# Comparative In Vitro Activity of Sitafloxacin Against Bacteria Isolated from Thai Patients with Urinary Tract Infections and Lower Respiratory Tract Infections in 2016

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**Objective:** *To determine in vitro activity of sitafloxacin compared with other antibiotics against the bacteria isolated from Thai patients with urinary tract infections and those with lower respiratory tract infections.*

**Material and Method:** *One thousand one hundred thirty six clinical isolates of Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Staphylococcus aureus isolated from different Thai patients with urinary tract infections or lower respiratory tract infections in 2016 were included. The minimum inhibitory concentrations (MICs) of sitafloxacin, ciprofloxacin, levofloxacin, amoxicillin-clavulanate, ceftriaxone, ceftazidime, piperacillin-tazobactam, tigecycline, imipenem, meropenem, and colistin 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 and ciprofloxacin. Sitafloxacin was more active than levofloxacin, ciprofloxacin, amoxicillin-clavulanate, ceftriaxone, and ceftazidime, but it was less active than piperacillin-tazobactam, tigecycline, imipenem, meropenem, and colistin against extended-spectrum beta-lactamase (ESBL)-producing E. coli isolates. Sitafloxacin was more active than levofloxacin, ciprofloxacin, amoxicillin-clavulanate, ceftriaxone, and ceftazidime against ESBL-producing K. pneumoniae. The activity of sitafloxacin against ESBL-producing K. pneumoniae was comparable to piperacillin-tazobactam, but it was less active than tigecycline, imipenem, meropenem, and colistin. Sitafloxacin was more active than levofloxacin, ciprofloxacin, ceftazidime, piperacillin-tazobactam, imipenem, and meropenem, but it was less active than colistin against A. baumannii isolates. The activity of sitafloxacin against P. aeruginosa isolates was comparable to levofloxacin, ciprofloxacin, ceftazidime, piperacillin-tazobactam, imipenem, and meropenem, but it was less active than colistin. The in vitro activity of sitafloxacin against methicillin-resistant S. aureus (MRSA) isolates was more than levofloxacin, but it was less than vancomycin. The activities of sitafloxacin against tested bacteria isolated from the patients in 2016 were not significantly different from those isolated in 2010.*

**Conclusion:** *Sitafloxacin remains active against the common antibiotic-resistant bacteria causing urinary tract infections and lower respiratory tract infections in Thai patients isolated in 2016, including ESBL-producing E. coli, ESBL-producing K. pneumoniae, A. baumannii, P. aeruginosa, and S. aureus, after its use in Thailand for five years.*

**Keywords:** *In vitro activity, Sitafloxacin, Fluoroquinolone*

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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 approved in Japan for the treatment of respiratory tract infections and genitourinary tract infections[1]. In vitro activity studies of sitafloxacin reported from Japan revealed that sitafloxacin was very active against a variety of bacteria, including *Streptococcus pneumoniae*, *Staphylococcus aureus*, Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Bacteroides fragilis*[2-11]. The in vitro activity of sitafloxacin against common causative bacteria isolated from Thai patients with urinary tract infections and

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those with lower respiratory tract infections in 2010 revealed that sitafloxacin was more active than levofloxacin, ciprofloxacin, moxifloxacin, and many other antibiotics against isolated bacteria from Thai patients with urinary tract and those with lower respiratory infections, including antibiotic resistant bacteria, such as methicillin-resistant *S. aureus* (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacilli, and carbapenem-resistant *A. baumannii*[12]. Sitafloxacin has been available in Thailand since 2012. Therefore, the objective of the present study was to determine the in vitro activity of sitafloxacin compared with other antibiotics against common antibiotic resistant bacteria isolated from Thai patients with urinary tract infections and those with lower respiratory tract infections in 2016, after sitafloxacin has been used on Thai patients for five years.

## Material and Method

### *Microorganisms*

One thousand one hundred thirty six clinical isolates of bacteria were collected from different patients with urinary tract infections and those with lower respiratory tract infections. The collected isolates were *Escherichia coli* (n = 304), *Klebsiella pneumoniae* (n = 317), *A. baumannii* (n = 190), *P. aeruginosa* (n = 203), and *S. aureus* (n = 122). There were 569 isolates from the patients with urinary tract infections, and 567 isolates from the patients with lower respiratory tract infections, all of whom attended five tertiary care hospitals in Thailand in 2016. Extended-spectrum beta-lactamase (ESBL) producing *E. coli* and *K. pneumoniae* isolates were detected by double-disk synergy test.

### *Antimicrobial agents*

Standard powders of amoxicillin, clavulanate, and ceftriaxone were purchased from Sigma-Aldrich, USA. Standard powders of ceftazidime, piperacillin, tazobactam, tigecycline, colistin, and vancomycin were purchased from Chem-Impex International, USA. Standard powders of ciprofloxacin, imipenem, and meropenem were purchased from Fluka, Switzerland USA, Gold Biotechnology, USA, and United States Pharmacopeia (USP), USA, respectively. Standard powders of levofloxacin 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 concentration (MIC) of an antibiotic was determined by standard agar dilution method according to the Clinical and Laboratory Standards Institute (CLSI) 2015. Mueller-Hinton II agar (BBL, Becton Dickinson, USA) was used for MIC determination of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, and *S. aureus*. Inoculum preparations of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii* were made by the growth method, adjusted to 0.5 McFarland turbidity, and then the bacterial suspension was diluted with cation-adjusted Mueller-Hinton broth (BBL, Becton Dickinson, USA) to $10^6$ CFU/mL. The inoculum preparation of *S. aureus* was made by a direct colony suspension adjusted to 0.5 McFarland turbidity, and then the bacterial suspension was diluted with cation-adjusted Mueller-Hinton broth to $10^6$ CFU/mL. Final inocula of $10^6$ CFU/mL were used and applied to the medium using multipoint spot inoculation. The inoculated agars were incubated at 35°C for 16 to 20 hours, except the inoculated agar with vancomycin (24 hours in ambient air). 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, *P. aeruginosa* ATCC 27853, and *S. aureus* ATCC 29213.

