

Comparative Activity of Gatifloxacin Against *P. aeruginosa* and Enterobacteriaceae Isolated from Hospitalized Patients in the United States

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ABSTRACT

Background: Fluoroquinolones such as ciprofloxacin, levofloxacin and ofloxacin have been used extensively to treat infections of the respiratory tract, urinary tract, skin and soft tissue, genital tract and blood stream. The long-term effect that such fluoroquinolones may have upon pathogens with varying degrees of intrinsic resistance to these agents is currently unknown. The activity of gatifloxacin against respiratory isolates of gram-negative rods recovered from laboratories across the United States has not been previously demonstrated. In this study we examined the activity of gatifloxacin and three comparators against a collection of *P. aeruginosa* and Enterobacteriaceae isolated from sputum and bronchial specimens of patients in general medicine wards of 108 investigative centers in the U.S. as part of a large national surveillance study during 1999/2000.

Methods: MIC's to gatifloxacin and comparators were determined using Etest® strips and interpreted following manufacturer's instructions and NCCLS guidelines as appropriate.

Results: MIC₅₀ and MIC₉₀ (µg/ml), and % Susceptible are shown in the following table:

	<i>P. aeruginosa</i> (n=143)			Enterobacteriaceae (n=251)		
	MIC ₅₀	MIC ₉₀	%S	MIC ₅₀	MIC ₉₀	%S
Gatifloxacin	1	>32	65.0	0.06	1	94.4
Ciprofloxacin	0.25	>32	67.6	0.06	1	93.2
Levofloxacin	1	>32	65.0	0.12	1	94.0
Ceftriaxone	>32	>256	9.8	0.12	>32	86.5

Conclusions: Based on percentages of susceptible isolates, gatifloxacin was as active as ciprofloxacin and levofloxacin and more active than ceftriaxone against sputum and bronchial isolates of *P. aeruginosa* and Enterobacteriaceae. However, ciprofloxacin MIC₅₀ was 4-fold lower than either gatifloxacin or levofloxacin against *P. aeruginosa*.

INTRODUCTION

The fluoroquinolones are useful antimicrobial agents in the treatment of respiratory tract infections. Their use is increasing in this regard, partly due of the resistance to the beta-lactams and macrolides, and partly due to the enhanced activity of the newer fluoroquinolones in Gram-positive organisms. However, from 1989, the year ciprofloxacin was introduced, to present, the incidence of fluoroquinolone resistance has steadily increased among all the Enterobacteriaceae and *Pseudomonas aeruginosa*. For

example, in 1993, ciprofloxacin MIC₉₀s were reported at 0.5 µg/ml but in more recent studies they have ranged from 4 µg/ml to >32 µg/ml. Although less common than their Gram-positive respiratory counterparts, Gram-negative organisms are significant respiratory pathogens, especially in general medical and intensive care wards. Gatifloxacin is an enhanced activity compound, an 8-methoxy fluoroquinolone, effective against many Gram-positive respiratory pathogens while maintaining broad Gram-negative activity. Irrespective of isolate source, gatifloxacin is generally 2 to 8 fold more active than ciprofloxacin and levofloxacin against Gram-positive bacteria, Acinetobacter

and non-*Pseudomonas aeruginosa* pseudomonads with similar activity to other quinolones versus Enterobacteriaceae.

The *in vitro* activity of gatifloxacin against Gram-negative respiratory pathogens in the United States has not previously been documented. In this study, gatifloxacin and comparative antimicrobial agents were tested against 143 *Pseudomonas aeruginosa* and 251 Enterobacteriaceae respiratory pathogens collected as part of a larger surveillance study conducted by 108 medical centers within the United States between July 1999 and May 2000. The *in vitro* activities of gatifloxacin and three comparative agents were determined in respiratory isolates from general medical wards only. The data are presented below.

MATERIALS & METHODS

- Isolates were collected between July 1999 and May 2000 from 108 study centers from the United States.
- Each center was instructed to collect up to 10 Gram-negative pathogens associated with respiratory tract infections. The specimens presented are those from general medical wards only.
- Each isolate was identified and determined to be the causative agent of a recent respiratory infection using local laboratory criteria. Only one isolate per patient was accepted.
- Organism collection, transport, storage and antimicrobial susceptibility testing, as well as construction and management of a centralized database, was coordinated by International Health Management Associates, Inc. (IHMA, Rolling Meadows, IL).

