skin and soft tissue infections are treatable on an outpatient basis with elevation of the effected body part and administration of oral antimicrobial agents (5, 12). Those injuries which present for medical attention within 8 h after the incident and which are classified as moderate to severe, including those involving the hands, require a short course of oral antimicrobial prophylaxis (12). Since it is not cost-effective to culture wounds from patients presenting early after being bitten and many laboratories would have difficulty isolating and identifying the diverse, fastidious veterinary bacteria from infected bite wounds, even if they were cultured (2, 4, 7, 15, 16), the basis for the selection of oral antimicrobial therapy is often the published literature. However, published studies of the in vitro activities of new antimicrobial agents typically report aerobic isolates and rarely include all the genera and species isolated from bite wounds (6, 10, 27, 28, 35). Consequently, microbiologic surveys must be performed periodically in order to assist the physician in selecting clinically appropriate antimicrobial therapy.

Bay 12-8039 is a new oral 8-methoxyquinolone agent {1-cyclopropyl-7[(*S*,*S*)-2,8 diazabicyclo [4.3.0] non-8-yl]-6-fluoro-6-methoxy-1,4-dihydro-4-oxo-3-quinolone carboxylic acid} that appears to be appropriate for once-daily dosing (22, 31) and that is safe without evidence of phototoxicity (34). Bay 12-8039 has been noted to possess activity against aerobic gram-positive and gram-negative bacteria as well as anaerobes (1, 8, 9, 17, 29, 35). While these preliminary studies have examined the quinolone's activity against a broad range of clinical pathogens, they have not previously examined its activity against the fastidious bacterial strains that are typically isolated from human and animal bite wounds. Consequently, we tested recent isolates from clinical bite wounds and 17 American Type Culture Collection (ATCC) strains against Bay 12-8039 and 11 other oral antimicrobial agents with potential clinical utility in bite wound infection therapy.

MATERIALS AND METHODS

Most of the strains (263 isolates) were recent, pretherapy clinical isolates (1995 and 1996), and the remainder (127 isolates) were from our collection of isolates from infected skin and soft tissue bite wounds in humans. All isolates were identified by standard criteria (18–20, 23, 32). The specific sources were dog bites (n = 155), cat bites (n = 154), human bites (n = 54), squirrel bites (n = 2), pig bites (n = 1), monkey bites (n = 2), bites of other animals (n = 6), and bites of unknown animal origin (n = 6). Seventeen ATCC strains were also tested. The numbers and species of isolates tested are given in Table 1.

Standard laboratory powders of the following antimicrobial agents were supplied by the indicated companies: Bay 12-8039 and ciprofloxacin, Bayer Corp., West Haven, Conn.; ofloxacin and levofloxacin, R. W. Johnson Pharmaceutical Research Institute, Raritan, N.J.; sparfloxacin, Parke-Davis Pharmaceutical Research Division of Warner Lambert Co., Ann Arbor, Mich.; cefpodoxime, The Upjohn Co., Kalamazoo, Mich.; cefuroxime, Glaxo Welcome, Research Triangle Park, N.C.; amoxicillin clavulanate, SmithKline Beecham Pharmaceuticals, Philadelphia, Pa.; azithromycin and doxycycline, Pfizer Inc., New York, N.Y.; clarithromycin, Abbott Pharmaceuticals Inc., Abbott Park, Ill.; and penicillin G, Eli Lilly & Co., Indianapolis, Ind.