### *Data analysis*

The susceptibility breakpoints (BP) of the tested antibiotics were those recommended in the CLSI 2017 guidelines and EUCAST 2017 if they were available[13,14]. The susceptibility rate of the tested bacteria against sitafloxacin was calculated according to the MIC BPs of 1 mg/L or less and 2 mg/L or less. $MIC_{50}$ is the amount of antibiotic that inhibits 50% of bacterial isolates whereas $MIC_{90}$ is the amount of antibiotic that inhibits 90% of bacterial isolates. The percentage of antibiotic susceptibility was calculated based on the criteria. The susceptibilities of the antibiotics were comparable when the difference between those susceptibilities was within 10%.

## Results

The values of $MIC_{50}$, $MIC_{90}$, and the MIC ranges of the tested antibiotics, and the susceptibility rates of all of the tested organisms, are at Table 1. The in vitro activities of sitafloxacin and the other antimicrobial agents against bacteria isolated from the patients with urinary tract infections and those with lower respiratory tract infections are at Table 2 and 3, respectively.

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

| Organisms/antimicrobial agents | CLSI MIC breakpoints (mg/L) | MICs (mg/L) | | | |
|---|---|---|---|---|---|
| | | Range | $MIC_{50}$ | $MIC_{90}$ | % susceptibility |
| *E. coli* (304 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.004 to 32 | 1 | 4 | 72.4, 88.2 |
| Levofloxacin | ≤2 | 0.004 to >32 | 8 | 32 | 33.9 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 32 | >32 | 32.9 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to 256 | 16 | 32 | 37.5 |
| Ceftriaxone | ≤1 | 0.016 to >256 | 32 | 256 | 34.5 |
| Ceftazidime | ≤4 | 0.06 to >256 | 4 | 64 | 53.0 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 2 | 8 | 95.7 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 4 | 0.12 | 0.5 | 99.7 |
| Imipenem | ≤1 | 0.03 to 4 | 0.12 | 0.25 | 98.7 |
| Meropenem | ≤1 | 0.008 to 2 | 0.016 | 0.03 | 98.7 |
| Colistin | ≤2 | 0.25 to 4 | 0.5 | 0.5 | 97.7 |
| *E. coli*: ESBL-negative (105 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.004 to 32 | 0.06 | 2 | 87.6, 92.4 |
| Levofloxacin | ≤2 | 0.004 to >32 | 0.25 | 32 | 64.8 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.12 | >32 | 64.8 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to 128 | 16 | 32 | 48.6 |
| Ceftriaxone | ≤1 | 0.016 to 1 | 0.03 | 0.12 | 100 |
| Ceftazidime | ≤4 | 0.06 to 4 | 0.25 | 0.5 | 100 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to 8 | 1 | 4 | 100 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 0.5 | 0.06 | 0.12 | 100 |
| Imipenem | ≤1 | 0.03 to 0.25 | 0.12 | 0.12 | 100 |
| Meropenem | ≤1 | 0.008 to 0.03 | 0.016 | 0.016 | 100 |
| Colistin | ≤2 | 0.25 to 1 | 0.5 | 0.5 | 100 |
| *E. coli*: ESBL-producing (199 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 1 | 4 | 64.3, 85.4 |
| Levofloxacin | ≤2 | 0.03 to >32 | 16 | 32 | 17.6 |
| Ciprofloxacin | ≤1 | 0.008 to >32 | 32 | >32 | 16.6 |
| Amoxicillin-clavulanate | ≤8/4 | 4 to 256 | 16 | 32 | 31.7 |
| Ceftriaxone | ≤1 | 2 to >256 | 64 | 256 | 0 |
| Ceftazidime | ≤4 | 0.25 to >256 | 16 | 128 | 28.1 |
| Piperacillin-tazobactam | ≤16/4 | 0.5to >256 | 2 | 8 | 93.5 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 4 | 0.12 | 0.5 | 99.5 |
| Imipenem | ≤1 | 0.06 to 4 | 0.12 | 0.25 | 98.0 |
| Meropenem | ≤1 | 0.008 to 2 | 0.03 | 0.03 | 98.0 |
| Colistin | ≤2 | 0.25 to 4 | 0.5 | 0.5 | 97.0 |
| *K. pneumoniae* (317 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to >32 | 0.5 | 8 | 67.2, 77.9 |
| Levofloxacin | ≤2 | 0.03 to >32 | 4 | >32 | 49.8 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 8 | >32 | 42.3 |
| Amoxicillin-clavulanate | ≤8/4 | 1 to >256 | 32 | 128 | 31.9 |
| Ceftriaxone | ≤1 | 0.008 to >256 | 64 | >256 | 32.2 |
| Ceftazidime | ≤4 | 0.06 to >256 | 32 | >256 | 37.5 |
| Piperacillin-tazobactam | ≤16/4 | 0.25 to >256 | 8 | 256 | 77.6 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 4 | 0.25 | 0.5 | 98.1 |
| Imipenem | ≤1 | 0.06 to 32 | 0.25 | 1 | 90.2 |
| Meropenem | ≤1 | 0.016 to 32 | 0.03 | 1 | 90.2 |
| Colistin | ≤2 | 0.25 to 16 | 0.5 | 1 | 92.4 |
| *K. pneumoniae*: ESBL-negative (102 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 0.016 | 4 | 86.3, 88.2 |
| Levofloxacin | ≤2 | 0.03 to >32 | 0.06 | 16 | 86.3 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.03 | 16 | 84.3 |
| Amoxicillin-clavulanate | ≤8/4 | 1 to 256 | 4 | 16 | 83.3 |
| Ceftriaxone | ≤1 | 0.008 to 1 | 0.06 | 0.12 | 100 |
| Ceftazidime | ≤4 | 0.06 to 16 | 0.25 | 0.5 | 98 |
| Piperacillin-tazobactam | ≤16/4 | 0.25 to 64 | 2 | 4 | 99 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 1 | 0.12 | 0.25 | 100 |
| Imipenem | ≤1 | 0.06 to 0.5 | 0.12 | 0.25 | 100 |
| Meropenem | ≤1 | 0.016 to 0.03 | 0.03 | 0.03 | 100 |
| Colistin | ≤2 | 0.25 to 1 | 0.5 | 1 | 100 |

CLSI = Clinical and Laboratory Standards Institute; MIC = minimum inhibitory concentration; ESBL = extended-spectrun beta-lactamase; MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*; NA = not applicable

