Comparative *In Vitro* Activity of Sitafloxacin against Bacteria Isolated from Thai Patients with Urinary Tract Infections and Lower Respiratory Tract Infections

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Objective: *To determine comparative in vitro activity of sitafloxacin against clinical isolates of bacteria from Thai patients with urinary tract infection and those with lower respiratory tract infection.*
Material and Method: *1,255 clinical isolates of Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Acinetobacter baumannii, Enterococcus spp, Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae and Moraxella catarrhalis isolated from different Thai patients with urinary tract infection and those with lower respiratory tract infection in 2010 were included. The minimum inhibitory concentrations (MICs) of sitafloxacin, ciprofloxacin, levofloxacin, moxifloxacin, imipenem, amikacin, ampicillin, ceftazidime, ceftriaxone, penicillin, piperacillin/tazobactam, vancomycin, azithromycin and trimethoprim/sulfamethoxazole were determined by standard agar dilution method.*
Results: *The MIC_{50} and MIC_{90} values of sitafloxacin against all tested bacteria were lowest when compared with those of levofloxacin, ciprofloxacin and moxifloxacin. Sitafloxacin was active against 51% of methicillin-resistant S. aureus (MRSA) isolates. The activity of sitafloxacin against multidrug-resistant (MDR) Gram-negative bacteria, such as, extended spectrum beta-lactamase (ESBL)-producing E. coli and K. pneumomiae, P. aeruginosa and A. baumannii was comparable to or more than that of some beta-lactam/beta-lactamase inhibitors, cephalosporins or carbapenems.*
Conclusion: *Sitafloxacin is more active than levofloxacin, ciprofloxacin and moxifloxacin against isolated bacteria from Thai patients with urinary tract and lower respiratory infections including antibiotic resistant bacteria, such as MRSA, ESBL-producing Gram-negatives, carbapenem-resistant A. baumannii.*

Keywords: *In vitro activity, Sitafloxacin, Floroquinolone*

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Sitafloxacin (DU 6859a), a broad-spectrum oral fluoroquinolone that is very active against many Gram-positive, Gram-negative and anaerobic bacteria including the strains resistant to other fluoroquinolones, was recently approved in Japan for the treatment of respiratory tract infection and genitourinary tract infection[1]. Several *in vitro* activity studies of sitafloxacin were conducted many years ago showing that sitafloxacin was very active against a variety of bacteria including *Streptococcus pneumoniae*, *Staphylococcus aureus*, Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Bacteroides fragilis*[2-6]. However, the aforementioned studies were conducted when antibiotic resistant pathogens, such as, extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, multi-drug resistant (MDR) *P. aeruginosa* and *A. baumannii* were not commonly observed. Therefore, the objective of the present study was to determine *in vitro* activity of

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sitafloxacin and other antibotics against common causative bacteria isolated from Thai patients with urinary tract infections and those with lower respiratory tract infections in 2010.

Material and Method

Microorganisms

A total of 1,255 clinical isolates were collected from different patients with urinary tract infections or lower respiratory tract infections who attended five tertiary care hospitals in Thailand from January to June 2010. The collected isolates were *Escherichia coli* (n = 140), *Klebsiella pneumonia* (n = 196), *Proteus mirabilis* (n = 100), *Pseudomonas aeruginosa* (n = 216), *Acinetobacter baumannii* (n = 198), *Enterococcus faecalis* (n = 50), *Enterococcus faecium* (n = 50), *Streptococcus pneumonia* (n = 100), methicillin-resistant *Staphylococcus aureus*, MRSA (n = 55), methicillin-susceptible *Staphylococcus aureus*, MSSA (n = 50), *Haemophilus influenzae* (n = 50) and *Moraxella catarrhalis* (n = 50).

Antimicrobial agents

Standard powders of amikacin, ampicillin, ceftazidime, ceftriaxone, penicillin, piperacillin, tazobactam, vancomycin and trimethoprim were purchased from Sigma-Aldrich, USA. Standard powders of azithromycin, ciprofloxacin and sulfamethoxazole were purchased from Fluka, Switzerland. Standard powder of amoxicillin, clavulanate was purchased from USP, USA. Standard powders of levofloxacin, moxifloxacin, imipenem and sitafloxacin were generously provided by Daiichi Sankyo, Thailand. The stock solutions of these antimicrobial agents were prepared using appropriate solvents or/and diluents, and they were kept frozen at -80°C until used.

Antimicrobial susceptibility test

The minimum inhibitory concentrations (MICs) were determined by standard agar dilution method according to the Clinical and Laboratory Standards Institute (CLSI) 2010. Mueller Hinton II agar (BBL, Becton Dickinson, USA) was used for MIC determination of *E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, A. baumannii, E. faecalis, E. faecium*, MRSA and MSSA. The Mueller Hinton II agar supplemeneted with 5% sheep blood was used for MIC determination of *S. pneumoniae* and *M. catarrhalis*. The Mueller Hinton II agar plus Haemophilus test medium supplement (Oxoid, UK) was used for MIC determination of *H. influenzae*. Inoculum preparations of *E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa* and *A. baumannii* were made by broth method, adjusted to 0.5 McFarland turbidity and then diluted the bacterial suspension with cation adjusted Mueller Hinton broth (BBL, Becton Dickinson, USA) to 10^6 CFU/mL. Inoculum preparations of *S. aureus*, *Enterococcus* spp, *S. pneumoniae, H. influenzae* and *M. catarrhalis* were made by direct colony suspension adjusted to 0.5 McFarland turbidity and then the bacterial suspension diluted with cation adjusted Mueller Hinton broth to 10^6 CFU/mL. Final inocula of approximately 10^6 CFU/mL were used and applied to the medium by multipoints spot inoculators. The inoculated agars were incubated at 35°C for 18-24 hours in ambient air. The inoculated agars of *S. pneumoniae* and *H. influenzae* were incubated in 5% CO_2. The MIC was defined as the lowest concentration of antimicrobial agent that inhibited visible growth on agar. The control strains were *E. coli* ATCC 25922, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, *S. pneumoniae* ATCC 49619 and *H. influenzae* ATCC 49247. The susceptibility breakpoints (BP) of tested antibiotics were those recommended in the CLSI 2010 guidelines, if they were available, as shown in Table 1-3[7,8]. The susceptibility rate of tested bacteria against sitafloxacin was calculated according to the MIC BPs of $\leq$ 1 mg/L and $\leq$ 2 mg/L as also shown in Table 1-3.