Frozen cultures were transferred twice onto Trypticase soy agar supplemented with 5% sheep blood or chocolate agar for the aerobes and brucella agar supplemented with hemin, vitamin K_1, and 5% sheep blood for the anaerobes to ensure purity and good growth. Susceptibility testing was performed according to

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TABLE 1. In vitro activity of Bay 12-8039 compared to those of 11 other oral antimicrobial agents against 250 aerobic isolates from wounds caused by human and animal bites

Isolate (no. of isolates) and antimicrobial agent	MIC (μg/ml)		
	Range	50%	90%
Actinobacillus and *Haemophilus* spp.[a] (11)			
Bay 12-8039	0.008–0.06	0.016	0.06
Levofloxacin	0.008–0.06	0.008	0.06
Ofloxacin	0.008–0.125	0.016	0.125
Sparfloxacin	0.004–0.016	0.004	0.016
Ciprofloxacin	0.008–0.125	0.016	0.125
Azithromycin	0.125–4.0	0.25	4.0
Clarithromycin	0.06–16	1.0	16
Penicillin G	0.16–4.0	0.06	4.0
Amoxicillin clavulanate	0.016–0.5	0.25	0.5
Cefuroxime	0.03–2.0	0.06	1.0
Cefpodoxime	0.016–0.25	0.03	0.125
Doxycycline	0.03–1.0	0.25	1.0
Capnocytophaga spp. (7)			
Bay 12-8039	0.004–1.0	0.03	
Levofloxacin	0.008–1.0	0.03	
Ofloxacin	0.03–1.0	0.06	
Sparfloxacin	0.004–0.25	0.016	
Ciprofloxacin	0.016–1.0	0.06	
Azithromycin	0.06–1.0	0.5	
Clarithromycin	0.03–0.25	0.06	
Penicillin G	0.03–0.5	0.125	
Amoxicillin clavulanate	0.03–0.25	0.125	
Cefuroxime	0.016–1.0	0.25	
Cefpodoxime	0.016–0.25	0.016	
Doxycycline	0.03–0.5	0.06	
Corynebacterium spp. (15)			
Bay 12-8039	0.002–1.0	0.03	0.25
Levofloxacin	0.008–1.0	0.06	0.5
Ofloxacin	0.016–4.0	0.25	1.0
Sparfloxacin	0.002–4.0	0.016	0.125
Ciprofloxacin	0.004–0.5	0.06	0.5
Azithromycin	0.016–16	0.03	2.0
Clarithromycin	0.016–8.0	0.016	1.0
Penicillin G	0.016–1.0	0.016	1.0
Amoxicillin clavulanate	0.016–1.0	0.06	0.5
Cefuroxime	0.016–2.0	0.06	1.0
Cefpodoxime	0.016–>4	0.25	4.0
Doxycycline	0.016–4.0	0.06	0.25
EF-4b (21)			
Bay 12-8039	0.004–0.5	0.016	0.25
Levofloxacin	0.002–0.06	0.008	0.016
Ofloxacin	0.008–0.5	0.03	0.5
Sparfloxacin	0.001–0.008	0.002	0.008
Ciprofloxacin	0.002–0.25	0.008	0.125
Azithromycin	0.03–0.25	0.03	0.125
Clarithromycin	0.06–2.0	0.125	2.0
Penicillin G	0.06–2.0	0.25	2.0
Amoxicillin clavulanate	0.06–1.0	0.25	0.5
Cefuroxime	0.016–8.0	1.0	1.0
Cefpodoxime	0.016–0.5	0.06	0.125
Doxycycline	0.125–0.5	0.25	0.25
Eikenella corrodens (22)			
Bay 12-8039	0.008–0.125	0.016	0.06
Levofloxacin	0.004–0.03	0.008	0.016
Ofloxacin	0.008–0.125	0.016	0.06
Sparfloxacin	0.002–0.03	0.016	0.03