[1] No susceptible breakpoints in CLSI 2017, used EUCAST 2017 breakpoints

[2] No EUCAST 2017 breakpoints for *A. baumannii*, used breakpoints for Enterobacteriaceae

[3] No susceptible breakpoints in CLSI 2017 and EUCAST 2017 for *P. aeruginosa*

**Table 1.** (cont.)

| Organisms/antimicrobial agents | CLSI MIC breakpoints (mg/L) | MICs (mg/L) | | | |
|---|---|---|---|---|---|
| | | Range | $MIC_{50}$ | $MIC_{90}$ | % susceptibility |
| *K. pneumoniae*: ESBL-producing (215 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.016 to >32 | 1 | 8 | 57.7, 72.6 |
| Levofloxacin | ≤2 | 0.06 to >32 | 4 | >32 | 32.6 |
| Ciprofloxacin | ≤1 | 0.03 to >32 | 32 | >32 | 22.3 |
| Amoxicillin-clavulanate | ≤8/4 | 4 to >256 | 32 | >256 | 7.4 |
| Ceftriaxone | ≤1 | 2 to >256 | 256 | >256 | 0 |
| Ceftazidime | ≤4 | 0.5 to >256 | 128 | >256 | 8.8 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 16 | >256 | 67.4 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 4 | 0.25 | 0.5 | 97.2 |
| Imipenem | ≤1 | 0.06 to 32 | 0.25 | 4 | 85.6 |
| Meropenem | ≤1 | 0.016 to 32 | 0.03 | 4 | 85.6 |
| Colistin | ≤2 | 0.25 to 16 | 0.5 | 4 | 88.8 |
| *A. baumannii* (190 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 16 | 1 | 4 | 57.9, 87.9 |
| Levofloxacin | ≤2 | 0.03 to >32 | 8 | 16 | 20.5 |
| Ciprofloxacin | ≤1 | 0.06 to >32 | >32 | >32 | 18.4 |
| Ceftazidime | ≤8 | 2 to >256 | >256 | >256 | 18.9 |
| Piperacillin-tazobactam | ≤16/4 | 0.06 to >256 | >256 | >256 | 18.4 |
| Tigecycline[2] | ≤1 (EUCAST; Enterobacteriaceae) | 0.03 to 4 | 0.5 | 2 | 88.9 |
| Imipenem | ≤2 | 0.12 to >128 | 32 | 64 | 18.9 |
| Meropenem | ≤2 | 0.06 to >128 | 32 | 64 | 18.9 |
| Colistin | ≤2 | 0.5 to 2 | 1 | 1 | 100 |
| *P. aeruginosa* (203 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.004 to >32 | 0.12 | 16 | 69.5, 73.4 |
| Levofloxacin | ≤2 | 0.008 to >32 | 0.5 | >32 | 65.0 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.12 | >32 | 67.5 |
| Ceftazidime | ≤8 | 1 to >256 | 2 | >256 | 65.5 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 4 | 128 | 71.4 |
| Tigecycline[3] | NA | 0.012 to >4 | 4 | >4 | NA |
| Imipenem | ≤2 | 0.25 to >256 | 2 | 256 | 60.1 |
| Meropenem | ≤2 | 0.06 to >256 | 0.5 | 128 | 65.0 |
| Colistin | ≤2 | 0.25 to 16 | 2 | 2 | 100 |
| *S. aureus* (122 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 8 | 0.5 | 4 | 62.3, 66.4 |
| Levofloxacin | ≤1 | 0.06 to >32 | 4 | >32 | 47.5 |
| Vancomycin | ≤2 | 0.5 to 1 | 1 | 1 | 100 |
| *S. aureus*: MSSA (42 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 0.5 | 0.016 | 0.03 | 100, 100 |
| Levofloxacin | ≤1 | 0.06 to 8 | 0.12 | 0.25 | 95.2 |
| Vancomycin | ≤2 | 0.5 to 0.5 | 0.5 | 0.5 | 100 |
| *S. aureus*: MRSA (80 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 8 | 4 | 4 | 42.5, 48.8 |
| Levofloxacin | ≤1 | 0.06 to >32 | 16 | >32 | 22.5 |
| Vancomycin | ≤2 | 0.5 to 1 | 1 | 1 | 100 |

CLSI = Clinical and Laboratory Standards Institute; MIC = minimum inhibitory concentration; ESBL = extended-spectrun beta-lactamase; MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*; NA = not applicable

[1] No susceptible breakpoints in CLSI 2017, used EUCAST 2017 breakpoints

[2] No EUCAST 2017 breakpoints for *A. baumannii*, used breakpoints for Enterobacteriaceae

[3] No susceptible breakpoints in CLSI 2017 and EUCAST 2017 for *P. aeruginosa*

### *In vitro activity of sitafloxacin compared with other fluoroquinolones*

The values of $MIC_{50}$ and $MIC_{90}$ of sitafloxacin against all of the tested bacteria were lowest when compared with those of levofloxacin and ciprofloxacin. Sitafloxacin was active against 88 to 92% of ESBL-negative *E. coli* isolates, compared with 65% for levofloxacin and ciprofloxacin. Sitafloxacin was active against 64 to 85% of ESBL-producing *E. coli* isolates, compared with 17 to 18% for ciprofloxacin and levofloxacin. Sitafloxacin was active against 86 to 88% of ESBL-negative *K. pneumoniae* isolates, compared with 84 to 86% for ciprofloxacin and levofloxacin. Sitafloxacin was active against 58 to 73% of ESBL-producing *K. pneumoniae* isolates, compared with 22 to 33% for ciprofloxacin and levofloxacin. Sitafloxacin was active against 58 to 88% of *A. baumannii* isolates, compared with 18 to 21% for ciprofloxacin and levofloxacin. Sitafloxacin was active against 70 to 73% of *P. aeruginosa* isolates, compared with 65 to 68%

