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In vitro Activity of Gemifloxacin Against Recent Clinical Isolates of Bacteria in Korea

Gemifloxacin is an enhanced-affinity fluoroquinolone with broad-spectrum antibacterial activity. In Korea, resistant bacteria are relatively more prevalent than in other industrialized countries. In this study, we studied the in vitro activities of gemifloxacin, gatifloxacin, moxifloxacin, levofloxacin, ciprofloxacin, and other commonly used antimicrobial agents against 1,689 bacterial strains isolated at four Korean university hospitals during 1999-2000. Minimum inhibitory concentrations (MICs) were determined using the agar dilution method of National Committee for Clinical Laboratory Standards. Gemifloxacin had the lowest MICs for the respiratory pathogens: 90% of *Streptococcus pneumoniae, Moraxella catarrhalis*, and *Haemophilus influenzae* were inhibited by 0.06, 0.03, and 0.03 mg/L, respectively. Gemifloxacin was more active than the other fluoroquinolones against methicillin-susceptible *Staphylococcus aureus*, coagulase-negative staphylococci, streptococci, and *Enterococcus faecalis*. The MIC_{90}s of gemifloxacin for *Klebsiella oxytoca, Proteus vulgaris*, and non-typhoidal *Salmonella* spp. were 0.25, 1.0, and 0.12 mg/L, respectively, while those for other Gram-negative bacilli were 4-64 mg/L. In conclusion, gemifloxacin was the most active among the comparative agents against Gram-positive species, including respiratory pathogens isolated in Korea.

Key Words : *Fluoroquinolone; Gemifloxacin; Korea; Streptococcus pneumoniae; Haemophilus influenzae*

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INTRODUCTION

In the face of the increasing worldwide problem of antimicrobial resistance, many classes of antimicrobial agents have become less useful for therapy (1). Fluoroquinolones continued to be used for the treatment of various infections, because they are active against both Gram-positive, and Gram-negative bacteria (2-4). However, resistance to the second-generation fluoroquinolones has increased against many bacterial species. Gemifloxacin is a new fluoroquinolones under development with enhanced affinity for topoisomerase IV, and DNA gyrase, and has the lowest minimum inhibitory concentrations (MICs) against clinical isolates of *Streptococcus pneumoniae* (5-7). In Korea, resistant bacteria are relatively more prevalent than in other industrialized countries, and are a serious problem currently (8). In this study, we tested the in vitro activity of gemifloxacin, and comparative agents against recent Korean bacterial isolates.

MATERIALS AND METHODS

A total of 1,689 clinical bacterial isolates were collected from four Korean university hospitals during 1999-2000. *Neisseria gonorrhoeae* isolates were obtained, mostly from female patients. Identifications of species were performed by conventional methods or through the usage of commercial kits. Isolates were stored in skim milk at -70˚C until required.

Antimicrobial susceptibility was determined, using the National Committee for Clinical Laboratory Standards (NCCLS) agar dilution method (9) with Mueller-Hinton agar (BBL, Cockeysville, MD, U.S.A.), except for streptococci, *N. gonorrhoeae,* and *Haemophilus influenzae*, for which 5% lysed sheep blood-supplemented Mueller-Hinton agar, IsoVitaleX (BBL)-supplemented GC agar, and Haemophilus Test Medium, respectively, were used.

The antimicrobial agents used were: gemifloxacin (LGCI, Seoul, Korea), gatifloxacin (Bristol-Myers Squibb, Princeton,

NJ, U.S.A.), ciprofloxacin, and moxifloxacin (Bayer, Wuppertal, Germany), levofloxacin (Daiichi Pharmaceutical, Tokyo, Japan), amoxicillin-clavulanic acid, and ceftazidime (GlaxoSmithKline, Harlow, U.K.), ceftriaxone (Roche, Basel, Switzerland), imipenem (MSD, Elkton, VA, U.S.A.), spectinomycin (Upjohn, Bridgewater, NJ, U.S.A.), and penicillin G, ampicillin, oxacillin, cefuroxime, erythromycin, gentamicin, tetracycline, and vancomycin (Sigma, St. Louis, MO, U.S.A.). The ratio of amoxicillin to clavulanic acid was 2:1. As the breakpoints of ciprofloxacin for *S. pneumoniae* is not defined by the NCCLS, the criteria used by Doern et al. (10) were applied, i.e., an MIC ≥ 4 mg/L as resistant, and ≤ 1 mg/L as susceptible. Quality controls were performed using *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* 29212, *S. pneumoniae* ATCC 49619, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *N. gonorrhoeae* ATCC 49226, *H. influenzae* ATCC 49247 or *H. influenzae* ATCC 49766, depending on test organisms.