Ciprofloxacin	0.008–0.06	0.008	0.016
Azithromycin	0.125–4.0	1.0	4.0
Clarithromycin	0.125–4.0	2.0	4.0
Penicillin G	0.016–4.0	0.5	2.0
Amoxicillin clavulanate	0.03–1.0	0.5	1.0
Cefuroxime	0.25–16	2.0	8.0
Cefpodoxime	0.06–1.0	0.125	0.5
Doxycycline	0.125–2.0	0.5	2.0
Moraxella spp. (12)			
Bay 12-8039	0.004–0.03	0.004	0.03
Levofloxacin	0.001–0.03	0.002	0.016
Ofloxacin	0.004–0.06	0.008	0.06
Sparfloxacin	0.002–0.016	0.002	0.008
Ciprofloxacin	0.001–0.03	0.002	0.03
Azithromycin	0.016–0.25	0.06	0.06
Clarithromycin	0.03–1.0	0.125	0.25
Penicillin G	0.016–0.25	0.06	0.125
Amoxicillin clavulanate	0.016–0.25	0.125	0.125
Cefuroxime	0.03–0.5	0.25	0.5
Cefpodoxime	0.016–0.6	0.06	0.06
Doxycycline	0.016–0.125	0.125	0.125
Neisseria weaveri (18)			
Bay 12-8039	0.004–0.25	0.03	0.06
Levofloxacin	0.004–0.06	0.008	0.008
Ofloxacin	0.008–0.25	0.06	0.06
Sparfloxacin	0.002–0.06	0.004	0.016
Ciprofloxacin	0.008–0.25	0.016	0.03
Azithromycin	0.06–0.25	0.125	0.25
Clarithromycin	0.03–0.5	0.25	0.5
Penicillin G	0.016–2.0	1.0	2.0
Amoxicillin clavulanate	0.03–0.5	0.25	0.5
Cefuroxime	0.125–1.0	0.5	1.0
Cefpodoxime	0.016–0.125	0.016	0.06
Doxycycline	0.03–0.25	0.25	0.25
Pasteurella canis (9)			
Bay 12-8039	0.004–0.016	0.008	
Levofloxacin	0.004–0.008	0.008	
Ofloxacin	0.008–0.03	0.016	
Sparfloxacin	0.002–0.004	0.002	
Ciprofloxacin	0.002–0.004	0.004	
Azithromycin	0.125–0.125	0.125	
Clarithromycin	0.5–4.0	1.0	
Penicillin G	0.03–0.5	0.03	
Amoxicillin clavulanate	0.03–0.06	0.06	
Cefuroxime	0.016–0.125	0.03	
Cefpodoxime	0.016–0.016	0.016	
Doxycycline	0.06–0.5	0.06	
Pasteurella multocida subsp. *multocida* (19)			
Bay 12-8039	0.008–0.026	0.008	0.016
Levofloxacin	0.008–0.016	0.008	0.016
Ofloxacin	0.016–0.03	0.016	0.03
Sparfloxacin	0.001–0.004	0.002	0.004
Ciprofloxacin	0.002–0.016	0.008	0.008
Azithromycin	0.06–0.25	0.125	0.25
Clarithromycin	0.5–2.0	1.0	2.0
Penicillin G	0.06–0.06	0.06	0.06
Amoxicillin clavulanate	0.06–0.125	0.06	0.125
Cefuroxime	0.06–0.06	0.06	0.06
Cefpodoxime	0.016–0.03	0.03	0.03
Doxycycline	0.03–0.125	0.03	0.06
Pasteurella multocida subsp. *septica* (13)			
Bay 12-8039	0.008–0.016	0.016	0.016
Levofloxacin	0.008–0.016	0.008	0.016
Ofloxacin	0.016–0.03	0.03	0.03
Sparfloxacin	0.001–0.004	0.004	0.004
Ciprofloxacin	0.004–0.008	0.008	0.008
Azithromycin	0.03–0.25	0.125	0.25
Clarithromycin	0.25–2.0	1.0	1.0
Penicillin G	0.03–0.06	0.06	0.06
Amoxicillin clavulanate	0.06–0.125	0.06	0.125
Cefuroxime	0.03–0.06	0.06	0.06
Cefpodoxime	0.016–0.03	0.03	0.03
Doxycycline	0.03–0.125	0.03	0.06