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

| Organisms/antimicrobial agents | CLSI MIC breakpoints(mg/L) | MICs (mg/L) | | | |
|---|---|---|---|---|---|
| | | Range | $MIC_{50}$ | $MIC_{90}$ | % susceptibility |
| *E. coli* (152 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 1 | 8 | 67.1, 86.2 |
| Levofloxacin | ≤2 | 0.016 to >32 | 16 | 32 | 28.3 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 32 | >32 | 27.6 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to 256 | 16 | 32 | 32.9 |
| Ceftriaxone | ≤1 | 0.016 to >256 | 32 | 256 | 33.6 |
| Ceftazidime | ≤4 | 0.12 to >256 | 4 | 64 | 54.6 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 2 | 4 | 96.7 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 1 | 0.12 | 0.12 | 100 |
| Imipenem | ≤1 | 0.03 to 4 | 0.12 | 0.25 | 99.3 |
| Meropenem | ≤1 | 0.008 to 2 | 0.016 | 0.03 | 99.3 |
| Colistin | ≤2 | 0.25 to 4 | 0.5 | 0.5 | 97.4 |
| *E. coli* ESBL-negative (51 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 0.06 | 1 | 90.2, 96.1 |
| Levofloxacin | ≤2 | 0.016 to >32 | 0.5 | 16 | 56.9 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.25 | >32 | 56.9 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to 64 | 16 | 32 | 45.1 |
| Ceftriaxone | ≤1 | 0.016 to 0.25 | 0.06 | 0.12 | 100 |
| Ceftazidime | ≤4 | 0.12 to 1 | 0.25 | 0.5 | 100 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to 8 | 2 | 4 | 100 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 0.5 | 0.06 | 0.12 | 100 |
| Imipenem | ≤1 | 0.03 to 0.25 | 0.12 | 0.12 | 100 |
| Meropenem | ≤1 | 0.008 to 0.03 | 0.016 | 0.016 | 100 |
| Colistin | ≤2 | 0.25 to 1 | 0.5 | 1 | 100 |
| *E. coli* ESBL-producing (101 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 1 | 8 | 54.5, 80.2 |
| Levofloxacin | ≤2 | 0.03 to >32 | 16 | 32 | 12.9 |
| Ciprofloxacin | ≤1 | 0.008 to >32 | 32 | >32 | 11.9 |
| Amoxicillin-clavulanate | ≤8/4 | 4 to 256 | 16 | 32 | 26.7 |
| Ceftriaxone | ≤1 | 4 to >256 | 64 | 256 | 0 |
| Ceftazidime | ≤4 | 1 to >256 | 16 | 64 | 31.7 |
| Piperacillin-tazobactam | ≤16/4 | 0.5to >256 | 2 | 8 | 94.1 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 1 | 0.12 | 0.12 | 100 |
| Imipenem | ≤1 | 0.06 to 4 | 0.12 | 0.25 | 99.0 |
| Meropenem | ≤1 | 0.016 to 2 | 0.03 | 0.03 | 99.0 |
| Colistin | ≤2 | 0.25 to 4 | 0.5 | 0.5 | 96.0 |
| *K. pneumoniae* (162 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 0.5 | 8 | 64.2, 75.9 |
| Levofloxacin | ≤2 | 0.03 to >32 | 4 | >32 | 46.9 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 16 | >32 | 38.9 |
| Amoxicillin-clavulanate | ≤8/4 | 1 to >256 | 32 | 128 | 31.5 |
| Ceftriaxone | ≤1 | 0.016 to >256 | 64 | >256 | 32.1 |
| Ceftazidime | ≤4 | 0.06 to >256 | 32 | 256 | 37.7 |
| Piperacillin-tazobactam | ≤16/4 | 0.25 to >256 | 4 | >256 | 76.5 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 2 | 0.25 | 0.5 | 98.1 |
| Imipenem | ≤1 | 0.06 to 32 | 0.25 | 2 | 89.5 |
| Meropenem | ≤1 | 0.016 to 32 | 0.03 | 4 | 89.5 |
| Colistin | ≤2 | 0.25 to 16 | 0.5 | 4 | 88.3 |
| *K. pneumoniae* ESBL-negative (52 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 16 | 0.016 | 8 | 78.8, 80.8 |
| Levofloxacin | ≤2 | 0.03 to >32 | 0.06 | 32 | 78.8 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.03 | >32 | 75.0 |
| Amoxicillin-clavulanate | ≤8/4 | 1 to 256 | 4 | 32 | 78.9 |
| Ceftriaxone | ≤1 | 0.016 to 1 | 0.06 | 0.12 | 100 |
| Ceftazidime | ≤4 | 0.06 to 16 | 0.25 | 1.0 | 96.2 |
| Piperacillin-tazobactam | ≤16/4 | 0.25 to 64 | 2 | 8 | 98.1 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 1 | 0.12 | 0.5 | 100 |
| Imipenem | ≤1 | 0.06 to 0.5 | 0.12 | 0.25 | 100 |
| Meropenem | ≤1 | 0.016 to 0.03 | 0.03 | 0.03 | 100 |
| Colistin | ≤2 | 0.25 to 1 | 0.5 | 1 | 100 |

[1] No susceptible breakpoints in CLSI 2017, used EUCAST 2017 breakpoints
[2] No EUCAST 2017 breakpoints for *A. baumannii*, used breakpoints for Enterobacteriaceae
[3] No susceptible breakpoints in CLSI 2017 and EUCAST 2017 for *P. aeruginosa*