RESULTS AND DISCUSSION

The activities of gemifloxacin, and the other antimicrobial agents against common respiratory pathogens are shown in Table 1. All isolates of *S. pneumoniae*, except one, were inhibited by ≤ 0.25 mg/L of gemifloxacin. One *S. pneumoniae* isolate with a gemifloxacin MIC of 2 mg/L was inhibited by 32 mg/L of levofloxacin, 64 mg/L of ciprofloxacin, 8 mg/L of moxi-

Table 1. In vitro activity of gemifloxacin, and other antimicrobial agents against recent clinical isolates of *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*

Organism (no. of isolates tested), and antimicrobial agent	MIC (mg/L)		
	Range	50%	90%
Streptococcus pneumoniae, all (103)			
Gemifloxacin	0.015-2	0.03	0.06
Moxifloxacin	0.12-8	0.25	0.25
Gatifloxacin	0.03-8	0.5	0.5
Levofloxacin	0.5-32	1	2
Ciprofloxacin	0.5-64	2	4
Penicillin	≤0.008-8	2	4
Ceftriaxone	0.015-4	1	2
Erythromycin	0.03->128	128	>128
S. pneumoniae, Penicillin susceptible (9)			
Gemifloxacin	0.03-0.06	0.03	
Moxifloxacin	0.12-0.25	0.25	
Gatifloxacin	0.5	0.5	
Levofloxacin	1-2	1	
Ciprofloxacin	1-4	2	
Penicillin	≤0.008-0.06	0.015	
Ceftriaxone	0.015-1	0.03	
Erythromycin	0.03->128	0.06	
S. pneumoniae, Penicillin intermediate (16)			
Gemifloxacin	0.015-0.12	0.03	0.06
Moxifloxacin	0.12-0.25	0.25	0.25
Gatifloxacin	0.06-0.5	0.25	0.5
Levofloxacin	1-2	1	2
Ciprofloxacin	0.5-4	1	4
Penicillin	0.12-1	0.5	1
Ceftriaxone	0.015-4	0.25	1
Erythromycin	0.03->128	64	>128
S. pneumoniae, Penicillin resistant (78)			
Gemifloxacin	0.015-2	0.03	0.06
Moxifloxacin	0.12-8	0.25	0.25
Gatifloxacin	0.03-8	0.5	0.5
Levofloxacin	0.5-32	1	2
Ciprofloxacin	1-64	2	4
Penicillin	2-8	4	4
Ceftriaxone	0.12-4	1	2
Erythromycin	0.03->128	128	>128
Haemophilus influenzae, all (73)			
Gemifloxacin	≤0.008-0.12	≤0.008	0.03
Moxifloxacin	≤0.008-1	0.015	0.06
Gatifloxacin	≤0.008-0.5	0.015	0.03
Levofloxacin	≤0.008-0.25	0.015	0.06
Ciprofloxacin	≤0.008-0.25	0.015	0.03
Ampicillin	0.06->128	16	128
Cefuroxime	≤0.03-16	1	4
Ceftriaxone	≤0.008-32	≤0.008	0.06
Amoxicillin-clavulanic acid	≤0.008-16	1	8
H. influenzae, β-lactamase positive (48)			
Gemifloxacin	≤0.008-0.12	≤0.008	0.03
Moxifloxacin	≤0.008-1	0.03	0.06
Gatifloxacin	≤0.008-0.25	0.015	0.03
Levofloxacin	≤0.008-0.25	0.015	0.12
Ciprofloxacin	≤0.008-0.12	0.015	0.03
Ampicillin	4->128	32	128
Cefuroxime	≤0.03-16	1	4
Ceftriaxone	≤0.008-32	≤0.008	0.06
Amoxicillin-clavulanic acid	≤0.008-16	2	8
H. influenzae, β-lactamase negative (25)			
Gemifloxacin	≤0.008-0.03	≤0.008	0.03
Moxifloxacin	≤0.008-0.06	0.015	0.06
Gatifloxacin	≤0.008-0.5	0.015	0.03
Levofloxacin	≤0.008-0.12	0.015	0.06
Ciprofloxacin	≤0.008-0.25	0.015	0.03
Ampicillin	0.06-2	0.5	2
Cefuroxime	0.015-4	0.5	2
Ceftriaxone	≤0.008-1	0.015	0.06
Amoxicillin-clavulanic acid	0.015-16	1	4
Moraxella catarrhalis (60)			
Gemifloxacin	≤0.008-0.03	0.015	0.03
Moxifloxacin	≤0.008-0.12	0.03	0.06
Gatifloxacin	0.03-0.25	0.03	0.06
Levofloxacin	0.03-0.5	0.06	0.06
Ciprofloxacin	≤0.008-1	0.03	0.06
Penicillin	0.5-32	16	32
Erythromycin	0.12-1	0.25	0.5
Tetracycline	0.25-1	0.5	1