Results

The MIC_{50} and MIC_{90} and MIC range values of tested antibiotics and susceptibility rate of tested organisms are shown in Table 1-3.

In vitro activity of sitafloxacin compared with other fluoroquinolones. The MIC_{50} and MIC_{90} of sitafloxacin against tested bacteria were lowest when compared with those of levofloxacin, ciprofloxacin and moxifloxacin. All studied isolates of *H. influenzae* and *M. catarrhalis* were susceptible to all tested fluoroquinolones. All studied isolates of *S. pneumoniae* and MSSA were susceptible to sitafloxacin whereas 69% to 99% of such isolates were susceptible to other fluoroquinolones. Sitafloxacin was active against 51% of MRSA isolates compared with nearly none for other fluoroquinolones. Sitafloxacin was active against 43% to 59% of *Enterococcus* spp isolates compared with 31% to 36% for other fluoroquinolones. *E. faecalis* isolates were more susceptible to sitafloxacin than *E. faecium* isolates (58% to 82% vs. 24% to 29%). Sitafloxacin was active against 75% to 90% of ESBL-negative *E. coli* isolates compared with 40% to 42% for other fluoroquinolones. Sitafloxacin was active against

Table 1. *In vitro* activities of sitafloxacin and other comparative antimicrobial agents against all bacteria isolated from the patients with urinary tract infections and lower respiratory tract infections

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
E. coli (140)	Sitafloxacin[1]	≤ 0.004-> 32	1	4	65.7, 87.1	≤ 1, ≤ 2
	Levofloxacin	0.032-> 32	16	32	24.3	≤ 2
	Ciprofloxacin	≤ 0.004-> 32	32	>32	24.3	≤ 1
	Moxifloxacin[2]	0.016-> 32	16	>32	23.6, 25.0	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	2/1-> 256/128	16/8	32/16	42.1	≤ 8/4
	Pipercillin/Tazobactam	1/4-> 256/4	32/4	128/4	47.9	≤ 16/4
	Ceftriaxone	≤ 0.016-> 256	16	256	40.0	≤ 1
	Imipenem	0.063-> 16	0.25	0.25	98.6	≤ 1
	Amikacin	≤ 0.25-16	2	8	97.9	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	1/19	>16/304	37.1	≤ 2/38
K. pneumoniae (196)	Sitafloxacin[1]	≤ 0.004-32	0.25	4	74.0, 79.6	≤ 1, ≤ 2
	Levofloxacin	0.016-> 32	1	32	62.2	≤ 2
	Ciprofloxacin	≤ 0.004-> 32	2	>32	49.5	≤ 1
	Moxifloxacin[2]	0.016-> 32	2	>32	45.4, 62.2	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	1/0.5-128/64	8/4	32/16	51.0	≤ 8/4
	Pipercillin/Tazobactam	1/4-> 256/4	32/4	256/4	43.4	≤ 16/4
	Ceftriaxone	≤ 0.016-> 256	4	>256	46.9	≤ 1
	Imipenem	0.125-16	0.25	0.25	98.0	≤ 1
	Amikacin	≤ 0.25-> 16	2	4	97.5	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14-> 16/304	16/304	>16/304	43.9	≤ 2/38
K. pneumoniae ESBL-positive (103)	Sitafloxacin[1]	0.016-> 32	0.5	8	62.1, 71.8	≤ 1, ≤ 2
	Levofloxacin	0.063-> 32	8	32	46.6	≤ 2
	Ciprofloxacin	0.016-> 32	8	>32	20.4	≤ 1
	Moxifloxacin[2]	0.063-> 32	8	>32	15.5, 44.7	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	4/2-128/64	16/8	32/16	16.5	≤ 8/4
	Pipercillin/Tazobactam	16/4-> 256/4	128/4	256/4	3.9	≤ 16/4
	Ceftriaxone	1-> 256	128	>256	2.9	≤ 1
	Imipenem	0.125-2	0.25	0.25	98.1	≤ 1
	Amikacin	0.5->16	4	8	95.2	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.25/4.75-> 16/304	>16/304	>16/304	15.5	≤ 2/38
K. pneumoniae ESBL-negative (93)	Sitafloxacin[1]	≤ 0.004-32	0.016	2	87.1, 91.4	≤ 1, ≤ 2
	Levofloxacin	0.016-> 32	0.063	32	79.6	≤ 2
	Ciprofloxacin	≤ 0.004-> 32	0.032	>32	81.7	≤ 1
	Moxifloxacin[2]	0.016->32	0.063	32	78.5, 81.7	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	1/0.5-128/64	2/1	16/8	89.3	≤ 8/4
	Pipercillin/Tazobactam	1/4-256/4	4/4	32/4	87.1	≤ 16/4
	Ceftriaxone	≤ 0.016->256	0.063	0.5	95.7	≤ 1
	Imipenem	0.125-16	0.25	0.25	97.9	≤ 1
	Amikacin	≤ 0.25-8	1	2	100	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	0.5/9.5	>16/304	75.3	≤ 2/38
P. mirabilis (100)	Sitafloxacin[1]	0.008-4	0.016	1	92, 99	≤ 1, ≤ 2
	Levofloxacin	0.032-32	0.063	8	79	≤ 2
	Ciprofloxacin	0.008-32	0.016	8	78	≤ 1
	Moxifloxacin[2]	0.032->32	0.25	>32	68, 70	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	0.25/0.125-64/32	1/0.5	4/2	97	≤ 8/4
	Pipercillin/Tazobactam	≤ 0.25/4-128/4	0.5/4	4/4	98	≤ 16/4
	Ceftriaxone	≤ 0.016-128	≤ 0.016	0.125	94	≤ 1
	Imipenem	0.004-4	0.25	0.5	99	≤ 1
	Amikacin	1->128	2	4	98	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	0.12/2.28	>16/304	72	≤ 2/38

Table 1. Cont.