**Table 2.** (cont.)

| Organisms/antimicrobial agents | CLSI MIC breakpoints(mg/L) | MICs (mg/L) | | | |
|---|---|---|---|---|---|
| | | Range | $MIC_{50}$ | $MIC_{90}$ | % susceptibility |
| *K. pneumoniae* ESBL-producing (110 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.016 to 32 | 1 | 8 | 60.0, 77.1 |
| Levofloxacin | ≤2 | 0.06 to >32 | 8 | >32 | 31.8 |
| Ciprofloxacin | ≤1 | 0.03 to >32 | 32 | >32 | 21.8 |
| Amoxicillin-clavulanate | ≤8/4 | 8 to >256 | 32 | 256 | 9.1 |
| Ceftriaxone | ≤1 | 2 to >256 | 128 | >256 | 0 |
| Ceftazidime | ≤4 | 0.5 to >256 | 64 | >256 | 10.0 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 8 | >256 | 66.4 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 2 | 0.25 | 0.5 | 97.3 |
| Imipenem | ≤1 | 0.06 to 32 | 0.25 | 4 | 84.5 |
| Meropenem | ≤1 | 0.016 to 32 | 0.03 | 4 | 84.5 |
| Colistin | ≤2 | 0.25 to 16 | 0.5 | 8 | 82.7 |
| *A. baumannii* (101 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 4 | 1 | 4 | 57.4, 89.1 |
| Levofloxacin | ≤2 | 0.03 to >32 | 4 | 16 | 19.8 |
| Ciprofloxacin | ≤1 | 0.06 to >32 | >32 | >32 | 18.8 |
| Ceftazidime | ≤8 | 2 to >256 | >256 | >256 | 19.8 |
| Piperacillin-tazobactam | ≤16/4 | 0.06 to >256 | >256 | >256 | 19.8 |
| Tigecycline[2] | ≤1 (EUCAST; Enterobacteriaceae) | 0.06 to 4 | 1 | 2 | 85.1 |
| Imipenem | ≤2 | 0.25 to >128 | 32 | 64 | 20.8 |
| Meropenem | ≤2 | 0.06 to >128 | 32 | 64 | 20.8 |
| Colistin | ≤2 | 0.5 to 2 | 0.5 | 1 | 100 |
| *P. aeruginosa* (102 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.03 to >32 | 0.25 | 32 | 60.8, 62.7 |
| Levofloxacin | ≤2 | 0.12 to >32 | 1 | >32 | 57.8 |
| Ciprofloxacin | ≤1 | 0.03 to >32 | 0.25 | >32 | 57.8 |
| Ceftazidime | ≤8 | 1 to >256 | 4 | >256 | 58.8 |
| Piperacillin-tazobactam | ≤16/4 | 2 to >256 | 8 | 128 | 66.7 |
| Tigecycline[3] | NA | 1 to >4 | 4 | >4 | NA |
| Imipenem | ≤2 | 0.5 to >256 | 2 | 256 | 59.8 |
| Meropenem | ≤2 | 0.06 to >256 | 0.5 | 256 | 63.7 |
| Colistin | ≤2 | 0.5 to 16 | 2 | 2 | 98.0 |
| *S. aureus* (52 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 4 | 0.5 | 4 | 67.3, 75.0 |
| Levofloxacin | ≤1 | 0.12 to >32 | 4 | >32 | 44.2 |
| Vancomycin | ≤2 | 0.5 to 1 | 0.5 | 1 | 100 |
| *S. aureus*: MSSA (19 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 0.5 | 0.016 | 0.03 | 100, 100 |
| Levofloxacin | ≤1 | 0.12 to 8 | 0.12 | 0.5 | 89.5 |
| Vancomycin | ≤2 | 0.5 to 0.5 | 0.5 | 0.5 | 100 |
| *S. aureus*: MRSA (33 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.016 to 4 | 2 | 4 | 48.5, 60.6 |
| Levofloxacin | ≤1 | 0.12 to >32 | 16 | >32 | 18.2 |
| Vancomycin | ≤2 | 0.5 to 1 | 1 | 1 | 100 |

[1] No susceptible breakpoints in CLSI 2017, used EUCAST 2017 breakpoints
[2] No EUCAST 2017 breakpoints for *A. baumannii*, used breakpoints for Enterobacteriaceae
[3] No susceptible breakpoints in CLSI 2017 and EUCAST 2017 for *P. aeruginosa*

for levofloxacin and ciprofloxacin. Sitafloxacin was active against all isolates of methicillin-susceptible *S. aureus* (MSSA), compared with 95% for levofloxacin. Sitafloxacin was active against 43 to 49% of MRSA isolates, compared with 23% for levofloxacin.

### *In vitro activity of sitafloxacin compared with other antibiotic classes*

Sitafloxacin was more active than amoxicillin-clavulanate against ESBL-negative *E. coli*. Sitafloxacin was slightly less active than ceftriaxone, ceftazidime, piperacillin-tazobactam, tigecycline, imipenem, meropenem, and colistin against ESBL-negative *E. coli* isolates. Sitafloxacin was more active than amoxicillin-clavulanate, ceftriaxone, and ceftazidime against ESBL-producing *E. coli*. Sitafloxacin was less active than piperacillin-tazobactam, tigecycline, imipenem, meropenem, and colistin against ESBL-producing *E. coli* isolates. The activity of sitafloxacin was comparable to amoxicillin-clavulanate against ESBL-negative *K. pneumoniae*. Sitafloxacin was less active than ceftriaxone, ceftazidime, piperacillin-tazobactam, tigecycline, imipenem, meropenem, and colistin against ESBL-negative *K. pneumoniae* isolates. Sitafloxacin