Continued

TABLE 1—*Continued*

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TABLE 1—*Continued*

Isolate (no. of isolates) and antimicrobial agent	MIC (μg/ml)		
	Range	50%	90%
Pasteurella spp. (other)[b] (14)			
Bay 12-8039	0.004–0.06	0.008	0.03
Levofloxacin	0.004–0.016	0.008	0.016
Ofloxacin	0.008–0.06	0.016	0.03
Sparfloxacin	0.002–0.016	0.002	0.008
Ciprofloxacin	0.004–0.008	0.004	0.008
Azithromycin	0.06–0.25	0.125	0.5
Clarithromycin	0.125–8.0	1.0	4.0
Penicillin G	0.03–0.25	0.06	0.125
Amoxicillin clavulanate	0.03–0.25	0.06	0.125
Cefuroxime	0.016–0.125	0.03	0.06
Cefpodoxime	0.016–0.06	0.016	0.03
Doxycycline	0.06–0.5	0.125	0.125
Staphylococcus aureus (18)			
Bay 12-8039	0.016–0.06	0.03	0.03
Levofloxacin	0.03–0.125	0.06	0.125
Ofloxacin	0.125–0.25	0.25	0.25
Sparfloxacin	0.016–0.06	0.03	0.03
Ciprofloxacin	0.06–0.5	0.25	0.5
Azithromycin	0.06–0.25	0.25	0.25
Clarithromycin	0.06–0.5	0.125	0.5
Penicillin G	0.06–32	2.0	8.0
Amoxicillin clavulanate	0.06–1.0	0.5	0.5
Cefuroxime	0.06–1.0	0.5	1.0
Cefpodoxime	0.25–4.0	2.0	2.0
Doxycycline	0.06–4.0	0.06	1.0
Staphylococcus epidermidis (15)			
Bay 12-8039	0.03–0.06	0.06	0.06
Levofloxacin	0.06–0.25	0.125	0.125
Ofloxacin	0.125–1.0	0.25	0.25
Sparfloxacin	0.03–0.06	0.03	0.06
Ciprofloxacin	0.03–0.5	0.06	0.125
Azithromycin	0.125–>16	0.25	>16
Clarithromycin	0.03–>32	0.125	>32
Penicillin G	0.016–>16	0.25	4.0
Amoxicillin clavulanate	0.03–1.0	0.25	0.5
Cefuroxime	0.06–2.0	0.25	2.0
Cefpodoxime	0.125–8.0	1.0	4.0
Doxycycline	0.06–4.0	0.25	4.0
Staphylococcus spp. (other)[c] (9)			
Bay 12-8039	0.03–0.125	0.03	
Levofloxacin	0.06–0.25	0.06	
Ofloxacin	0.125–1.0	0.25	
Sparfloxacin	0.016–0.06	0.03	
Ciprofloxacin	0.06–0.25	0.06	
Azithromycin	0.06–>16	0.25	
Clarithromycin	0.03–>32	0.25	
Penicillin G	0.03–16	0.016	
Amoxicillin clavulanate	0.03–2.0	0.125	
Cefuroxime	0.06–8.0	0.125	
Cefpodoxime	0.06–>8.0	0.25	
Doxycycline	0.03–8.0	0.125	
Streptococcus spp.[d] (32)			
Bay 12-8039	0.002–0.5	0.06	0.25
Levofloxacin	0.008–0.5	0.25	0.5
Ofloxacin	0.001–2.0	1.0	1.0
Sparfloxacin	0.004–0.5	0.06	0.25
Ciprofloxacin	0.001–2.0	0.5	1.0
Azithromycin	0.016–>16	0.03	2.0
Clarithromycin	0.016–>32	0.03	2.0
Penicillin G	0.006–8.0	0.03	0.25
Amoxicillin clavulanate	0.016–2.0	0.03	0.25
Cefuroxime	0.016–8.0	0.125	2.0
Cefpodoxime	0.016–>8.0	0.125	4.0
Doxycycline	0.016–16	0.06	4.0
Weeksella zoohelcum (10)			
Bay 12-8039	0.004–0.016	0.008	0.016
Levofloxacin	0.001–0.03	0.016	0.016
Ofloxacin	0.06–0.125	0.06	0.125
Sparfloxacin	0.004–0.008	0.008	0.008
Ciprofloxacin	0.002–0.06	0.03	0.06
Azithromycin	0.03–0.5	0.5	0.5
Clarithromycin	0.016–0.06	0.03	0.06
Penicillin G	0.016–0.125	0.016	0.06
Amoxicillin clavulanate	0.016–0.25	0.06	0.25
Cefuroxime	0.016–0.5	0.03	0.25
Cefpodoxime	0.016–0.125	0.016	0.016
Doxycycline	0.025–0.5	0.5	0.5
Miscellaneous[e] (5)			