ANTIMICROBIAL SUSCEPTIBILITY TESTING

- Gatifloxacin, levofloxacin, ciprofloxacin, and ceftriaxone inhibitory concentrations (MICs, µg/ml) were determined using Etest® strips (AB Biodisk, Solna, Sweden) according to the manufacturer's recommendations.
- Plates were inoculated with bacterial suspensions equivalent to a 0.5 McFarland standard and incubated at 35°C for 18-24 hours.
- The antimicrobial breakpoints used for data analysis were those recommended by the NCCLS (M100-S11, 2001) for broth dilution susceptibility testing.
- Control strains used were *E. coli* ATCC 35218; *P. aeruginosa* ATCC 27853 and *H. influenzae* ATCC 49247 and 49766. Test isolate results were accepted into the final analysis only if the quality control isolate MICs were within the acceptable range defined by NCCLS guidelines (M100-S11, 2001).

RESULTS

Results are shown in the following Tables and Figures.

Table 1. *In Vitro* Activity (µg/ml) of Gatifloxacin and Comparators Against Gram-Negative Respiratory Pathogens from 108 Centers in the United States.

Organism	Antimicrobial	MIC ₅₀	MIC ₉₀	Range	%Sus ^a	%Int	%Res
<i>Pseudomonas aeruginosa</i> (n=143)	Gatifloxacin	1	>32	0.094 ->32	65.0	4.9	30.1
	Ciprofloxacin	0.25	>32	0.032 ->32	67.6	7.7	24.6
	Levofloxacin	1	>32	0.094 ->32	65.0	3.5	31.5
	Ceftriaxone	>32	256	0.032 ->256	9.8	12.6	77.6
Enterobacteriaceae (n=251)	Gatifloxacin	0.064	0.75	0.008 ->32	94.4	1.6	4.0
	Ciprofloxacin	0.064	0.75	0.008 ->32	93.2	1.2	5.6
	Levofloxacin	0.125	1	0.008 ->32	94.0	0.4	5.6
	Ceftriaxone	0.125	>32	0.016 ->256	86.5	2.8	10.8

^a Interpretive standards derived from NCCLS publication M100-S11, 2001.

Figure 1. *Pseudomonas aeruginosa* Cumulative Percent Inhibited (%) for Gatifloxacin, Levofloxacin and Ciprofloxacin for 143 Respiratory Isolates from the United States