floxacin, and 8 mg/L of gatifloxacin. Gemifloxacin (MIC_{90} 0.06 mg/L) was 4 to 64-fold more potent than the other quinolones (MIC_{90} 0.25-4 mg/L), and ≥32-fold more potent than the non-quinolone comparators (MIC_{90} 2->128 mg/L) for *S. pneumoniae*. The percentage of strains with a ciprofloxacin MICs of ≥4 mg/L was 14%, and those with a levofloxacin MICs of ≥8 mg/L was 1.5%. These results indicate that the resistance rates were higher than in the United States (11), and in Japan (12).

Ninety-one percent of *S. pneumoniae* (94/103) were penicillin non-susceptible, but 90% of the isolates were inhibited by ≤0.06 mg/L of gemifloxacin. These results were similar to those from other reports (6, 7), although two studies from North America showed a statistically significant association between resistance to penicillin, and fluoroquinolone (13, 14).

In this study, the rates of β-lactamase-producing *H. influenzae,* and *Moraxella catarrhalis* were found to be higher than those reported in other countries, 66%, and 95%, respectively

Table 2. In vitro activity of gemifloxacin, and other antimicrobial agents against other Gram-positive aerobes

Organism (no. of isolates tested), and antimicrobial agent	MIC (mg/L)		
	Range	50%	90%
Methicillin-susceptible *Staphylococcus aureus* (86)			
Gemifloxacin	0.015-0.5	0.06	0.12
Moxifloxacin	0.03-32	0.12	0.25
Gatifloxacin	0.03-4	0.12	0.25
Levofloxacin	0.015-4	0.25	0.5
Ciprofloxacin	1-32	0.5	1
Oxacillin	≤0.12-2	0.5	1
Erythromycin	≤0.12->128	0.5	>128
Gentamicin	≤0.12->128	1	64
Vancomycin	≤0.12-2	1	1
Methicillin-resistant *S. aureus* (88)			
Gemifloxacin	0.03->128	4	>128
Moxifloxacin	0.015->128	16	128
Gatifloxacin	0.06->128	8	>128
Levofloxacin	0.25->128	32	>128
Ciprofloxacin	0.25->128	64	>128
Oxacillin	4->128	>128	>128
Erythromycin	0.25->128	>128	>128
Gentamicin	0.5->128	128	>128
Vancomycin	0.5-2	1	2
Methicillin-susceptible coagulase-negative staphylococci (60)			
Gemifloxacin	≤0.008-1	0.03	0.12
Moxifloxacin	0.015-4	0.12	0.25
Gatifloxacin	0.015-4	0.12	0.25