[a] *Actinobacillus actinomycetemcomitans*, *n* = 4; *Haemophilus parainfluenzae*, *n* = 2; *Haemophilus aphrophilus*, *n* = 1; other *Haemophilus* species, *n* = 4.

[b] *P. dagmatis*, *n* = 4; *P. haemolytica*, *n* = 1; *P. multocida* subsp. *gallicida*, *n* = 2; *P. pneumotropica*, *n* = 1; *P. stomatis*, *n* = 5; *P. testudinis*, *n* = 1.

[c] *S. intermedius*, *n* = 4; *S. hyicus*, *n* = 1; *S. hominis*, *n* = 2; *S. capitis*, *n* = 1; *S. haemolyticus*, *n* = 1.

[d] *S. mitis*, *n* = 8; *S. mutans*, *n* = 1; *S. sanguis*, *n* = 9; group C, *n* = 1; group F, *n* = 1; *S. equinus*, *n* = 1; *S. constellatus*, *n* = 3; other *Streptococcus* species, *n* = 8.

[e] *Flavobacterium* spp., *n* = 3; *Rothia dentocariosa*, *n* = 1; *Brevibacterium* sp., *n* = 1.

the standards of the National Committee for Clinical Laboratory Standards (25, 26). Brucella agar supplemented with hemin, vitamin K_1, and 5% laked sheep blood was the basal medium used for anaerobic species and for *Eikenella corrodens*, *Weeksella zoohelicum*, and *Capnocytophaga* species. Mueller-Hinton agar was used for staphylococci, and Mueller-Hinton agar supplemented with 5% sheep blood was used for the remainder of the organisms. Antimicrobial agents were reconstituted according to the manufacturers' instructions. Serial twofold dilutions of antimicrobial agents were prepared on the day of the test and were added to the media at various concentrations.

The agar plates were inoculated with a Steers replicator (Craft Machine Inc., Chester, Pa.). The inoculum used for aerobic bacteria was 10^4 CFU per spot, and the inoculum used for *E. corrodens* and anaerobic bacteria was 10^5 CFU per spot. Control plates without antimicrobial agents were inoculated before and after each set of drug-containing plates was inoculated. Plates with aerobic isolates were incubated at 35°C in an aerobic environment for 24 h and then examined. *E. corrodens* and streptococci were incubated in 5% CO_2 for 48 h and were then examined. Plates with anaerobes were incubated in an anaerobic chamber (Anaerobe Systems) at 35°C for 48 h and were then examined.

The control strains tested included *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Bacteroides fragilis* ATCC 25285, and *Eubacterium lentum* ATCC 43055. The ATCC strains included in the analysis were *E. corrodens* ATCC 23834, *Pasteurella multocida* subsp. *multocida* ATCC 43137 and ATCC 12947, *Pasteurella haemolytica* ATCC 33396, *P. multocida* subsp. *gallicida* ATCC 51689, *P. multocida* subsp. *septica* ATCC 51688, *Pasteurella stomatis* ATCC 43327, *Pasteurella dagmatis* ATCC 43325, *Pasteurella canis* ATCC 43326, *Pasteurella testudinis* ATCC 33688, *Moraxella osloensis* ATCC 19976, and *Moraxella lacunata* ATCC 17967. These strains were tested simultaneously with the appropriate plates and environments. The MIC was defined as the lowest concentration of an agent that yielded no growth or a marked change in the appearance of growth compared to that on the growth control plate.