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
P. aeruginosa (216)	Sitafloxacin[1]	0.016->32	0.5	8	55.9, 66.2	≤ 1, ≤ 2
	Levofloxacin	0.125->32	2	>32	51.8	≤ 2
	Ciprofloxacin	0.016->32	0.5	>32	54.9	≤ 1
	Moxifloxacin[2]	0.063->32	4	>32	30.3, 46.2	≤ 1, ≤ 2
	Piperacillin/Tazobactam	2/4->256/4	8/4	128/4	78.0	≤ 64/4
	Ceftazidime	0.125->256	4	>256	56.4	≤ 8
	Imipenem	0.032->128	4	128	60.0	≤ 4
	Amikacin	0.5->128	4	>128	64.6	≤ 16
A. baumannii (198)	Sitafloxacin[1]	0.008-32	1	2	66.9, 94.1	≤ 1, ≤ 2
	Levofloxacin	0.032->32	8	16	14.8	≤ 2
	Ciprofloxacin	0.016->32	32	>32	11.2	≤ 1
	Moxifloxacin[2]	0.032->32	16	16	11.2, 11.8	≤ 1, ≤ 2
	Piperacillin/Tazobactam	2/4->256/4	>256/4	>256/4	10.7	≤ 16/4
	Ceftazidime	0.25->256	>256	>256	13.0	≤ 8
	Imipenem	0.125-128	32	64	18.9	≤ 4
	Amikacin	2->128	>128	>128	21.9	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.125/2.38->16/304	>16/304	>16/304	30.8	≤ 2/38
H .influenzae (50)	Sitafloxacin[1]	≤ 0.004	≤ 0.004	≤ 0.004	100	≤ 1, ≤ 2
	Levofloxacin	≤ 0.004-0.032	0.016	0.016	100	≤ 2
	Ciprofloxacin	≤ 0.004-0.016	0.008	0.008	100	≤ 1
	Moxifloxacin	≤ 0.004-0.125	0.016	0.032	100	≤ 1
	Ampicillin	0.25->32	2	32	38	≤ 1
	Amoxicillin/Clavulanate	< 0.5/0.25-4/2	1/0.5	4/2	100	≤ 4/2
	Ceftriaxone	≤ 0.016-0.032	≤ 0.016	≤ 0.016	100	≤ 2
	Azithromycin	0.25-32	2	4	98	≤ 4
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	2/38	16/304	46	≤ 0.5/9.5
M. catarrhalis[3] (50)	Sitafloxacin[1]	≤ 0.004-0.125	0.008	0.016	100, 100	≤ 1, ≤ 2
	Levofloxacin	0.032-1	0.063	0.063	100	≤ 2
	Ciprofloxacin	0.016-0.5	0.032	0.032	100	≤ 1
	Moxifloxacin	0.032-0.25	0.063	0.063	100	≤ 1
	Ampicillin	0.5-16	2	8	21.6	≤ 1
	Amoxicillin/Clavulanate	≤ 0.063/0.032-2/1	≤ 0.063/ 0.032	≤ 0.063/ 0.032	100	≤ 4/2
	Ceftriaxone	≤ 0.016-1	0.125	0.5	100	≤ 2
	Azithromycin	≤ 0.016-2	0.032	0.032	100	≤ 4
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14-2/38	0.5/9.5	1/19	78.4	≤ 0.5/9.5
S. pneumoniae (100)	Sitafloxacin[1]	0.032-0.25	0.063	0.063	100, 100	≤ 1, ≤ 2
	Levofloxacin	0.5-16	1	1	99	≤ 2
	Ciprofloxacin[4]	0.5-32	1	2	69	≤ 1
	Moxifloxacin	0.125-4	0.125	0.25	99	≤ 1
	Penicillin	≤ 0.016-4	1	2	91	≤ 2[5]
	Amoxicillin/Clavulanate	≤ 0.016/0.008-4/2	0.25/0.125	1/0.5	97	≤ 2/1
	Ceftriaxone	≤ 0.016-4	0.5	1	50, 95	≤ 0.5[6], ≤ 1[7]
	Azithromycin	0.25->32	16	>32	23	≤ 0.5
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	4/76	16/304	23	≤ 0.5/9.5
S. aureus(105)	Sitafloxacin[1]	≤ 0.004-8	0.5	8	69.6, 69.6	≤ 1, ≤ 2
	Levofloxacin	0.125->32	16	>32	33.7	≤ 1
	Ciprofloxacin	0.125->32	32	>32	33.7	≤ 1
	Moxifloxacin	0.016->32	4	>32	33.7	≤ 0.5
	Azithromycin	0.25->32	>32	>32	33.7	≤ 2
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	≤ 0.06/ 1.14	16/304	79.3	≤ 2/38
	Vancomycin	0.5-1	1	1	100	≤ 2

Table 1. Cont.

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
Enterococcus spp (100)	Sitafloxacin[1]	0.063->16	2	16	43, 59	≤ 1, ≤ 2
	Levofloxacin	0.5->32	32	>32	34	≤ 2
	Ciprofloxacin	0.5->32	32	>32	31	≤ 1
	Moxifloxacin[2]	0.125->32	16	32	34, 36	≤ 1, ≤ 2
	Penicillin	≤ 0.125->32	4	>32	59	≤ 8
	Ampicillin	0.25->32	4	>32	60	≤ 8
	Vancomycin	0.5-4	1	1	100	≤ 4

[1]No susceptible breakpoints in CLSI 2010, [2]No susceptible breakpoints in CLSI 2010 for *E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, A. baumannii* and *Enterococcus* spp, [3]The susceptible breakpoints used as those of *H. influenzae* (CLSI 2010), [4]No susceptible breakpoints in CLSI 2010 for *S. pneumoniae*, [5]For penicillin parenteral (non-meningitis breakpoint), [6]For meningitis breakpoint, [7]For non-meningitis breakpoint

Table 2. *In vitro* activities of sitafloxacin and other comparative antimicrobial agents against bacteria isolated from the patients with urinary tract infections