Levofloxacin	0.03-8	0.25	0.25
Ciprofloxacin	0.015-8	0.25	0.5
Oxacillin	≤0.12-0.25	0.25	0.25
Erythromycin	≤0.12->128	0.25	>128
Gentamicin	≤0.12-128	0.5	16
Vancomycin	≤0.12-2	1	2
Methicillin-resistant coagulase-negative staphylococci (63)			
Gemifloxacin	≤0.008-8	0.12	1
Moxifloxacin	0.015-8	0.25	4
Gatifloxacin	0.03-8	0.25	4
Levofloxacin	0.12-32	0.25	8
Ciprofloxacin	0.015->128	0.25	128
Oxacillin	0.5->128	4	128
Erythromycin	≤0.12->128	64	>128
Gentamicin	0.25->128	64	128
Vancomycin	≤0.12-2	1	2
Enterococcus faecalis (78)			
Gemifloxacin	≤0.008-8	0.25	8
Moxifloxacin	0.06-32	0.5	16
Gatifloxacin	0.12-32	0.5	16
Levofloxacin	0.5-64	1	64
Ciprofloxacin	0.25-64	1	32
Ampicillin	0.25-8	1	4
Erythromycin	0.25->128	>128	>128
Tetracycline	0.5-128	64	128
Vancomycin	0.5-4	2	4
Enterococcus faecium (82)			
Gemifloxacin	0.015-128	16	64
Moxifloxacin	0.03-64	16	32
Gatifloxacin	0.015-128	16	32
Levofloxacin	0.015->128	32	64
Ciprofloxacin	≤0.008->128	32	>128
Ampicillin	0.5->128	>128	>128
Erythromycin	≤0.12->128	>128	>128
Tetracycline	0.25->128	0.5	64
Vancomycin	0.25->128	1	>128
S. pyogenes (41)			
Gemifloxacin	0.015-0.25	0.06	0.25
Moxifloxacin	0.015-0.5	0.25	0.5
Gatifloxacin	0.03-0.5	0.12	0.5
Levofloxacin	0.015-2	0.5	1
Ciprofloxacin	0.06-2	0.5	1
Penicillin	≤0.008-0.5	0.015	0.06
Ceftriaxone	≤0.008-0.06	0.015	0.03
Erythromycin	0.015->128	0.06	4
S. agalactiae (30)			
Gemifloxacin	0.015-0.25	0.06	0.25
Moxifloxacin	≤0.008-0.25	0.25	0.25
Gatifloxacin	0.12-0.5	0.25	0.25
Levofloxacin	0.25-2	0.5	1
Ciprofloxacin	0.5-4	2	1
Penicillin	≤0.008-1	0.06	0.25
Ceftriaxone	0.015-0.5	0.06	0.12
Erythromycin	0.06->128	0.25	>128
Viridans streptococci (28)			
Gemifloxacin	≤0.008-2	0.06	0.25
Moxifloxacin	≤0.008-8	0.25	0.5
Gatifloxacin	≤0.008-4	0.25	1
Levofloxacin	≤0.008-32	1	2
Ciprofloxacin	≤0.008-64	1	4
Penicillin	≤0.008-32	0.25	4
Ceftriaxone	≤0.008-32	0.12	2
Erythromycin	≤0.008->128	0.06	>128

Table 3. In vitro activity of gemifloxacin, and other antimicrobial agents against Enterobacteriaceae, glucose-nonfermenters, and *Neisseria gonorrhoeae (Table 3. Continued nest)*