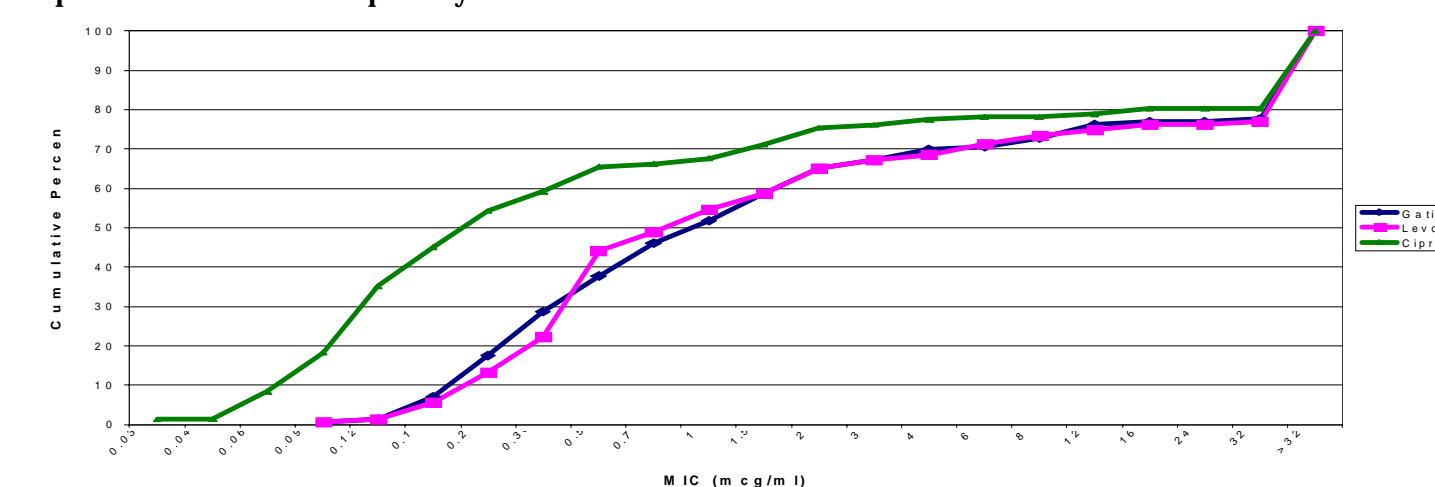
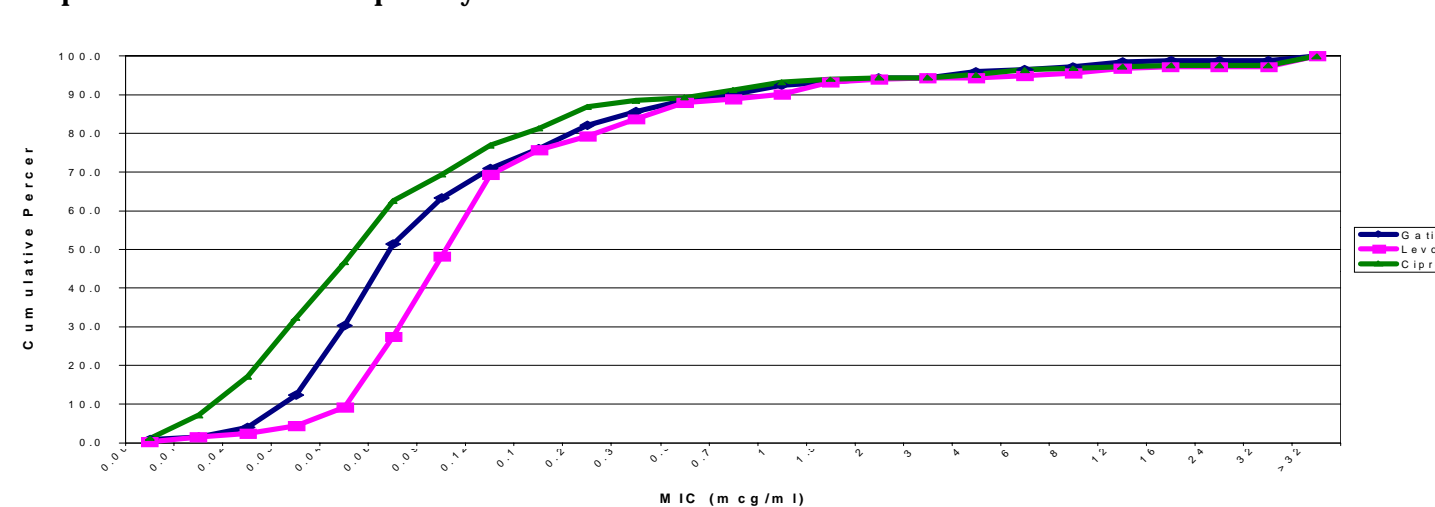


Figure 2. Enterobacteriaceae Cumulative Percent Inhibited (%) for Gatifloxacin, Levofloxacin and Ciprofloxacin for 251 Respiratory Isolates from the United States



CONCLUSIONS

- Gatifloxacin was as active as ciprofloxacin and levofloxacin and more active than ceftriaxone against respiratory isolates of *Pseudomonas aeruginosa* and Enterobacteriaceae.
- Ciprofloxacin MIC₅₀ was 4 fold lower than gatifloxacin and levofloxacin for *Pseudomonas aeruginosa*.
- Resistance to ciprofloxacin is increasing in *Pseudomonas aeruginosa* species.
- Large-scale surveillance programs are beneficial in providing ongoing susceptibility data for antimicrobial agents.