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
E. coli (140)	Sitafloxacin[1]	≤ 0.004->32	1	4	65.7, 87.1	≤ 1, ≤ 2
	Levofloxacin	0.032->32	16	32	24.3	≤ 2
	Ciprofloxacin	≤ 0.004->32	32	>32	24.3	≤ 1
	Moxifloxacin[2]	0.016->32	16	>32	23.6, 25.0	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	2/1->256/128	16/8	32/16	42.1	≤ 8/4
	Pipercillin/Tazobactam	1/4->256/4	32/4	128/4	47.9	≤ 16/4
	Ceftriaxone	≤ 0.016->256	16	256	40.0	≤ 1
	Imipenem	0.063->16	0.25	0.25	98.6	≤ 1
	Amikacin	≤ 0.25-16	2	8	97.9	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	1/19	>16/304	37.1	≤ 2/38
E. coli ESBL-positive(73)	Sitafloxacin[1]	0.008->32	1	4	57.5, 84.9	≤ 1, ≤ 2
	Levofloxacin	0.032->32	16	32	9.6	≤ 2
	Ciprofloxacin	0.016->32	32	>32	9.6	≤ 1
	Moxifloxacin[2]	0.032->32	16	>32	8.2, 9.6	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	2/1->256/128	16/8	32/16	35.6	≤ 8/4
	Piperacillin/Tazobactam	4/4->256/4	32/4	128/4	24.7	≤ 16/4
	Ceftriaxone	8->256	128	>256	0	≤ 1
	Imipenem	0.125->16	0.25	0.5	98.6	≤ 1
	Amikacin	0.5->16	2	8	95.9	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	>16/304	>16/304	21.9	≤ 2/38
E. coli ESBL-negative(67)	Sitafloxacin[1]	≤ 0.004-8	0.5	4	74.6, 89.6	≤ 1, ≤ 2
	Levofloxacin	0.032->32	8	32	40.3	≤ 2
	Ciprofloxacin	≤ 0.004->32	16	>32	40.3	≤ 1
	Moxifloxacin[2]	0.016->32	8	32	40.3, 41.8	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	2/1-64/32	16/8	32/16	49.25	≤ 8/4
	Piperacillin/Tazobactam	1/4-128/4	8/4	64/4	73.1	≤ 16/4
	Ceftriaxone	≤ 0.016-64	0.063	16	83.6	≤ 1
	Imipenem	0.063-2	0.25	0.25	98.5	≤ 1
	Amikacin	≤ 0.25-16	2	8	100	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	1/19	>16/304	53.7	≤ 2/38
K. pneumoniae (101)	Sitafloxacin[1]	≤ 0.004 - 32	0.5	8	65.474.3	≤ 1≤ 2
	Levofloxacin	0.016 - >32	2	>32	50.5	≤ 2

Table 2. Cont.

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
	Ciprofloxacin	≤ 0.004->32	4	>32	39.6	≤ 1
	Moxifloxacin[2]	0.016->32	4	>32	36.6, 49.5	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	1/0.5-64/32	16/8	32/16	47.5	≤ 8/4
	Piperacillin/Tazobactam	1/4->256/4	32/4	256/4	38.6	≤ 16/4
	Ceftriaxone	≤ 0.016->256	2	>256	47.5	≤ 1
	Imipenem	0.125-2	0.25	0.25	99.0	≤ 1
	Amikacin	≤ 0.25->16	2	8	96.0	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	>16/304	>16/304	34.7	≤ 2/38
K. pneumoniae ESBL-positive (55)	Sitafloxacin[1]	0.032-32	1	16	54.6, 65.5	≤ 1, ≤ 2
	Levofloxacin	0.125->32	8	>32	34.5	≤ 2
	Ciprofloxacin	0.125->32	32	>32	14.5	≤ 1
	Moxifloxacin[2]	0.063->32	16	>32	10.9, 32.7	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	4/2-64/32	16/8	64/32	14.5	≤ 8/4
	Piperacillin/Tazobactam	16/4->256/4	128/4	256/4	3.6	≤ 16/4
	Ceftriaxone	1-256	128	>256	3.6	≤ 1
	Imipenem	0.125-2	0.25	0.5	98.2	≤ 1
	Amikacin	1->16	4	16	92.7	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.25/4.75->16/304	>16/304	>16/304	10.9	≤ 2/38
K. pneumoniae ESBL-negative (46)	Sitafloxacin[1]	≤ 0.004-32	0.016	4	78.3, 84.8	≤ 1, ≤ 2
	Levofloxacin	0.016-32	0.063	>32	69.6	≤ 2
	Ciprofloxacin	≤ 0.004->32	0.032	>32	69.6	≤ 1
	Moxifloxacin[2]	0.016->32	0.063	>32	67.4, 69.6	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	1/0.5-64/32	4/2	16/8	87.0	≤ 8/4
	Piperacillin/Tazobactam	1/4-64/4	4/4	32/4	80.4	≤ 16/4
	Ceftriaxone	≤ 0.016-1	0.063	0.5	100	≤ 1
	Imipenem	0.125-0.5	0.25	0.25	100	≤ 1
	Amikacin	≤ 0.25-8	1	2	100	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	0.5/9.5	>16/304	63.0	≤ 2/38
P. mirabilis (100)	Sitafloxacin[1]	0.008-4	0.016	1	92, 99	≤ 1, ≤ 2
	Levofloxacin	0.032-32	0.063	8	79	≤ 2
	Ciprofloxacin	0.008-32	0.016	8	78	≤ 1
	Moxifloxacin[2]	0.032->32	0.25	>32	68, 70	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	0.25/0.125-64/32	1/0.5	4/2	97	≤ 8/4
	Piperacillin/Tazobactam	≤ 0.25/4-128/4	0.5/4	4/4	98	≤ 16/4
	Ceftriaxone	≤ 0.016-128	≤ 0.016	0.125	94	≤ 1
	Imipenem	0.004-4	0.25	0.5	99	≤ 1
	Amikacin	1->128	2	4	98	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	0.12/2.28	>16/304	72	≤ 2/38
P. aeruginosa (100)	Sitafloxacin[1]	0.016->32	2	16	48, 60	≤ 1, ≤ 2
	Levofloxacin	0.125->32	16	>32	47	≤ 2
	Ciprofloxacin	0.063->32	16	>32	47	≤ 1
	Moxifloxacin[2]	0.063->32	16	>32	29, 50	≤ 1, ≤ 2
	Piperacillin/Tazobactam	2/4->128/4	64/4	128/4	72	≤ 64/4
	Ceftazidime	1->256	64	>256	43	≤ 8
	Imipenem	0.032->128	4	>128	60	≤ 4
	Amikacin	2->128	64	>128	56	≤ 16
A. baumannii (100)	Sitafloxacin[1]	0.016->32	1	4	65, 87	≤ 1, ≤ 2
	Levofloxacin	0.063->32	8	16	18	≤ 2
	Ciprofloxacin	0.063->32	32	>32	14	≤ 1
	Moxifloxacin[2]	0.032->32	16	32	14, 14	≤ 1, ≤ 2
	Piperacillin/Tazobactam	8/4->256/4	256/4	>256/4	12	≤ 16/4
	Ceftazidime	1->256	>256	>256	13	≤ 8

Table 2. Cont.