RESULTS AND DISCUSSION

The activities of the antimicrobial agents against the bite wound isolates tested are presented in Tables 1 and 2. There was no difference in the antimicrobial susceptibilities of isolates from human bite and other animal bite wounds when they were represented in a single genus or species (e.g., *S. aureus*, streptococci, *E. corrodens*, fusobacteria, and *Prevotella* species). Bay 12-8039 was active against all aerobic isolates, both gram-positive and gram-negative, at ≤1.0 μg/ml (MICs at which 90% of isolates are inhibited [MIC_{90}s], ≤0.25 μg/ml).

TABLE 2. In vitro activity of Bay 12-8039 compared to those of 11 other oral antimicrobial agents against 140 anaerobic isolates from wounds caused by human and animal bites

Isolate (no. of isolates) and antibacterial agent	MIC (μg/ml)		
	Range	50%	90%
Bacteroides tectum (22)			
Bay 12-8039	0.03–0.25	0.06	0.125
Levofloxacin	0.125–1.0	0.125	0.25
Ofloxacin	0.25–2.0	0.25	0.5
Sparfloxacin	0.125–0.5	0.25	0.25
Ciprofloxacin	0.5–2.0	0.25	1.0
Azithromycin	0.5–2.0	1.0	1.0
Clarithromycin	0.125	0.125	0.125
Penicillin G	0.016–16	0.016	0.06
Amoxicillin clavulanate	0.03–0.5	0.06	0.125
Cefuroxime	0.03–>8	0.06	0.25
Cefpodoxime	0.125–>8	0.25	1.0
Doxycycline	0.03–8.0	0.06	2.0
Fusobacterium nucleatum (21)			
Bay 12-8039	0.008–8.0	1.0	4.0
Levofloxacin	0.06–>16	8.0	>16
Ofloxacin	0.03–>16	4.0	>16
Sparfloxacin	0.016–>16	16	16
Ciprofloxacin	0.06–>16	8	>16
Azithromycin	0.016–4	1.0	4
Clarithromycin	0.016–>16	8	16
Penicillin G	0.008–16	0.03	0.5
Amoxicillin clavulanate	0.016–0.125	0.06	0.125
Cefuroxime	0.016–8.0	0.25	8.0
Cefpodoxime	0.008–8.0	0.05	4.0
Doxycycline	0.06–2.0	0.125	2.0
Fusobacterium spp. (other)[a] (15)			
Bay 12-8039	0.03–8.0	4	8
Levofloxacin	0.125–>16	16	>16
Ofloxacin	0.06–>16	>16	>16
Sparfloxacin	0.008–>16	16	16
Ciprofloxacin	0.03–>16	16	>16
Azithromycin	0.06–4	0.25	4
Clarithromycin	0.016–>16	2	>16
Penicillin G	0.008–0.125	0.03	0.125
Amoxicillin clavulanate	0.016–0.25	0.06	0.25
Cefuroxime	0.008–8.0	0.06	8.0
Cefpodoxime	0.008–>8.0	0.125	>8.0
Doxycycline	0.016–0.05	0.125	0.5
Peptostreptococcus spp. (9)			
Bay 12-8039	0.03–0.5	0.25	
Levofloxacin	0.125–4	1.0	
Ofloxacin	0.5–8	1.0	
Sparfloxacin	0.03–1.0	0.25	
Ciprofloxacin	0.25–4	2	
Azithromycin	0.016–>16	0.5	
Clarithromycin	0.016–>16	0.06	
Penicillin G	0.008–0.5	0.25	
Amoxicillin clavulanate	0.016–1.0	0.25	
Cefuroxime	0.06–4.0	1.0	
Cefpodoxime	0.06–4.0	2.0	