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

| Organisms/antimicrobial agents | CLSI MIC breakpoints(mg/L) | MICs (mg/L) | | | |
|---|---|---|---|---|---|
| | | Range | $MIC_{50}$ | $MIC_{90}$ | % susceptibility |
| *E. coli* (152 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.004 to 16 | 1 | 4 | 77.6, 89.5 |
| Levofloxacin | ≤2 | 0.004 to >32 | 8 | 32 | 40.1 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 16 | >32 | 38.8 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to 256 | 16 | 32 | 42.1 |
| Ceftriaxone | ≤1 | 0.016 to >256 | 32 | 256 | 35.5 |
| Ceftazidime | ≤4 | 0.06 to >256 | 4 | 64 | 51.3 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 1 | 8 | 94.7 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 4 | 0.12 | 0.5 | 99.3 |
| Imipenem | ≤1 | 0.06 to 4 | 0.12 | 0.25 | 98.0 |
| Meropenem | ≤1 | 0.008 to 2 | 0.016 | 0.03 | 98.0 |
| Colistin | ≤2 | 0.25 to 4 | 0.5 | 0.5 | 98.0 |
| *E. coli* ESBL-negative (54 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.004 to 16 | 0.03 | 4 | 85.2, 88.9 |
| Levofloxacin | ≤2 | 0.004 to >32 | 0.25 | 32 | 72.2 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.016 | 32 | 72.2 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to 128 | 8 | 32 | 51.9 |
| Ceftriaxone | ≤1 | 0.016 to 1 | 0.03 | 0.12 | 100 |
| Ceftazidime | ≤4 | 0.06 to 4 | 0.25 | 0.5 | 100 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to 8 | 1 | 2 | 100 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 0.5 | 0.06 | 0.12 | 100 |
| Imipenem | ≤1 | 0.06 to 0.25 | 0.12 | 0.25 | 100 |
| Meropenem | ≤1 | 0.008 to 0.03 | 0.016 | 0.016 | 100 |
| Colistin | ≤2 | 0.25 to 1 | 0.5 | 0.5 | 100 |
| *E. coli* ESBL-producing (98 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 16 | 1 | 4 | 73.5, 89.8 |
| Levofloxacin | ≤2 | 0.03 to >32 | 16 | 32 | 22.4 |
| Ciprofloxacin | ≤1 | 0.008 to >32 | 32 | >32 | 20.4 |
| Amoxicillin-clavulanate | ≤8/4 | 4 to 256 | 16 | 64 | 36.7 |
| Ceftriaxone | ≤1 | 2 to >256 | 64 | >256 | 0 |
| Ceftazidime | ≤4 | 0.25 to >256 | 16 | 128 | 24.5 |
| Piperacillin-tazobactam | ≤16/4 | 0.5to >256 | 2 | 16 | 91.8 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.03 to 4 | 0.12 | 0.5 | 99.0 |
| Imipenem | ≤1 | 0.06 to 4 | 0.12 | 0.25 | 96.9 |
| Meropenem | ≤1 | 0.008 to 2 | 0.016 | 0.06 | 96.9 |
| Colistin | ≤2 | 0.25 to 4 | 0.5 | 0.5 | 96.9 |
| *K. pneumoniae* (155 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to >32 | 0.5 | 8 | 70.3, 80.0 |
| Levofloxacin | ≤2 | 0.03 to >32 | 2 | >32 | 52.9 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 4 | >32 | 45.8 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to >256 | 32 | 128 | 32.3 |
| Ceftriaxone | ≤1 | 0.008 to >256 | 128 | >256 | 32.3 |
| Ceftazidime | ≤4 | 0.06 to >256 | 32 | >256 | 37.4 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 8 | 128 | 78.7 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 4 | 0.25 | 0.5 | 98.1 |
| Imipenem | ≤1 | 0.12 to 32 | 0.12 | 0.5 | 91.0 |
| Meropenem | ≤1 | 0.016 to 32 | 0.03 | 0.25 | 91.0 |
| Colistin | ≤2 | 0.25 to 16 | 0.5 | 1 | 96.8 |
| *K. pneumoniae* ESBL-negative (50 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 32 | 0.016 | 0.12 | 94.0, 96.0 |
| Levofloxacin | ≤2 | 0.03 to >32 | 0.06 | 1 | 94.0 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.03 | 0.5 | 94.0 |
| Amoxicillin-clavulanate | ≤8/4 | 2 to32 | 4 | 16 | 88.0 |
| Ceftriaxone | ≤1 | 0.008 to 0.5 | 0.06 | 0.06 | 100 |
| Ceftazidime | ≤4 | 0.06 to 1 | 0.25 | 0.25 | 100 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to 16 | 2 | 4 | 100 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 1 | 0.12 | 0.25 | 100 |
| Imipenem | ≤1 | 0.12 to 0.5 | 0.12 | 0.25 | 100 |
| Meropenem | ≤1 | 0.016 to 0.03 | 0.03 | 0.03 | 100 |
| Colistin | ≤2 | 0.25 to 1 | 0.5 | 1 | 100 |

[1] No susceptible breakpoints in CLSI 2017, used EUCAST 2017 breakpoints
[2] No EUCAST 2017 breakpoints for *A. baumannii*, used breakpoints for Enterobacteriaceae
[3] No susceptible breakpoints in CLSI 2017 and EUCAST 2017 for *P. aeruginosa*

**Table 3.** (cont.)

| Organisms/antimicrobial agents | CLSI MIC breakpoints(mg/L) | MICs (mg/L) | | | |
|---|---|---|---|---|---|
| | | Range | $MIC_{50}$ | $MIC_{90}$ | % susceptibility |
| *K. pneumoniae* ESBL-producing (105 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.016 to >32 | 1 | 8 | 50.5, 72.4 |
| Levofloxacin | ≤2 | 0.06 to >32 | 4 | >32 | 33.3 |
| Ciprofloxacin | ≤1 | 0.03 to >32 | 32 | >32 | 22.9 |
| Amoxicillin-clavulanate | ≤8/4 | 4 to >256 | 32 | >256 | 5.7 |
| Ceftriaxone | ≤1 | 2 to >256 | 256 | >256 | 0 |
| Ceftazidime | ≤4 | 1 to >256 | 128 | >256 | 7.6 |
| Piperacillin-tazobactam | ≤16/4 | 1 to >256 | 16 | >256 | 68.6 |
| Tigecycline[1] | ≤1 (EUCAST) | 0.06 to 4 | 0.25 | 0.5 | 97.1 |
| Imipenem | ≤1 | 0.12 to 32 | 0.25 | 4 | 86.7 |
| Meropenem | ≤1 | 0.03 to 32 | 0.06 | 4 | 86.7 |
| Colistin | ≤2 | 0.5 to 16 | 0.5 | 1 | 95.2 |
| *A. baumannii* (89 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 16 | 1 | 4 | 58.4, 86.5 |
| Levofloxacin | ≤2 | 0.03 to >32 | 8 | 16 | 21.3 |
| Ciprofloxacin | ≤1 | 0.06 to >32 | >32 | >32 | 18.0 |
| Ceftazidime | ≤8 | 4 to >256 | >256 | >256 | 18.0 |
| Piperacillin-tazobactam | ≤16/4 | 0.06 to >256 | >256 | >256 | 18.0 |
| Tigecycline[2] | ≤1 (EUCAST; Enterobacteriaceae) | 0.03 to 4 | 0.5 | 1 | 93.3 |
| Imipenem | ≤2 | 0.12 to 128 | 64 | 64 | 16.9 |
| Meropenem | ≤2 | 0.25 to 128 | 32 | 64 | 16.9 |
| Colistin | ≤2 | 0.5 to 2 | 1 | 1 | 100 |
| *P. aeruginosa* (101 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.004 to 16 | 0.12 | 4 | 78.2, 85.1 |
| Levofloxacin | ≤2 | 0.008 to >32 | 0.5 | >32 | 72.3 |
| Ciprofloxacin | ≤1 | 0.004 to >32 | 0.12 | 32 | 77.2 |
| Ceftazidime | ≤8 | 1 to >256 | 2 | >256 | 72.3 |
| Piperacillin-tazobactam | ≤16/4 | 0.5 to >256 | 4 | 64 | 76.2 |
| Tigecycline[3] | NA | 0.12 to >4 | 4 | >4 | NA |
| Imipenem | ≤2 | 0.25 to >256 | 2 | 64 | 60.4 |
| Meropenem | ≤2 | 0.06 to >256 | 0.5 | 64 | 66.3 |
| Colistin | ≤2 | 0.25 to 16 | 2 | 2 | 99.0 |
| *S. aureus* (70 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 8 | 0.03 | 4 | 58.6, 60.0 |
| Levofloxacin | ≤1 | 0.06 to >32 | 0.25 | >32 | 50.0 |
| Vancomycin | ≤2 | 0.5 to 1 | 1 | 1 | 100 |
| *S. aureus*: MSSA (23 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 0.03 | 0.016 | 0.03 | 100, 100 |
| Levofloxacin | ≤1 | 0.06 to 0.25 | 0.12 | 0.25 | 100 |
| Vancomycin | ≤2 | 0.5 to 0.5 | 0.5 | 0.5 | 100 |
| *S. aureus*: MRSA (47 isolates) | | | | | |
| Sitafloxacin | ≤1, ≤2 | 0.008 to 8 | 4 | 4 | 38.3, 40.4 |
| Levofloxacin | ≤1 | 0.06 to >32 | 32 | >32 | 25.5 |
| Vancomycin | ≤2 | 0.5 to 1 | 1 | 1 | 100 |