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
	Imipenem	0.125-128	32	64	23	≤ 4
	Amikacin	1->128	>128	>128	23	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.25/4.75->16/304	>16/304	>16/304	37	≤ 2/38
Enterococcus spp.*(100)*	Sitafloxacin[1]	0.063->16	2	16	43, 59	≤ 1, ≤ 2
	Levofloxacin	0.5->32	32	>32	34	≤ 2
	Ciprofloxacin	0.5->32	32	>32	31	≤ 1
	Moxifloxacin[2]	0.125->32	16	32	34, 36	≤ 1, ≤ 2
	Penicillin	≤ 0.125->32	4	>32	59	≤ 8
	Ampicillin	0.25->32	4	>32	60	≤ 8
	Vancomycin	0.5-4	1	1	100	≤ 4
Enterococcus faecalis(50)	Sitafloxacin[1]	0.063-16	0.125	4	58, 82	≤ 1, ≤ 2
	Levofloxacin	0.5->32	2	>32	54	≤ 2
	Ciprofloxacin	0.5->32	2	>32	48	≤ 1
	Moxifloxacin[2]	0.125-32	0.5	32	54, 66	≤ 1, ≤ 2
	Penicillin	≤ 0.125->32	2	32	84	≤ 8
	Ampicillin	0.25->32	4	16	86	≤ 8
	Vancomycin	0.5-4	1	1	100	≤ 4
Enterococcus faecium(50)	Sitafloxacin[1]	0.063-16	8	16	24, 29	≤ 1, ≤ 2
	Levofloxacin	0.5->32	>32	>32	12	≤ 2
	Ciprofloxacin	0.5->32	>32	>32	10	≤ 1
	Moxifloxacin[2]	0.125->32	32	>32	12, 15	≤ 1, ≤ 2
	Penicillin	2->32	>32	>32	27	≤ 8
	Ampicillin	4->32	>32	>32	27	≤ 8
	Vancomycin	0.5-2	1	1	100	≤ 4

[1] No susceptible breakpoints in CLSI 2010

[2] No susceptible breakpoints in CLSI 2010 for *E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, A. baumannii* and *Enterococcus* spp

Table 3. *In vitro* activities of sitafloxacin and other comparative antimicrobial agents against bacteria isolated from the patients with lower respiratory tract infections

Organism(No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
K. pneumoniae (95)	Sitafloxacin[1]	0.008-32	0.125	4	83.2, 88.4	≤ 1, ≤ 2
	Levofloxacin	0.016->32	0.5	32	74.7	≤ 2
	Ciprofloxacin	0.008->32	0.5	>32	60.0	≤ 1
	Moxifloxacin[2]	0.032->32	1	32	54.7, 75.8	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	2/1-128/64	8/4	32/16	54.7	≤ 8/4
	Piperacillin/Tazobactam	1/4->256/4	32/4	256/4	48.4	≤ 16/4
	Ceftriaxone	≤ 0.016->256	8	256	46.3	≤ 1
	Imipenem	0.0125-16	0.25	0.25	96.8	≤ 1
	Amikacin	≤ 0.5->16	2	4	98.9	≤ 16
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	2/38	>16/304	53.7	≤ 2/38
K. pneumoniae ESBL-positive (48)	Sitafloxacin[1]	0.016-32	0.25	4	70.8, 79.2	≤ 1, ≤ 2
	Levofloxacin	0.063->32	1	32	60.4	≤ 2
	Ciprofloxacin	0.016->32	2	>32	27.1	≤ 1
	Moxifloxacin[2]	0.063->32	2	>32	20.8, 58.3	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	4/2-128/64	16/8	32/16	18.8	≤ 8/4
	Piperacillin/Tazobactam	16/4->256/4	128/4	256/4	4.2	≤ 16/4
	Ceftriaxone	1->256	128	>256	2.1	≤ 1
	Imipenem	0.125-2	0.25	0.25	97.9	≤ 1

Table 3. Cont.

Organism (No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
	Amikacin	0.5->16	2	4	97.9	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.25/4.75->16/304	>16/304	>16/304	18.8	≤ 2/38
K. pneumoniae ESBL-negative (47)	Sitafloxacin[1]	0.008-32	0.016	0.125	95.7, 97.9	≤ 1, ≤ 2
	Levofloxacin	0.016->32	0.063	1	89.4	≤ 2
	Ciprofloxacin	0.008->32	0.016	0.5	93.6	≤ 1
	Moxifloxacin[2]	0.032->32	0.063	2	89.4, 93.6	≤ 1, ≤ 2
	Amoxicillin/Clavulanate	2/1-128/64	2/1	8/4	91.5	≤ 8/4
	Piperacillin/Tazobactam	1/4-256/4	4/4	16/4	93.6	≤ 16/4
	Ceftriaxone	≤ 0.016->256	0.063	1	91.5	≤ 1
	Imipenem	0.125-16	0.25	0.25	95.7	≤ 1
	Amikacin	0.5-8	1	4	100	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.125/2.38->16/304	0.5/9.5	>16/304	85.1	≤ 2/38
P. aeruginosa(116)	Sitafloxacin[1]	0.016->32	0.25	8	61.2, 70.7	≤ 1, ≤ 2
	Levofloxacin	0.125->32	2	>32	56.1	≤ 2
	Ciprofloxacin	0.016->32	0.25	>32	60.3	≤ 1
	Moxifloxacin[2]	0.25->32	4	>32	31.1, 49.5	≤ 1, ≤ 2
	Piperacillin/Tazobactam	2/4->256/4	8/4	128/4	81.9	≤ 64/4
	Ceftazidime	0.125->256	4	>256	65.5	≤ 8
	Imipenem	0.5->128	4	32	60.3	≤ 4
	Amikacin	0.5->128	4	>128	70.7	≤ 16
A. baumannii(98)	Sitafloxacin[1]	0.008-16	1	2	68.4, 99.0	≤ 1, ≤ 2
	Levofloxacin	0.032->32	8	16	12.2	≤ 2
	Ciprofloxacin	0.016->32	32	>32	10.2	≤ 1
	Moxifloxacin[2]	0.032->32	16	16	10.2, 11.2	≤ 1, ≤ 2
	Piperacillin/Tazobactam	2/4->256/4	>256/4	>256/4	10.2	≤ 16/4
	Ceftazidime	0.25->256	>256	>256	13.3	≤ 8
	Imipenem	0.125-128	64	128	16.3	≤ 4
	Amikacin	2->128	>128	>128	21.4	≤ 16
	Trimethoprim/ Sulfamethoxazole	0.125/2.38->16/304	>16/304	>16/304	26.5	≤ 2/38
H. influenzae (50)	Sitafloxacin[1]	≤ 0.004	≤ 0.004	≤ 0.004	100, 100	≤ 1, ≤ 2
	Levofloxacin	≤ 0.004-0.032	0.016	0.016	100	≤ 2
	Ciprofloxacin	≤ 0.004-0.016	0.008	0.008	100	≤ 1
	Moxifloxacin	≤ 0.004-0.125	0.016	0.032	100	≤ 1
	Ampicillin	0.25->32	2	32	38	≤ 1
	Amoxicillin/Clavulanate	< 0.5/0.25-4/2	1/0.5	4/2	100	≤ 4/2
	Ceftriaxone	≤ 0.016-0.032	≤ 0.016	≤ 0.016	100	≤ 2
	Azithromycin	0.25-32	2	4	98	≤ 4
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	2/38	16 / 304	46	≤ 0.5/9.5
M. catarrhalis[3] (50)	Sitafloxacin[1]	≤ 0.004-0.125	0.008	0.016	100, 100	≤ 1, ≤ 2
	Levofloxacin	0.032-1	0.063	0.063	100	≤ 2
	Ciprofloxacin	0.016-0.5	0.032	0.032	100	≤ 1
	Moxifloxacin	0.032-0.25	0.063	0.063	100	≤ 1
	Ampicillin	0.5-16	2	8	21.6	≤ 1
	Amoxicillin/ Clavulanate	≤ 0.063/0.032-2/1	≤ 0.063/ 0.032	≤ 0.063/ 0.032	100	≤ 4/2
	Ceftriaxone	≤ 0.016-1	0.125	0.5	100	≤ 2
	Azithromycin	≤ 0.016-2	0.032	0.032	100	≤ 4
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14-2/38	0.5/9.5	1/19	78.4	≤ 0.5/9.5
S. pneumoniae (100)	Sitafloxacin[1]	0.032-0.25	0.063	0.063	100, 100	≤ 1, ≤ 2
	Levofloxacin	0.5-16	1	1	99	≤ 2
	Ciprofloxacin[4]	0.5-32	1	2	69	≤ 1
	Moxifloxacin	0.125-4	0.125	0.25	99	≤ 1
	Penicillin	≤ 0.016-4	1	2	91	≤ 2[5]