Doxycycline	0.06–4.0	0.06	
Porphyromonas salivosa (11)			
Bay 12-8039	0.06–0.125	0.125	0.125
Levofloxacin	0.025–0.5	0.5	0.5
Ofloxacin	0.06–1.0	0.5	1.0
Sparfloxacin	0.03–0.5	0.5	0.5
Ciprofloxacin	0.5–1.0	1.0	1.0
Azithromycin	0.125–1.0	0.25	0.5
Clarithromycin	0.016–0.125	0.06	0.125
Penicillin G	0.008–1.0	0.5	1.0
Amoxicillin clavulanate	0.03–0.125	0.06	0.06
Cefuroxime	2.0–4.0	4.0	4.0
Cefpodoxime	0.25–4.0	1.0	2.0
Doxycycline	0.03–8.0	0.125	0.5
Porphyromonas gingivalis (10)			
Bay 12-8039	0.008–0.06	0.06	0.06
Levofloxacin	<0.016–0.125	0.125	0.125
Ofloxacin	0.016–0.25	0.25	0.25
Sparfloxacin	<0.016–0.125	0.06	0.125
Ciprofloxacin	0.06–0.5	0.25	0.5
Azithromycin	0.016–0.5	0.125	0.25
Clarithromycin	<0.016–0.016	0.016	0.016
Penicillin G	<0.008–0.03	0.008	0.03
Amoxicillin clavulanate	0.016–0.06	0.016	0.03
Cefuroxime	0.016–0.06	0.03	0.06
Cefpodoxime	0.016–0.03	0.016	0.03
Doxycycline	0.06–0.5	0.25	0.5
Porphyromonas spp. (other)[b] (14)			
Bay 12-8039	0.125–0.5	0.25	0.5
Levofloxacin	0.03–2	0.5	2
Ofloxacin	0.5–4	1.0	2
Sparfloxacin	0.125–1.0	0.25	1.0
Ciprofloxacin	0.125–2	1.0	2
Azithromycin	0.016–0.5	0.125	0.25
Clarithromycin	0.016–0.125	0.03	0.06
Penicillin G	0.008–0.5	0.016	0.016
Amoxicillin clavulanate	0.015–0.125	0.016	0.03
Cefuroxime	0.008–2.0	0.016	0.03
Cefpodoxime	0.008–2.0	0.06	0.06
Doxycycline	0.125–0.25	0.125	0.25
Prevotella heparinolytica (12)			
Bay 12-8039	0.125–0.25	0.125	0.125
Levofloxacin	0.25–0.5	0.25	0.5
Ofloxacin	0.25–1.0	1.0	1.0
Sparfloxacin	0.25	0.25	0.25
Ciprofloxacin	2–4	2	4
Azithromycin	0.25–0.5	0.5	0.5
Clarithromycin	0.03–0.125	0.06	0.06
Penicillin G	0.06–0.25	0.25	0.25
Amoxicillin clavulanate	0.125–0.5	0.25	0.25
Cefuroxime	0.03–1.0	0.5	1.0
Cefpodoxime	0.25–0.5	0.5	0.5
Doxycycline	0.06–8.0	0.125	8.0
Prevotella spp. (other)[c] (26)			
Bay 12-8039	0.03–2.0	0.25	0.5
Levofloxacin	0.125–2	0.25	0.5
Ofloxacin	0.25–4	1.0	1.0
Sparfloxacin	0.03–4	0.25	2
Ciprofloxacin	0.125–4	1.0	4
Azithromycin	0.06–2	0.5	1.0
Clarithromycin	0.016–0.25	0.06	0.125
Penicillin G	0.016–32	0.06	32
Amoxicillin clavulanate	0.016–0.5	0.125	0.5
Cefuroxime	0.016–>8.0	0.5	>8.0
Cefpodoxime	0.03–>8.0	0.5	8.0
Doxycycline	0.06–16	0.25	4.0

[a] *F. necrophorum*, $n = 3$; *F. russii*, $n = 7$; *F. gonidiaformans*, $n = 1$; other *Fusobacterium* spp., $n = 4$.

[b] *P. cangingivalis*, $n = 4$; *P. canoris*, $n = 5$; *P. cansulci*, $n = 2$; *P. circumdentaria*, $n = 2$; other *Porphyromonas* species, $n = 1$.