[1] No susceptible breakpoints in CLSI 2017, used EUCAST 2017 breakpoints
[2] No EUCAST 2017 breakpoints for *A. baumannii*, used breakpoints for Enterobacteriaceae
[3] No susceptible breakpoints in CLSI 2017 and EUCAST 2017 for *P. aeruginosa*

was more active than amoxicillin-clavulanate, ceftriaxone, and ceftazidime against ESBL-producing *K. pneumoniae*. The activity of sitafloxacin against ESBL-producing *K. pneumoniae* was comparable to piperacillin-tazobactam, but it was less active than tigecycline, imipenem, meropenem, and colistin.

Sitafloxacin was more active than ceftazidime, piperacillin-tazobactam, imipenem, and meropenem against *A. baumannii* isolates. The activity of sitafloxacin against *A. baumannii* isolates was comparable to that of tigecycline, but it was less active than colistin. The activity of sitafloxacin against *P. aeruginosa* isolates was comparable to ceftazidime, piperacillin-tazobactam, imipenem, and meropenem, but it was less active than colistin. The in vitro activity of sitafloxacin against MRSA isolates was less than that of vancomycin.

The activities of sitafloxacin against the tested bacteria isolated from the patients with urinary tract infections and those with lower respiratory tract infections were not significantly different.

The activities of sitafloxacin against the tested bacteria isolated from the patients in 2016 were not significantly different from those isolated

in 2010, although the activities of sitafloxacin against *A. baumannii* and MRSA collected in 2016 tended to be less than those collected in 2010.

## Discussion

The present study focused on common antibiotic resistant bacteria causing urinary tract infections and lower respiratory tract infections, i.e., ESBL-producing *E. coli*, ESBL-producing *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and MRSA, since other causative antibiotic non-resistant bacteria, such as *S. pneumoniae*, *Hemophilus influenzae*, *Moraxella catarrhalis*, and ESBL-negative Gram-negative bacilli, are usually susceptible to sitafloxacin and many other antibiotics.

CLSI and EUCAST have not officially recommended MIC BP for sitafloxacin. Several reports considered a MIC BP for sitafloxacin of 2 mg/L or less as susceptible for Gram-negative bacilli[10,15]. The MIC BP of sitafloxacin susceptibility used in this study were classified as 1 mg/L or less and 2 mg/L or less since the serum level of sitafloxacin after receiving a conventional dosage of sitafloxacin is not high[1]. However, most laboratories are unable to determine the MIC of sitafloxacin, and must use a disk diffusion test to determine susceptibility to sitafloxacin. It has been suggested that inhibition zone diameters of 16 mm or more and 18 mm or more seem to be the appropriate BP for susceptibility to sitafloxacin for resistant Gram-negative bacilli isolated from urine and blood, respectively[16].

The results of the present study indicated that sitafloxacin was more active than other fluoroquinolones and other oral or parenteral antibiotics against ESBL-producing *E. coli* and ESBL-producing *K. pneumoniae*, which is similar to the observations of previous studies[4-12]. The activity of sitafloxacin against *A. baumannii*, including the isolates resistant to carbapenems, confirmed the findings of several previous studies[12,15,17,18]. Moreover, most of the combinations of sitafloxacin and rifampin, colistin, sulbactam, or tigecycline exerted synergistic and/or partially synergistic and/or addictive effects against carbapenem-resistant *A. baumannii*[18]. Therefore, a clinical trial of colistin alone versus colistin plus sitafloxacin for the treatment of infections caused by carbapenem-resistant *A. baumannii* is being conducted. Sitafloxacin was also found to be as active as, or more active than, conventional anti-pseudomonas antibiotics against *P. aeruginosa*, which is similar to the observations of previous studies[12,19]. Tigecycline was found to be more active than sitafloxacin against *E. coli* and *K. pneumoniae*. However, the concentration of tigecycline in urine was very low, and it may not be appropriate for treatment of urinary tract infections[20]. Moreover, the treatment of infections with tigecycline was associated with increased mortality[21]. Colistin was also more active than sitafloxacin against *E. coli*, *K. pneumoniae*, *A. baumannii*, and *P. aeruginosa*. The effectiveness of therapy of antibiotic resistant Gram-negative infections with colistin was moderate, with frequent occurrences of nephrotoxicity[22]. The susceptibility rate of MRSA to sitafloxacin observed in the present study was comparable to the results from the previous studies[6,12].