Table 3. Cont.

Organism(No.)	Antimicrobial agent	MIC (mg/L)			Susceptible	
		Range	MIC_{50}	MIC_{90}	%	MIC BP
	Amoxicillin/Clavulanate	≤ 0.016/0.008-4/2	0.25/0.125	1/0.5	97	≤ 2/1
	Ceftriaxone	≤ 0.016-4	0.5	1	50, 95	≤ 0.5[6], ≤ 1[7]
	Azithromycin	0.25->32	16	>32	23	≤ 0.5
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	4/76	16/304	23	≤ 0.5/9.5
MRSA (55)	Sitafloxacin[1]	0.125-8	1	8	50.9, 50.9	≤ 1, ≤ 2
	Levofloxacin	4->32	32	>32	0	≤ 1
	Ciprofloxacin	8->32	>32	>32	0	≤ 1
	Moxifloxacin	1->32	8	>32	1.8	≤ 0.5
	Azithromycin	0.25->32	>32	>32	1.8	≤ 2
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14->16/304	0.125/2.375	16/304	69.1	≤ 2/38
	Vancomycin	0.5-1	1	1	100	≤ 2
MSSA (50)	Sitafloxacin[1]	≤ 0.004-1	0.016	1	100, 100	≤ 1, ≤ 2
	Levofloxacin	0.125-32	0.25	16	86	≤ 1
	Ciprofloxacin	0.125->32	0.25	32	86	≤ 1
	Moxifloxacin	0.016-8	0.032	4	86	≤ 0.5
	Azithromycin	0.25-32	0.5	>32	84	≤ 2
	Trimethoprim/ Sulfamethoxazole	≤ 0.06/1.14-16/304	≤ 0.06/1.14	0.25/4.75	98	≤ 2/38
	Vancomycin	0.5-1	1	1	100	≤ 2

[1] No susceptible breakpoints in CLSI 2010, [2] No susceptible breakpoints in CLSI 2010 for *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, *A. baumannii* and *Enterococcus* spp, [3] The susceptible breakpoints used as those of *H. influenzae* (CLSI 2010), [4] No susceptible breakpoints in CLSI 2010 for *S. pneumoniae*, [5] For penicillin parenteral (non-meningitis breakpoint), [6] For meningitis breakpoint, [7] For non-meningitis breakpoint

58% to 85% of ESBL-positive *E. coli* isolates compared with 8% to 10% for other fluoroquinolones. Sitafloxacin was active against 87% to 91% of ESBL-negative *K. pneumoniae* isolates compared with 79% to 82% for other fluoroquinolones. Sitafloxacin was active against 62% to 72% of ESBL-positive *K. pneumoniae* isolates compared with 16% to 47% for other fluoroquinolones. Sitafloxacin was active against 92% to 99% of *P. mirabilis* isolates compared with 68% to 79% for other fluoroquinolones. Sitafloxacin was active against 56% to 66% of *P. aeruginosa* isolates compared with 30% to 55% for other fluoroquinolones. Sitafloxacin was active against 67% to 94% of *A. baumanni* isolates compared with 11% to 15% for other fluoroquinolones.

In vitro activity of sitafloxacin compared with other antibiotic classes

In vitro activity of sitafloxacin against *S. pneumoniae* isolates was comparable to that of ceftriaxone and amoxicillin/clavulanate and more than that of azithromycin and trimethoprim/sulfamethoxazole. *In vitro* activity of sitafloxacin against MRSA isolates was comparable to that of trimethoprim/sulfamethoxazole and less than that of vancomycin. *In vitro* activity of sitafloxacin against *Enterococcus* spp. isolates was comparable to that of penicillin and ampicillin and less than that of vancomycin. *In vitro* activity of sitafloxacin against *H. influenzae* and *M. catarrhalis* isolates was comparable to that of amoxicillin/clavulanate, ceftriaxone and azithromycin, and more than that of ampicillin and trimethoprim/sulfamethoxazole. *In vitro* activity of sitafloxacin against *P. mirabilis* isolates was comparable to that of amoxicillin/clavulanate, ceftriaxone, imipenem, amikacin and piperacillin/tazobactam. *In vitro* activity of sitafloxacin against ESBL-negative *E. coli* isolates was comparable to piperacillin/tazobactam and ceftriaxone, and more than that of amoxicillin/clavulanate and trimethoprim/sulfamethoxazole and less than that of imipenem and amikacin. *In vitro* activity of sitafloxacin against ESBL-negative *K. pneumoniae* isolates was comparable to amoxicillin/clavulanate and piperacillin/tazobactam, more than that of trimethoprim/sulfamethoxazole and less than that of ceftriaxone, imipenem and amikacin. *In vitro* activity of sitafloxacin against ESBL-positive *E. coli* and ESBL-positive *K.*