Organism (no. of isolates tested), and antimicrobial agent	MIC (mg/L)		
	Range	50%	90%
Escherichia coli (81)			
Gemifloxacin	≤0.008->128	0.12	64
Moxifloxacin	≤0.008-128	0.25	64
Gatifloxacin	≤0.008-64	0.06	8
Levofloxacin	≤0.008-128	0.25	16
Ciprofloxacin	≤0.008->128	0.12	>128
Ampicillin	2->128	>128	>128
Cefuroxime	1->128	4	32
Ceftriaxone	≤0.008->128	0.06	16
Imipenem	0.03-1	0.25	0.25
Amoxicillin-clavulanic acid	2->128	32	64
Gentamicin	0.25->128	1	>128
Klebsiella pneumoniae (81)			
Gemifloxacin	0.03->128	0.06	4
Moxifloxacin	0.06->128	0.25	4
Gatifloxacin	0.015->128	0.06	2
Levofloxacin	0.03->128	0.06	4
Ciprofloxacin	≤0.008->128	0.03	2
Ampicillin	4->128	>128	>128
Cefuroxime	0.5->128	4	>128
Ceftriaxone	0.015->128	0.06	128
Imipenem	0.03-4	0.25	4
Amoxicillin-clavulanic acid	0.5->128	8	64
Gentamicin	0.25->128	0.5	>128
Klebsiella oxytoca (55)			
Gemifloxacin	≤0.008-8	0.06	0.25
Moxifloxacin	0.03-8	0.12	1
Gatifloxacin	0.015-2	0.06	0.12
Levofloxacin	0.03-2	0.06	0.12
Ciprofloxacin	≤0.008-2	0.015	0.06
Ampicillin	32->128	64	>128
Cefuroxime	1->128	4	64
Ceftriaxone	0.03->128	0.12	32
Imipenem	0.12-1	0.25	0.5
Amoxicillin-clavulanic acid	1->128	8	32
Gentamicin	0.25->128	0.5	2
Proteus vulgaris (42)			
Gemifloxacin	0.015-16	0.25	1
Moxifloxacin	0.12-16	0.5	4
Gatifloxacin	0.015-2	0.12	0.5
Levofloxacin	0.015-1	0.06	0.25
Ciprofloxacin	0.015-1	0.03	0.25
Ampicillin	2->128	>128	>128
Cefuroxime	1->128	>128	>128
Ceftriaxone	≤0.008-4	0.12	1
Imipenem	0.03-8	2	4
Amoxicillin-clavulanic acid	0.12->128	8	64
Gentamicin	0.25-16	0.5	4
P. mirabilis (63)			
Gemifloxacin	0.03-16	0.25	8
Moxifloxacin	0.06-64	1	8
Gatifloxacin	0.03-16	0.25	2
Levofloxacin	0.03-8	0.12	2
Ciprofloxacin	0.015-4	0.06	1
Ampicillin	1->128	128	>128
Cefuroxime	0.5->128	4	32
Ceftriaxone	≤0.008-64	0.015	2
Imipenem	0.06-8	1	4
Amoxicillin-clavulanic acid	0.5->128	4	64
Gentamicin	0.25->128	2	>128
Non-typhoidal Salmonella spp. (36)			
Gemifloxacin	≤0.008-0.5	0.03	0.12
Moxifloxacin	≤0.008-4	0.12	1
Gatifloxacin	≤0.008-0.5	0.06	0.25
Levofloxacin	0.015-0.5	0.06	0.5
Ciprofloxacin	≤0.008-0.5	0.015	0.25
Ampicillin	0.5->128	2	>128
Cefuroxime	2-16	8	8
Ceftriaxone	0.03-1	0.12	0.12
Imipenem	0.12-2	0.12	0.5
Amoxicillin-clavulanic acid	0.5->128	2	4
Gentamicin	0.5-16	0.5	2
Citrobacter freundii (62)			
Gemifloxacin	≤0.008-64	0.5	16
Moxifloxacin	0.015-128	1	16
Gatifloxacin	0.015-32	0.5	4
Levofloxacin	0.015-32	0.25	8
Ciprofloxacin	≤0.008-32	0.06	4
Ampicillin	2->128	>128	>128
Cefuroxime	2->128	64	>128
Ceftriaxone	0.015->128	0.5	>128
Imipenem	0.03-4	0.25	0.5
Amoxicillin-clavulanic acid	8->128	128	>128
Gentamicin	0.12->128	1	>128
Enterobacter cloacae (61)			
Gemifloxacin	≤0.008-64	0.25	16
Moxifloxacin	0.015-128	2	16
Gatifloxacin	0.015-32	0.25	16
Levofloxacin	≤0.008-32	0.12	16
Ciprofloxacin	≤0.008->128	0.12	16
Ampicillin	2->128	>128	>128
Cefuroxime	2->128	>128	>128
Ceftriaxone	0.03->128	16	>128
Imipenem	0.06-4	0.5	2
Amoxicillin-clavulanic acid	2->128	64	>128
Gentamicin	0.25->128	2	>128
Morganella morganii (44)			
Gemifloxacin	0.03-32	0.25	16
Moxifloxacin	0.03-64	1	32
Gatifloxacin	0.03-32	0.25	8
Levofloxacin	0.03-32	0.12	8
Ciprofloxacin	≤0.008-128	0.06	8
Ampicillin	16->128	>128	>128
Cefuroxime	8->128	128	>128
Ceftriaxone	≤0.008->128	0.5	32
Imipenem	1-4	2	4
Amoxicillin-clavulanic acid	64->128	>128	>128
Gentamicin	0.25->128	1	64
Providencia spp. (32)			
Gemifloxacin	0.06->128	2	16