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ACKNOWLEDGEMENTS

We acknowledge the following centers for their participation and contribution to this study (in alphabetical order): Allegheny University Hospital, MCP Philadelphia, PA; Altchuler Medical Foundation, New Orleans, LA; Baltimore Veterans Administration Med., Baltimore, MD; Baptist Medical Center, Little Rock, AR; Baptist Medical Center, Jacksonville, FL; Baptist Hospital, Miami, FL; Barnes-Jewish Hospital, St. Louis, MO; Baylor University Medical Center, Dallas, TX; Ben Taub General Hospital, Houston, TX; Beth Israel Deaconess Medical Center, Boston, MA; Beth Israel Medical Center, New York, NY; Boston Medical Center - ENC, Boston, MA; Brigham and Women's Hospital, Boston, MA; Christina Care Health Services, Wilmington, DE; Columbia Medical Center West, El Paso, TX; Columbia Memorial Hospital, Jacksonville, FL; Columbia Presbyterian Center of N.Y., New York, NY; Cottonwood Hospital & Medical Center, Murray, UT; Crozer - Chester Medical Center, Upland, PA; Desert Samaritan Medical Center, Phoenix, AZ; DSI Laboratories, Fort Myers, FL; East Texas Medical Center, Tyler, TX; Fairfax Hospital, Fairfax, VA; Florida Hospital, Orlando, FL; Forrest General Hospital, Hattiesburg, MS; Good Samaritan Regional Med. Ctr., Phoenix, AZ; Greenville Memorial Hospital, Greenville, SC; Gunderson Lutheran Clinic, Ltd., La Crosse, WI; Halifax Medical Center, Daytona Beach, FL; Harborview Medical Center, Seattle, WA; Health Alliance of Greater Cincinnati, Cincinnati, OH; Hermann Hospital, Houston, TX; Hoag Hospital, Newport Beach, CA; Holmes Regional Medical Center, Melbourne, FL; Illinois Masonic Medical Center, Chicago, IL; Indiana University Hospital, Indianapolis, IN; Infectious Disease Consultants, Wichita, KS; Iowa Methodist Medical Center, Des Moines, IA; Jackson Memorial Hospital, Miami, FL; Jackson Madison County General Hospital, Jackson, TN; Jewish Hospital, Louisville, KY; John Hopkins Hospital, Baltimore, MD; Kansas City VA Medical Center, Kansas City, MO; Lahey Clinic, Burlington, MA; LDS Hospital, Salt Lake City, UT; Loma Linda Mercantile, San Bernardino, CA; Long Beach Memorial Medical Center, Long Beach, CA; Long Island Jewish Medical Center, New Hyde Park, NY; LSU Medical Center, Shreveport, LA; Maine Medical Center, Portland, ME; Mayo Clinic Jacksonville, Jacksonville, FL; McKay-Dee Hospital Center, Ogden, UT; Medical Center of Central Georgia, Macon, GA; Medical College of Wisconsin, Milwaukee, WI; Methodist Hospital/Clarian Health, Indianapolis, IN; Miami Valley Hospital, Dayton, OH; Morristown Memorial Hospital, Morristown, NJ; Mount Sinai Medical Center, Miami Beach, FL; Mount Sinai Medical Center, New York, NY; New England Medical Center, Boston, MA; New Hanover Regional Medical Center, Wilmington, NC; New York University Medical Center, New York, NY; New York Hospital - Cornell Medical C., New York, NY; Presbyterian Hospital, Charlotte, NC; Primary Children's Medical Center, Salt Lake City, UT; Providence Portland Medical Center, Portland, OR; Regions Hospital, Saint Paul, MN; Rush-Presbyterian-St. Luke's Medical, Chicago, IL; San Francisco General Hospital, San Francisco, CA; San Francisco VA Hospital, San Francisco, CA; Sarasota Memorial Hospital, Sarasota, FL; Shands' Hospital-University Med. Center, Jacksonville, FL; Southwest Texas Methodist Hospital, San Antonio, TX; Spartanburg Regional Healthcare System, Spartanburg, SC; St. Joseph's Hospital and Medical Cent, Paterson, NJ; St. Luke's Hospital, Kansas City, MO; St. Luke's Episcopal Hospital, Houston, TX; St. Joseph's Hospital, Tampa, FL; Stanford University Medical Center, Stanford, CA; Summa Health System, Akron, OH; Sunrise Hospital & M.C. Sunrise Children, Las Vegas, NV; Sutter Roseville Medical Center, Roseville, CA; Temple Univ. Health Sciences C., Philadelphia, PA; The Cleveland Clinic Foundation, Cleveland, OH; The Methodist Hospital, Houston, TX; The Tampa General Hospital, Tampa, FL; Thomas Jefferson University Hospital, Philadelphia, PA; University Hospitals Of Cleveland, Cleveland, OH; University of Florida, Gainesville, FL; University Of Alabama At Birmingham, Birmingham, AL; University of Michigan Medical Center, Rochester Medical Center, University of Rochester Medical Center, NY; University of Kansas Medical Center, Kansas City, KS; University of Toledo College of Pharm., Toledo, OH; University Of Illinois Hospital, Chicago, IL; University Hospital, San Antonio, TX; University of Texas Medical Branch, Galveston, TX; University of Colorado Health Sciences, Denver, CO; University Of Washington Medical Center, Seattle, WA; University of Virginia Health System, Charlottesville, VA; Vanderbilt University Medical Center, Nashville, TN; Virginia Mason Hospital, Seattle, WA; Wake Forest University Baptist Medical, Winston Salem, NC; Wellstar Kennestone Hospital, Marietta, GA; Westchester County Medical Center, Valhalla, NY; William Beaumont Hospital, Royal Oak, MI; Wishard Memorial Hospital, Indianapolis, IN; Yale - New Haven Hospital, New Haven, CT.