pneumoniae isolates was more than that of trimethoprim/sulfamethoxazole, amoxicillin/clavulanate, piperacillin/tazobactam and ceftriaxone and less than that of imipenem and amikacin. *In vitro* activity of sitafloxacin against *P. aeruginosa* isolates was comparable to that of ceftazidime, imipenem, amikacin but slightly less than that of piperacillin/tazobactam. *In vitro* activity of sitafloxacin against *A. baumannii* isolates was much more than that of ceftazidime, imipenem, amikacin, piperacillin/tazobactam and trimethoprim/sulfamethoxazole. Sitafloxacin was active against 64% (BP $\leq$ 1 mg/L) to 96% (BP $\leq$ 2 mg/L) of carbapenem-resistant *A. baumannii* isolates.

Discussion

CLSI has not recommended MIC breakpoints for sitafloxacin. Therefore, the MIC breakpoints of sitafloxacin susceptibility used in the present study are classified as $\leq$ 1 mg/L and $\leq$ 2 mg/L. Sitafloxacin was more active than tested fluoroquinolones, ampicllin, azithromycin and trimethoprim/sulfamethoxazole against most of bacterial isolates collected from the patients with urinary tract or respiratory tract infections. Sitafloxacin was the only fluoroquinolone that contained significant activity against MRSA. The susceptibility rate of MRSA to sitafloxacin observed in the present study of 51% was comparable to the results from the previous study[6]. The activity of sitafloxacin against multidrug-resistant (MDR) Gram-negative bacteria, such as, ESBL-producing *E. coli* and *K. pneumomiae*, *P. aeruginosa* and *A. baumannii* was comparable to or more than that of some beta-lactam/beta-lactamase inhibitors, cephalosporins or carbapenems. Therefore, it is suggested that sitafloxacin could be used for infections caused by MDR Gram-negative bacteria. However, the efficacy of sitafloxacin for MDR Gram-negative infections should be established in clinical studies. Most of clinical studies of sitafloxacin were reported in Japanese journals. Sitafloxacin was found to be effective in the patients hospitalized with pneumonia comparable to imipenem/cilastatin[9]. Sitafloxacin was reported to be effective in the treatment of patients with infections caused by vancomycin-resistant enterococci and MRSA[10].

In addition to its activity against common bacteria causing urinary tract and respiratory tract infctions, sitafloxacin was observed to be active against other pathogens including *Campylobacter jejuni*[11], *Helicobacter pylori*[12], *Vibrio cholerae* O1[13], non-typhoidal *Salmonella enterica*[14] and *Bacteroides fragilis*[15]. Sitafloxacin has been available in Japan as an oral formulation with the recommended dose of 50 mg to 100 mg twice a day for therapy of respiratory tract or genitourinary tract infections. Pharmakokinetics of sitafloxacin was favorable[16]. Oral administration of 100 mg of sitafloxacin was rapidly absorbed with an absolute bioavailability up to 90%. Food intake did not affect the rate and extent of absorption. The mean maximum concentration in serum of sitafloxacin was 1 mg/L with elimination half-life of 5 hr. Sitafloxacin is primarily eliminated by the kidney. The area under the curve was 5.5 mg.h/L. The serum protein binding of the drug was approximately 50%. The apparent volume of distribution exceeded 1.8 L/kg suggesting good tissue penetration. The safety profiles of sitafloxacin were characterized from 1,059 patients who participated in 10 clinical trials observed that the most common adverse events with taking sitafloxacin 50 or 100 mg twice daily were gastrointestinal disorders (17.2%), mostly diarrhea and abnormal laboratory test results (16.2%), mostly liver enzyme elevations[1]. Sitafloxacin failed to demonstrate a clinically significant phototoxicity in Asian subjects but it was associated with a mild degree of cutaneous phototoxicity in Caucasians[17].

It is anticipated that sitafloxacin will be an effective antibiotic in the treatment of various infectious diseases in other locations in addition to Japan. Since sitafloxacin is available in oral formulation, its roles for therapy of infections are mainly for out-patients and hospitalized patients who do not required parenteral antibiotics, as well as a continued therapy after parenteral therapy with other antibiotics. Based on *in vitro* activity and *in vivo* efficacy, sitafloxacin should be effective for therapy of unrinary tract, genitourinary tract and gastrointestinal tract infections as well as for therapy of specific pathogens such as MRSA.

In summary, sitafloxacin is more *in vitro* active than levofloxacin, ciprofloxacin and moxifloxacin against isolated bacteria from Thai patients with urinary tract and lower respiratory infections including antibiotic resistant bacteria, such as MRSA, ESBL-producing gram negative bacilli, carbapenem-resistant *A. baumannii*.

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Potential conflicts of interest

None.

