ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 1990, p. 1609–1610
0066-4804/90/081609-02$02.00/0

Vol. 34, No. 8

In Vitro Susceptibility of *Xanthomonas (Pseudomonas) maltophilia* to Newer Antimicrobial Agents

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The susceptibilities of 45 clinical and 3 environmental isolates of *Xanthomonas maltophilia* to 14 antimicrobial agents was determined by broth microdilution. The newer quinolones PD117596, PD117558, PD127391, A-56620, amifloxacin, and fleroxacin were the most active agents tested, with 70 to 99% of isolates being susceptible to these agents. All isolates were resistant to trospectomycin. The new aminoglycosides SCH24120 and SCH22591 were active against 12 and 1% of isolates, respectively.

Xanthomonas maltophilia is an important cause of nosocomial infections, especially in immunocompromised patients. Although trimethoprim-sulfamethoxazole remains the drug of choice, a significant number of hospitalized patients are unable to tolerate this combination because of hypersensitivity reactions. Of the currently available antimicrobial agents, moxalactam, ticarcillin-clavulanic acid, cefoperazone, and ciprofloxacin were recently demonstrated to have variable in vitro activity against *X. maltophilia* (N. Khardori, L. Elting, E. Wong, B. Schable, and G. P. Bodey, Rev. Infect. Dis., in press). Because of the limited number of agents active against *X. maltophilia*, the identification of additional drugs which show in vitro activity is of practical importance. We evaluated the activities of 14 new antimicrobial agents against *X. maltophilia* by using the broth microdilution method.

Of a total of 69 isolates, 66 were from patients and 3 were from environmental sources at The University of Texas M. D. Anderson Cancer Center, Houston. The sources included sputum or throat (n = 32), blood (n = 16), wounds (n = 7), central venous catheters (n = 5), urine (n = 6), and environmental (n = 3). The results are reported on a single isolate from each patient (45 total) and on 3 environmental isolates. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were included as controls. All antimicrobial agents were obtained from their manufacturers in the form of standard laboratory powders and were stored at −70°C before use. Antimicrobial susceptibility was determined by a standard broth microdilution method as described by the National Committee for Clinical Laboratory Standards (7). Microtiter plates containing serial dilutions of antimicrobial agents were prepared by using the MIC-2000 system (Dynatech Laboratories, Inc., Alexandria, Va.). The range tested was 0.03 to 64 μg/ml for all agents except trospectomycin, for which the range was 0.15 to 25 μg/ml. The bacterial suspensions were standardized to yield a final inoculum size of 5×10^5 to 1×10^6 CFU/ml. The inoculum size and purity of all isolates were confirmed by plate counts.

The MIC was defined as the lowest concentration of antimicrobial agent that prevent visible growth after 18 to 24 h of incubation at 35°C. After thorough mixing of all the wells that showed no visible turbidity, a 0.01-ml sample was removed and spread on blood agar plates. The MBC was defined as the lowest concentration of antimicrobial agent that killed at least 99.9% of the original inoculum based on colony counts done on the inoculum.

The antimicrobial agents used and results obtained are shown in Table 1. These data were obtained with a single isolate from each patient and three environmental isolates. The newer quinolones, amifloxacin, fleroxacin, A-56620, PD117596, PD117558, and PD127391, were most active, with MICs for 90% of isolates tested of 0.5 to 8 μg/ml. The MICs of ciprofloxacin ranged from 0.5 to 32 μg/ml, and those of temafloxacin ranged from 0.25 to 16 μg/ml. Most of the isolates were resistant to S25930 and S25932. The new aminoglycosides SCH24120 and SCH22591 and the aminocyclitol trospectomycin were active against only 0 to 12% of the isolates.

X. maltophilia is emerging as an important nosocomial pathogen. The organism is isolated from a wide variety of clinical sources, including blood, the respiratory tract, urine, wounds, and spinal fluid, and from environmental sources, such as hospital water supplies, faucets, sinks, drains, and respiratory and disinfectant solutions (11). It is often resistant to antimicrobial agents that are used in the initial therapy of gram-negative bacterial infections, including those active against *P. aeruginosa* (2, 5, 6, 8, 12, 14).

Currently, the antimicrobial agent of choice against *X. maltophilia* is trimethoprim-sulfamethoxazole. Moody and Young (4) reported resistance of *X. maltophilia* to trimethoprim. However, most of their strains were susceptible to the combination of trimethoprim and sulfamethoxazole. The inhibition was largely dependent on susceptibility of this organism to sulfamethoxazole, with instances of minimal potentiation between the two drugs. Gentamicin and tobramycin were reported to be active against 8 and 12% isolates of *X. maltophilia*, respectively (13). Isolates generally appeared to be more resistant to the aminoglycosides when tested by a broth method than when tested by an agar method. Our results using two new aminoglycosides, SCH24120 and SCH22591, and broth microdilution methods are comparable to those obtained with the commercially available aminoglycosides. None of the isolates tested was susceptible to the aminocyclitol, trospectomycin. Other investigators have demonstrated the activity of some of the 4-quinolone agents against *X. maltophilia*, with ciprofloxacin being the most active agent (1, 3, 9, 10). Our results are in

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TABLE 1. In vitro susceptibilities of 48 isolates[a] of *X. maltophilia* to newer antimicrobial agents

Antimicrobial agent	MIC (μg/ml)[b]			MBC (μg/ml)[b]		% Susceptible
	Range	50%	90%	50%	90%	
Quinolones						
Ciprofloxacin	0.5–32	2	8	16	>64	61
Norfloxacin	4–>64	16	64	>64	>64	7
Amifloxacin	1–>64	4	8	64	64	87
A-56620	0.5–64	2	4	16	>64	86
Fleroxacin	1–>64	4	8	16	>64	70
PD117558	0.25–32	1	4	4	16	83
PD117596	0.12–8	0.5	2	1	4	97
PD127391	0.06–8	0.12	0.5	0.5	4	99
S25930	2–>64	8	16	64	>64	12
S25932	8–>64	32	64	>64	>64	1
Temafloxacin	0.25–16	2	4	8	64	64
Aminoglycosides						
SCH24120	1–>64	64	>64	>64	>64	12
SCH22591	0.5–>64	16	64	>64	>64	1
Aminocyclitol: trospectomycin	>256	>256	>256	>256	>256	0

[a] One isolate each from 45 patients and three environmental isolates.
[b] 50% and 90%, MIC or MBC for 50 and 90% of isolates tested, respectively.

agreement with those of previously published reports and extend the observations to the newer quinolone agents.

Our data indicate that some of the newer quinolone agents have greater activity against *X. maltophilia*, with 97 and 99% of isolates being susceptible to PD117596 and PD127391, respectively. In comparison, ciprofloxacin was active against 61% of isolates.

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