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In Vitro Susceptibilities of 393 Recent Clinical Isolates to WIN 49375, Cefotaxime, Tobramycin, and Piperacillin

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The in vitro susceptibilities of 393 recent clinical isolates to WIN 49375, a new quinolone derivative, were determined and concurrently tested with cefotaxime, tobramycin, and piperacillin. In general, members of the family *Enterobacteriaceae* were not as susceptible to tobramycin and piperacillin as they were to WIN 49375. Methicillin-resistant and -susceptible *Staphylococcus aureus* were equally susceptible to WIN 49375.

WIN 49375 is a new quinolone derivative developed by the Sterling-Winthrop Research Institute. This promising new antibacterial agent demonstrates a wide range of activity against both aerobic gram-positive cocci and aerobic gram-negative rods. We have compared the activity of WIN 49375 to three commercially available agents, cefotaxime, tobramycin, and piperacillin, which generally demonstrate an antibacterial spectrum against members of the family *Enterobacteriaceae* similar to that of WIN 49375 (2–5, 8; Sterling-Winthrop Research Institute, personal communication).

The clinical isolates tested were obtained from the Henry Ford Hospital bacteriology laboratory. WIN 49375 was a gift from the Sterling-Winthrop Research Institute, cefotaxime was from Hoechst-Roussel Pharmaceuticals Inc., piperacillin was from Lederle Laboratories, and tobramycin was from Eli Lilly & Co.

All MICs were determined by the microtube dilution method, using Mueller-Hinton broth (BBL Microbiology Systems). Upper-limit concentrations of WIN 49375, cefotaxime, and tobramycin were 50 μg/ml, and the upper-limit concentration of piperacillin was 500 μg/ml. The final inoculum contained 10^5 CFU/ml. Test systems were incubated at 35°C for 18 h. The MIC was defined as the lowest concentration of antimicrobial agent at which the inoculum did not show growth. Cephalothin, gentamicin, and methicillin susceptibility and resistance were defined by the National Committee for Clinical Laboratory Standards (7).

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The comparative activities are shown in Table 1. The majority of members of the family *Enterobacteriaceae* were either more or as susceptible to WIN 49375 as to cefotaxime. In general, members of the family *Enterobacteriaceae* were not as susceptible to tobramycin and piperacillin as they were to WIN 49375 and cefotaxime. Staphylococci and *Pseudomonas aeruginosa* were inhibited by relatively low concentrations of WIN 49375; however, the susceptibility of these organisms to WIN 49375 was considerably less than that of *Enterobacteriaceae*. Cephalothin-resistant *Escherichia coli*, gentamicin-resistant *P. aeruginosa*, and methicillin-resistant *Staphylococcus aureus* proved to be as susceptible to WIN 49375 as their respective antibiotic-susceptible varieties.

Compared with other new quinolone derivatives, WIN 49375 demonstrated similar activity to ciprofloxacin and to norfloxacin against *Enterobacteriaceae* (1, 6). The MICs required to inhibit 50 and 90% of isolates for WIN 49375, ciprofloxacin, and norfloxacin were generally within two twofold dilutions of each other when comparing their activity against *Enterobacteriaceae*, pseudomonads, and staphylococci.

TABLE 1. Comparative activity of WIN 49375 with cefotaxime, tobramycin, and piperacillin

Organism (no. of isolates)	Agent	MIC (μg/ml)[a]		
		Range	50%	90%
Acinetobacter calcoaceticus (22)	WIN 49375	0.195–1.56	0.39	0.78
	Cefotaxime	6.24–50.0	12.5	25.0
	Tobramycin	0.097–3.12	0.39	0.78
	Piperacillin	4.0–125.0	15.6	62.4
Citrobacter diversus (12)	WIN 49375	≤0.024	≤0.024	≤0.024
	Cefotaxime	≤0.024–0.048	≤0.024	≤0.024
	Tobramycin	0.048–0.195	0.195	0.195
	Piperacillin	2.0–4.0	2.0	4.0
Citrobacter freundii (14)	WIN 49375	≤0.024–0.195	0.048	0.097
	Cefotaxime	≤0.024–25.0	0.097	12.5
	Tobramycin	0.195–1.56	0.39	0.78
	Piperacillin	0.48–62.4	2.0	25.6
Enterobacter aerogenes (7)	WIN 49375	≤0.024–0.048	≤0.024	0.048
	Cefotaxime	≤0.024–25.0	≤0.024	25.0
	Tobramycin	0.048–50.0	0.39	50.0
	Piperacillin	≤0.24–31.2	1.0	31.2