References

1. Anderson DL. Sitafloxacin hydrate for bacterial infections. Drugs Today (Barc) 2008; 44: 489-501.
2. Marshall SA, Jones RN, Murray PR, Washington JA, Allen SD, Gerlach EH, et al. In-vitro comparison of DU-6859a, a novel fluoroquinolone, with other quinolones and oral cephalosporins tested against 5086 recent clinical isolates. J Antimicrob Chemother 1993; 32: 877-84.
3. Deshpande LM, Jones RN. Antimicrobial activity of advanced-spectrum fluoroquinolones tested against more than 2000 contemporary bacterial isolates of species causing community-acquired respiratory tract infections in the United States (1999). Diagn Microbiol Infect Dis 2000; 37: 139-42.
4. Milatovic D, Schmitz FJ, Brisse S, Verhoef J, Fluit AC. In vitro activities of sitafloxacin (DU-6859a) and six other fluoroquinolones against 8,796 clinical bacterial isolates. Antimicrob Agents Chemother 2000; 44: 1102-7.
5. Wang M, Sahm DF, Jacoby GA, Zhang Y, Hooper DC. Activities of newer quinolones against Escherichia coli and Klebsiella pneumoniae containing the plasmid-mediated quinolone resistance determinant qnr. Antimicrob Agents Chemother 2004; 48: 1400-1.
6. Yamaguchi K, Ohno A, Ishii Y, Tateda K, Iwata M, Kanda M, et al. In vitro susceptibilities to levofloxacin and various antibacterial agents of 12,919 clinical isolates obtained from 72 centers in 2007. Jpn J Antibiot 2009; 62: 346-70.
7. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; Twentieth information supplement (January 2010) M100-S20. Wayne, PA: CLSI; 2010.
8. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; Twentieth information supplement (June 2010 Update) M100-S20-U. Wayne, PA: CLSI; 2010.
9. Feldman C, White H, O'Grady J, Flitcroft A, Briggs A, Richards G. An open, randomised, multi-centre study comparing the safety and efficacy of sitafloxacin and imipenem/cilastatin in the intravenous treatment of hospitalised patients with pneumonia. Int J Antimicrob Agents 2001; 17: 177-88.
10. Shetty N, Wilson AP. Sitafloxacin in the treatment of patients with infections caused by vancomycin-resistant enterococci and methicillin-resistant Staphylococcus aureus. J Antimicrob Chemother 2000; 46: 633-8.
11. Lehtopolku M, Hakanen AJ, Siitonen A, Huovinen P, Kotilainen P. In vitro activities of 11 fluoroquinolones against 226 Campylobacter jejuni strains isolated from Finnish patients, with special reference to ciprofloxacin resistance. J Antimicrob Chemother 2005; 56: 1134-8.
12. Murakami K, Okimoto T, Kodama M, Tanahashi J, Fujioka T, Ikeda F, et al. Sitafloxacin activity against Helicobacter pylori isolates, including those with gyrA mutations. Antimicrob Agents Chemother 2009; 53: 3097-9.
13. Okuda J, Ramamurthy T, Yamasaki S. The potent antibacterial activity of Sitafloxacin against fluoroquinolone-resistant clinical isolates of Vibrio cholerae O1. Microbiol Immunol 2007; 51: 467-9.
14. Kotilainen P, Pitkanen S, Siitonen A, Huovinen P, Hakanen AJ. In vitro activities of 11 fluoroquinolones against 816 non-typhoidal strains of Salmonella enterica isolated from Finnish patients with special reference to reduced ciprofloxacin susceptibility. Ann Clin Microbiol Antimicrob 2005; 4: 12.
15. Nord CE. In vitro activity of quinolones and other antimicrobial agents against anaerobic bacteria. Clin Infect Dis 1996; 23(Suppl 1): S15-8.
16. Nakashima M, Uematsu T, Kosuge K, Umemura K, Hakusui H, Tanaka M. Pharmacokinetics and tolerance of DU-6859a, a new fluoroquinolone, after single and multiple oral doses in healthy volunteers. Antimicrob Agents Chemother 1995; 39: 170-4.
17. Dawe RS, Ibbotson SH, Sanderson JB, Thomson EM, Ferguson J. A randomized controlled trial (volunteer study) of sitafloxacin, enoxacin, levofloxacin and sparfloxacin phototoxicity. Br J Dermatol 2003; 149: 1232-41.

การเปรียบเทียบฤทธิ์ของยา sitafloxacin ต่อแบคทีเรียที่แยกได้จากผู้ป่วยไทยที่ติดเชื้อที่ระบบปัสสาวะและระบบการหายใจ

สุรภี เทียนกริม, ธนะพันธ์ พิบูลย์บรรณกิจ, สุดาลักษณ์ ธัญญาหาร, วรพจน์ ตันติศิริวัฒน์, สมชาย สันติวัฒนกุล, วัฒนชัย สุแสงรัตน์, นัตฏิยา ศรีสุราช, อำนาจ มะลิทอง, ประภัสสร ศรีแสงจันทร์, วิษณุ ธรรมลิขิตกุล

วัตถุประสงค์: *เพื่อเปรียบเทียบฤทธิ์ของยา sitafloxacin ต่อแบคทีเรียที่แยกได้จากผู้ป่วยโรคติดเชื้อที่ระบบปัสสาวะและระบบการหายใจ*

วัสดุและวิธีการ: *แบคทีเรียจำนวน 1,255 สายพันธุ์ของ Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Acinetobacter baumannii, Enterococcus spp, Streptococcus pneumoniae, Staphylococcus aureus, Hemophilus influenzae and Moraxella catarrhalis ที่แยกได้จากผู้ป่วยไทยที่เป็นโรคติดเชื้อที่ระบบปัสสาวะและระบบการหายใจใน พ.ศ. 2553 ถูกนำมาทดสอบความไวต่อยา sitafloxacin, ciprofloxacin, levofloxacin, moxifloxacin, imipenem, amikacin, ampicillin, ceftazidime, ceftriaxone, penicillin, piperacillin/tazobactam, vancomycin, azithromycin, and trimethoprim/sulfamethoxazole โดยการวัด minimum inhibitory concentrations (MICs) ด้วยวิธี agar dilution*

ผลการศึกษา: *MIC_{50} และ MIC_{90} ของยา sitafloxacin ต่อแบคทีเรียที่นำมาทดสอบมีค่าน้อยกว่ายา levofloxacin, ciprofloxacin และ moxifloxacin ยา sitafloxacin มีฤทธิ์ต่อ MRSA ร้อยละ 51, ฤทธิ์ของยา sitafloxacin ต่อเชื้อแบคทีเรียกรัมลบที่ดื้อยาหลายชนิด เช่น ESBL-producing E. coli และ K. pneumomiae, P. aeruginosa และ A. baumannii ก็ใกล้เคียงหรือมากกว่ายาบางขนานในกลุ่ม beta-lactam/beta-lactamase inhibitors, cephalosporins และ carbapenems*

สรุป: *Sitafloxacin มีฤทธิ์ต่อแบคทีเรียที่แยกได้จากผู้ป่วยโรคติดเชื้อที่ระบบปัสสาวะและระบบการหายใจมากกว่ายา levofloxacin, ciprofloxacin และ moxifloxacin รวมทั้งเชื้อที่ดื้อต่อยาต้านจุลชีพหลายขนานด้วย เช่น MRSA, ESBL-producing Gram-negatives, carbapenem-resistant A. baumannii*