[c] *P. bivia*, $n = 5$; *P. buccae*, $n = 3$; *P. intermedia*, $n = 6$; *P. melaninogenica*, $n = 4$; *P. loeschii*, $n = 2$; *P. zoogleoformans*, $n = 2$; *P. denticola*, $n = 1$; other *Prevotella* spp., $n = 3$.

Almost all anaerobes were susceptible to ≤0.5 μg of Bay 12-8039 per ml; the exceptions were *Fusobacterium nucleatum* and other *Fusobacterium* species (MIC_{90}s, ≥4.0 μg/ml) and one strain of *Prevotella loeschii* (MIC, 2.0 μg/ml). In comparison, the other quinolones tested had similar activities against aerobes but were less active than Bay 12-8039 against the anaer-

obes, including the peptostreptococci and the *Porphyromonas* and *Prevotella* species tested. These results are in accord with those of our earlier studies (13, 14) that noted that ciprofloxacin, ofloxacin, and sparfloxacin have limited activities against certain anaerobic strains.

The fusobacteria were relatively resistant to all the agents tested, including the quinolones, macrolides, and cephalosporins, but were generally susceptible to penicillin G and amoxicillin clavulanate. One strain of *F. nucleatum*, isolated from a cat bite wound, was found to produce penicillinase, and the penicillin G MIC was 16 μg/ml for this isolate. While penicillinase-producing strains of *F. nucleatum* have been isolated previously, albeit rarely, from human infections, including bacteremia (3, 11, 33), we are unaware of previous animal source strains that were penicillinase producing.

Pasteurella species are recognized as common isolates cultured from infected animal bite wounds, but most studies do not differentiate the various species and subspecies (4, 15, 16, 30). In 1985, Mutters et al. (24) proposed the reclassification of *Pasteurella* into 13 taxa on the basis of DNA hybridization studies. Subsequently, Holst et al. (19) studied 159 strains recovered from 146 infected humans collected over a 3-year period. They found that *P. multocida* subsp. *multocida* and *P. multocida* subsp. *septica* were routinely recovered from the more serious infections. In addition, *P. multocida* subsp. *septica* was also thought to have a greater tropism for the central nervous system. They noted other ecological differences between species in that *P. canis* was recovered only from dog bite wounds, while most isolates of the other species and subspecies were recovered from cat bite and cat scratch wounds. The current study is unique in that all *Pasteurella* isolates were identified to the species level to evaluate if there were any differences in susceptibility patterns. We found all *Pasteurella* species and *P. multocida* subspecies tested to be susceptible to Bay 12-8039. They were also susceptible to all the other antimicrobial agents tested except clarithromycin. For a variety of *P. canis*, *P. dagmatis*, *P. stomatis*, and *P. testudinis* strains tested, clarithromycin MICs were 4 to 8 μg/ml.

Among the other antimicrobial agents tested, we found that doxycycline was less active against the gram-positive aerobes and anaerobes (*Corynebacterium* species, staphylococci, streptococci, and peptostreptococci) as well as some strains of *Bacteroides tectum*, *Porphyromonas salivosa*, and *Prevotella heparinolytica*. Cefuroxime and cefpodoxime were also less active against gram-positive aerobes and had limited activity against non-*P. heparinolytica Prevotella* species, fusobacteria, and some *B. tectum* strains.

In general, azithromycin was more active than clarithromycin by 2 to 4 dilutions against many aerobic species such as *Actinobacillus* and *Haemophilus* species, *Moraxella* species, all *Pasteurella* species, and *P. multocida* subspecies. Clarithromycin was more active than azithromycin against some anaerobes such as *B. tectum* and *Porphyromonas* and *Prevotella* species. This may be related to the relatively greater effect on azithromycin than clarithromycin of CO_2 in the incubation atmosphere and the resultant pH of the agar medium surface. Azithromycin has two basic groups and is expected to be more pH sensitive than clarithromycin to anaerobic test conditions.

This study suggests that Bay 12-8039 is active in vitro against a wide variety of aerobic and anaerobic bacteria that are encountered in animal and human bite wounds. The true value of this investigational quinolone, however, will depend on the findings of clinical trials.

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