Sitafloxacin has been available in Japan as an oral formulation with a recommended dose of 50 to 100 mg twice daily for therapy of respiratory tract or genitourinary tract infections. The pharmacokinetics (PK) of sitafloxacin has been shown to be favorable[23,24]. The oral administration of 100 mg of sitafloxacin was rapidly absorbed, with an absolute bioavailability of up to 90%. Food intake did not affect the rate or extent of absorption. The mean maximum concentration in serum of sitafloxacin was 1 mg/L, with an elimination half-life of five to six hours. Sitafloxacin was primarily eliminated by the kidney, and the concentration of sitafloxacin in urine was very high. In another population, the PK and pharmacodynamics (PD) of sitafloxacin in patients with community-acquired respiratory tract infections revealed that the PK-PD target values of sitafloxacin for the treatment of mild to moderate infections were considered to be fAUC(0-24h)/MIC 30 or more and fCmax/MIC 2 or more[25]. The PK-PD parameters at a regimen of 50 or 100 mg twice daily in patients with infections reached the target values[25].

The treatment of urinary tract infections, complicated urinary tract infections, and pyelonephritis in Japanese and Thai patients with sitafloxacin was satisfactory, with up to a 97% clinical response rate[26,27]. Sitafloxacin has also been found to be effective as a step-down therapy for the treatment of acute pyelonephritis caused by ESBL-producing *E. coli* in Thai patients after receiving parenteral carbapenem for three days[28]. A post-marketing surveillance of the efficacy and safety of sitafloxacin on more than 4,000 patients revealed that sitafloxacin had a high efficacy; in contrast, the incidence of adverse drug reactions was low (2 to 4%), with diarrhea and hepatic function disorders being the major adverse drug reactions[29,30].

In summary, sitafloxacin remains active against common antibiotic resistant bacteria causing

urinary tract infections and lower respiratory infections after it has been available in Thailand for five years. It is anticipated that sitafloxacin will be an important and effective antibiotic for the therapy of infections caused by antibiotic-resistant Gram-negative bacilli in outpatients and hospitalized patients who do not require parenteral antibiotics, as well as a continued therapy after parenteral therapy with other antibiotics.

**What is already known on this topic?**

Sitafloxacin was active against common bacteria causing urinary tract infections and lower respiratory tract infections isolated from Thai patients in 2010.

**What this study adds?**

In 2016, sitafloxacin remained active against common resistant bacteria, including ESBL-producing *E. coli*, ESBL-producing *K. pneumoniae* and *A. baumannii*, and *P. aeruginosa*, isolated from Thai patients with urinary tract infections and those with lower respiratory tract infections.

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**Potential conflicts of interest**

None.

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**การเปรียบเทียบฤทธิ์ของยา sitafloxacin ต่อแบคทีเรียที่แยกได้จากผู้ป่วยไทยติดเชื้อที่ระบบปัสสาวะและระบบการหายใจช่วงล่าง พ.ศ. 2559**

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**วัตถุประสงค์:** *เพื่อทราบฤทธิ์ของยา sitafloxacin เปรียบเทียบกับยาต้านจุลชีพขนานอื่น ๆ ต่อแบคทีเรียที่แยกได้จากผู้ป่วยโรคติดเชื้อที่ระบบปัสสาวะและระบบการหายใจช่วงล่าง*

**วัสดุและวิธีการ:** *แบคทีเรียจำนวน 1,136 สายพันธุ์ของ Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa และ Staphylococcus aureus ที่แยกจากผู้ป่วยไทยที่ติดเชื้อที่ระบบปัสสาวะและระบบการหายใจช่วงล่าง พ.ศ. 2559 ถูกนำมาทดสอบความไวต่อยา sitafloxacin, ciprofloxacin, levofloxacin, amoxicillin-clavulanate, ceftriaxone, ceftazidime, piperacillin-tazobactam, tigecycline, imipenem, meropenem และ colistin โดยการตรวจ minimum inhibitory concentrations (MICs) ด้วยวิธีมาตรฐาน agar dilution*

**ผลการศึกษา:** *ปริมาณ $MIC_{50}$ และ $MIC_{90}$ ของยา sitafloxacin ต่อแบคทีเรียที่นำมาทดสอบมีค่าน้อยกว่า levofloxacin และ ciprofloxacin ยา sitafloxacin มีฤทธิ์มากกว่า levofloxacin, ciprofloxacin, amoxicillin-clavulanate, ceftriaxone และ ceftazidime แต่มีฤทธิ์น้อยกว่า piperacillin-tazobactam, tigecycline, imipenem, meropenem และ colistin ต่อเชื้อ ESBL-producing E. coli ยา sitafloxacin มีฤทธิ์มากกว่า levofloxacin, ciprofloxacin, amoxicillin-clavulanate, ceftriaxone และ ceftazidime ต่อเชื้อ ESBL-producing K. pneumoniae ฤทธิ์ของยา sitafloxacin ต่อเชื้อ ESBL-producing K. pneumoniae ใกล้เคียงกับยา piperacillin-tazobactam แต่มีฤทธิ์น้อยกว่า tigecycline, imipenem, meropenem และ colistin ยา sitafloxacin มีฤทธิ์มากกว่า levofloxacin, ciprofloxacin, ceftazidime, piperacillin-tazobactam, imipenem, meropenem แต่มีฤทธิ์น้อยกว่า colistin ต่อเชื้อ A. baumannii ฤทธิ์ของยา sitafloxacin ต่อเชื้อ P. aeruginosa ใกล้เคียงกับ levofloxacin, ciprofloxacin, ceftazidime, piperacillin-tazobactam, imipenem และ meropenem แต่มีฤทธิ์น้อยกว่า colistin ฤทธิ์ของยา sitafloxacin ต่อเชื้อ S. aureus สายพันธุ์ที่ดื้อ methicillin มากกว่า levofloxacin แต่น้อยกว่า vancomycin ฤทธิ์ของยา sitafloxacin ต่อแบคทีเรียที่แยกจากผู้ป่วย พ.ศ. 2559 ไม่แตกต่างจากฤทธิ์ของยานี้ต่อแบคทีเรียที่แยกจากผู้ป่วย พ.ศ. 2553*

**สรุป:** *ยา sitafloxacin ยังมีฤทธิ์ดีต่อแบคทีเรียดื้อยาที่พบบ่อยที่แยกจากผู้ป่วยโรคติดเชื้อที่ระบบปัสสาวะและระบบการหายใจช่วงล่างใน พ.ศ. 2559 รวมถึง ESBL-producing E. coli, ESBL-producing K. pneumoniae, A. baumannii, P. aeruginosa และ S. aureus หลังจากที่ใช้ยานี้ในประเทศไทยมานาน 5 ปี*