(*Continued next page*)

Table 3. (*Continued from the previous page*) In vitro activity of gemifloxacin, and other antimicrobial agents against Enterobacteriaceae, glucose-nonfermenters, and *Neisseria gonorrhoeae*

Organism (no. of isolates tested), and antimicrobial agent	MIC (mg/L)		
	Range	50%	90%
Moxifloxacin	0.12->128	1	32
Gatifloxacin	0.12->128	2	32
Levofloxacin	0.06->128	1	32
Ciprofloxacin	0.03->128	0.5	64
Ampicillin	0.25->128	64	>128
Cefuroxime	≤0.06->128	2	64
Ceftriaxone	≤0.008->128	0.03	0.5
Imipenem	0.5-8	1	4
Gentamicin	0.25->128	8	128
Amoxicillin-clavulanic acid	0.25->128	64	>128
Serratia marcescens (61)			
Gemifloxacin	0.03->128	2	16
Moxifloxacin	0.25-64	8	16
Gatifloxacin	0.06-64	2	8
Levofloxacin	0.03-64	2	8
Ciprofloxacin	≤0.008-64	1	8
Ampicillin	8->128	>128	>128
Cefuroxime	32->128	>128	>128
Ceftriaxone	0.12->128	32	>128
Imipenem	0.5-64	2	8
Amoxicillin-clavulanic acid	8->128	>128	>128
Gentamicin	0.25->128	16	>128
Pseudomonas aeruginosa (83)			
Gemifloxacin	0.25->128	4	128
Moxifloxacin	0.5->128	16	128
Gatifloxacin	0.5-128	4	64
Levofloxacin	0.25-128	4	64
Ciprofloxacin	≤0.06-64	1	32
Ceftazidime	1-128	16	64
Imipenem	0.25-128	2	16
Gentamicin	0.5->128	8	>128
Acinetobacter baumannii (84)			
Gemifloxacin	0.015-64	8	64
Moxifloxacin	0.015-64	8	32
Gatifloxacin	0.03-32	4	16
Levofloxacin	0.06-32	4	16
Ciprofloxacin	0.06->128	32	128
Ampicillin	8->128	>128	>128
Cefuroxime	8->128	>128	>128
Ceftriaxone	4->128	>128	>128
Imipenem	0.06-32	1	8
Gentamicin	0.25->128	128	>128
Amoxicillin-clavulanic acid	0.5->128	16	128
Stenotrophomonas maltophilia (63)			
Gemifloxacin	0.12-16	1	4
Moxifloxacin	0.12-16	1	4
Gatifloxacin	0.06-8	0.5	4
Levofloxacin	0.015-16	0.5	4
Ciprofloxacin	0.5-32	2	16
Ampicillin	64->128	>128	>128
Cefuroxime	1->128	>128	>128
Ceftriaxone	32->128	>128	>128
Imipenem	32->128	>128	>128
Gentamicin	1->128	128	>128
Amoxicillin-clavulanic acid	16->128	64	>128
Neisseria gonorrhoeae (49)			
Gemifloxacin	≤0.008-8	0.12	0.5
Moxifloxacin	≤0.008-4	0.25	0.5
Gatifloxacin	≤0.008-4	0.12	0.25
Levofloxacin	≤0.008-8	0.5	0.5
Ciprofloxacin	≤0.008-32	0.5	0.5
Penicillin	0.25->128	32	>128
Ceftriaxone	≤0.008-0.12	0.03	0.06
Tetracycline	0.5-4	2	4
Spectinomycin	2-32	16	32

(15). Although all of the isolates were inhibited by ≤1 mg/L of all of the fluoroquinolones tested, gemifloxacin had the lowest MIC_{50}, and MIC_{90}, regardless of β-lactamase production. This finding is consistent with other reports (5-7, 16, 17).