TABLE 1—*Continued*

Organism (no. of isolates)	Agent	MIC (μg/ml)[a]		
		Range	50%	90%
Enterobacter agglomerans (2)	WIN 49375	0.097–0.39	0.097	0.39
	Cefotaxime	0.097–0.39	0.097	0.39
	Tobramycin	0.048–0.097	0.048	0.097
	Piperacillin	≤0.24–2.0	≤0.24	2.0
Enterobacter cloacae (25)	WIN 49375	≤0.024–0.78	0.048	0.195
	Cefotaxime	≤0.024–50.0	0.39	50.0
	Tobramycin	0.097–25.0	0.195	0.78
	Piperacillin	0.48–500.0	2.0	62.4
Escherichia coli (24) (cephalothin susceptible)	WIN 49375	≤0.024–0.097	≤0.024	0.048
	Cefotaxime	≤0.024–0.048	≤0.024	≤0.024
	Tobramycin	0.195–1.56	0.39	0.78
	Piperacillin	≤0.24–>500	0.48	125.0
Escherichia coli (20) (cephalothin resistant)	WIN 49375	≤0.024–0.39	≤0.024	0.048
	Cefotaxime	≤0.024–0.39	≤0.024	0.39
	Tobramycin	0.195–1.56	0.78	1.56
	Piperacillin	≤0.24–31.2	4.0	15.6
Klebsiella pneumoniae (24)	WIN 49375	0.097–0.39	0.097	0.195
	Cefotaxime	≤0.024–0.195	≤0.024	0.048
	Tobramycin	0.195–25.0	0.39	12.5
	Piperacillin	1.0–>500	4.0	>500
Morganella morganii (22)	WIN 49375	≤0.024–0.39	≤0.024	≤0.024
	Cefotaxime	≤0.024–6.24	0.097	0.39
	Tobramycin	0.195–6.24	0.39	0.78
	Piperacillin	≤0.24–>500	1.0	15.6
Proteus mirabilis (24)	WIN 49375	≤0.024–0.195	0.048	0.097
	Cefotaxime	≤0.024–0.097	≤0.024	≤0.024
	Tobramycin	0.097–1.56	0.78	1.56
	Piperacillin	≤0.24	≤0.24	≤0.24
Proteus vulgaris (7)	WIN 49375	≤0.024–0.39	0.048	0.39
	Cefotaxime	≤0.024–0.097	0.048	0.097
	Tobramycin	0.097–3.12	0.39	3.12
	Piperacillin	≤0.24–15.6	≤0.24	15.6
Providencia sp. (8)	WIN 49375	≤0.024–6.24	0.195	6.24
	Cefotaxime	≤0.024–3.12	≤0.024	3.12
	Tobramycin	0.39–25.0	3.12	25.0
	Piperacillin	≤0.24–250	2.0	250
Pseudomonas aeruginosa (56) (gentamicin susceptible)	WIN 49375	0.78–12.5	3.12	6.24
	Cefotaxime	12.5–>50.0	>50.0	>50.0
	Tobramycin	0.195–>50.0	0.78	3.12
	Piperacillin	2.0–500	8.0	62.5
Pseudomonas aeruginosa (28) (gentamicin resistant)	WIN 49375	0.39–6.24	1.56	6.24
	Cefotaxime	25.0–>50.0	>50.0	>50.0
	Tobramycin	3.12–>50.0	>50.0	>50.0
	Piperacillin	8.0–500.0	250.0	500.0
Pseudomonas maltophilia (7)	WIN 49375	1.56–3.12	3.12	3.12
	Cefotaxime	25.0–>50.0	>50.0	>50.0
	Tobramycin	0.78–>50.0	>50.0	>50.0
	Piperacillin	250–>500	>500	>500
Serratia marcescens (27)	WIN 49375	0.048–0.39	0.195	0.39
	Cefotaxime	0.097–>50.0	0.39	0.78
	Tobramycin	0.78–>50.0	25.0	>50.0
	Piperacillin	≤0.24–>500	8.0	62.5
Staphylococcus aureus (23) (methicillin susceptible)	WIN 49375	0.39–1.56	0.78	1.56
	Cefotaxime	1.56–3.12	3.12	3.12
	Tobramycin	≤0.024–0.39	0.097	0.195
	Piperacillin	≤0.24–125.0	8.0	31.2

TABLE 1—*Continued*

Organism (no. of isolates)	Agent	MIC (μg/ml)[a]		
		Range	50%	90%
Staphylococcus aureus (28) (methicillin resistant)	WIN 49375	0.39–1.56	0.78	1.56
	Cefotaxime	6.24–>50.0	>50.0	>50.0
	Tobramycin	>50.0	>50.0	>50.0
	Piperacillin	250.0	250.0	250.0
Staphylococcus saprophyticus (13)	WIN 49375	1.56	1.56	1.56
	Cefotaxime	3.12–6.24	3.12	6.24
	Tobramycin	≤0.024	≤0.024	≤0.024
	Piperacillin	≤0.24–1.0	1.0	1.0

[a] 50% and 90%, MICs inhibiting 50 and 90% of isolates, respectively.

The MICs required to inhibit the pseudomonads and staphylococci were of particular interest in this initial in vitro investigation. WIN 49375 is a promising new antibacterial agent with a broad spectrum of in vitro activity which warrants in vivo investigation.

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