The MIC_{90}s of gemifloxacin for methicillin-susceptible *S. aureus* (MSSA), and methicillin-susceptible, and -resistant coagulase-negative staphylococci were 0.12, 0.12, and 1 mg/L, respectively (Table 2). In the present study, gemifloxacin was 2 to 128-fold more potent than the other quinolones (MIC_{90} 0.25-128 mg/L), and 2 to ≥128-fold more potent than the non-quinolone comparators (MIC_{90} 0.25->128 mg/L) for these isolates. Most of the methicillin-resistant *S. aureus* (MRSA) isolates were less susceptible than MSSA to all of the fluoroquinolones.

None of the *E. faecalis* isolates in this study were resistant to vancomycin, while 20% of the *Enterococcus faecium* isolates were vancomycin resistant (Table 2). The MIC_{50} (0.25 mg/L), and MIC_{90} (8 mg/L) of gemifloxacin were 2 to 8-fold lower than the other quinolones for *E. faecalis*. Gemifloxacin was the most potent of the fluoroquinolones studied against *E. faecalis*; however, strains with reduced gemifloxacin susceptibilities were noted, particularly in *E. faecium*. For streptococci other than *S. pneumoniae*, the MIC_{90} of gemifloxacin was 0.25 mg/L, which was 1- to 16-fold lower than that of the other quinolones.

The in vitro activity of fluoroquinolones against Gram-negative bacilli was found to vary significantly, depending on species. In general, the MICs of ciprofloxacin were lower than those of the other quinolones for Gram-negative bacilli, except for *E. coli,* Providencia spp., *Acinetobacter baumannii,* and *Stenotrophomonas maltophilia*. The MIC_{90}s of gemifloxacin for *K. oxytoca, Proteus vulgaris,* and non-typhoidal Salmonella were 0.25, 1.0, and 0.12 mg/L, respectively, while those for other Enterobacteriaceae were 4-64 mg/L, which were similar to or slightly higher than those of ciprofloxacin (Table 3). None of the *N. gonorrhoeae* isolates tested were susceptible to penicillin. The MIC_{90} of ciprofloxacin was 0.5 mg/L, and 92% of *N. gonorrhoeae* were non-susceptible to ciprofloxacin. This rate was higher than that of other reports. Ciprofloxacin-non-sus-

ceptible *N. gonorrhoeae* also showed reduced susceptibility to other fluoroquinolones, but the MIC_{50}s of gemifloxacin, and gatifloxacin were 4-fold lower than that of ciprofloxacin.

The quinolones are absorbed quickly, attaining maximum plasma concentration within 1-2 hr of oral administration. The maximum plasma concentrations (bronchial mucosa: plasma ratios) were 1.2 mg/L (7.2), 1.2 mg/L (2.1), 3.9 mg/L (1.7), 5.1 mg/L (1.6), and 2.3 mg/L (1.7) with a single oral administration of 320 mg gemifloxacin, 200 mg moxifloxacin, 400 mg gatifloxacin, 500 mg levofloxacin, and 500 mg ciprofloxacin, respectively (18, unpublished data). Therefore, it was considered those concentrations of fluoroquinolones in bronchial mucosa were 8.6, 2.5, 6.6, 8.2, 3.9 mg/L, respectively.

In conclusion, gemifloxacin was most active in vitro against Gram-positive species, including respiratory pathogens isolated in Korea. Therefore, gemifloxacin should be useful for the treatment of the majority of respiratory, and other infections, especially those due to Gram-positive cocci.

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