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Susceptibilities of *Mycoplasma hominis*, *Mycoplasma pneumoniae*, and *Ureaplasma urealyticum* to a New Quinolone, OPC 17116

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The susceptibilities of human mycoplasmas to OPC 17116 (Otsuka America Pharmaceutical, Inc., Rockville, Md.) and temafloxacin (Abbott Laboratories, Chicago, Ill.) were determined by the agar dilution method and were compared with those to sparfloxacin and ofloxacin. The MICs of OPC 17116 for 90% of *Mycoplasma pneumoniae* (0.25 μg/ml) and *Mycoplasma hominis* (0.125 μg/ml) isolates tested were closely similar to those of sparfloxacin and were four- to eightfold greater than those of ofloxacin. Temafloxacin was two- to fourfold more active than ofloxacin. *Ureaplasma urealyticum* was less susceptible; the MICs of OPC 17116 and temafloxacin for 90% of isolates tested were 2 and 4.0 μg/ml, respectively.

The findings that both respiratory and genitourinary tract bacterial pathogens show increased resistance to common antimicrobial agents (10) have resulted in substantial problems for antimicrobial chemotherapy and have led to a search for new antimicrobial agents. High-level resistance to such highly useful antimicrobial agents as penicillin, tetracyclines, and macrolides is common (10). Because of their lack of a cell wall, mycoplasmas and ureaplasmas are insusceptible to penicillins and other cell wall-specific agents. Although *Mycoplasma pneumoniae* remains susceptible to tetracycline, clinical isolates of both *Mycoplasma hominis* and *Ureaplasma urealyticum* increasingly show high-level resistance to tetracyclines because of the transposable determinant Tet(M) (11, 12). Considerable research has led to the development of newer quinolones that not only are active against gram-negative organisms but also have high levels of activity against gram-positive organisms (1–4, 13).

The purpose of the present study was to determine the susceptibilities of *M. pneumoniae*, *M. hominis*, and *U. urealyticum* to temafloxacin and OPC 17116 and to compare them with those to ofloxacin and sparfloxacin to determine the relative susceptibility rankings of these new quinolones in comparison with those of older quinolones. The agar dilution method was chosen because it gives conservative endpoints that can be consistently repeated (8).

The sources and culturing of clinical isolates and prototypic strains of *M. pneumoniae*, *M. hominis*, and *U. urealyticum* were described previously (6, 9), with the exception that the broth media used for the cultivation of strains were different. *M. pneumoniae* and *M. hominis* were grown in H broth (5) supplemented with 20% horse serum and 10% fresh yeast extract (with 10 mM arginine added for *M. hominis* and 5 mM glucose added for *M. pneumoniae*), whereas *U. urealyticum* was grown in U broth (5) supplemented with 10% fresh yeast extract–5 mM urea–10 mM morpholineethanesulfonic acid (MES)–20% horse serum (pH 6.2 to 6.4). Susceptibility testing was carried out by agar dilution (6, 9) with H agar (5) for *M. hominis* and *M. pneumoniae* and U agar (5) for *U. urealyticum*. The plates were inoculated with three 10-fold dilutions of organisms taken from cultures that were judged to be in the logarithmic phase of growth because they had just begun to show a color change (alkaline [red] for *U. urealyticum* and *M. hominis*, whereas *M. pneumoniae* gave an acid reaction [yellow]). Agar plates were incubated at 37°C in air for *M. pneumoniae* and in 2.5% CO_2 in air for both *U. urealyticum* and *M. hominis*. The endpoint was the least amount of antimicrobial agent that completely prevented the formation of 30 to 300 colonies in 5 days for *M. hominis*, 4 days for *U. urealyticum*, and 12 to 14 days for *M. pneumoniae* (6). The new quinolones tested were temafloxacin (Abbott Laboratories, Chicago, Ill.) and OPC 17116 (Otsuka America Pharmaceutical, Inc., Rockville, Md.). Although temafloxacin has been removed from the market, these data are the only results available by the agar dilution method and are important in determining the relative potencies of quinolones for mycoplasmas. The reference quinolones were ofloxacin (Ortho Pharmaceutical Co., Raritan, N.J.) and sparfloxacin (Parke-Davis, Ann Arbor, Mich.). The quinolones were dissolved in water at 1 mg/ml, but for ofloxacin, a small amount of 10 N NaOH was added to assist in solubilization. Quinolone solutions were filtered through a 0.22-μm-pore-size filter (Millipore Corp., Bedford, Mass.).

M. pneumoniae was as susceptible to OPC 17116 as it was to sparfloxacin (Table 1); the MICs of these two agents for 90% of strains tested (MIC_{90}s) were 0.25 μg/ml. Temafloxacin at 1 μg/ml was fourfold less active than OPC 17116 but was twofold more active than ofloxacin. *M. hominis* was highly susceptible to OPC 17116 and sparfloxacin (MIC_{90}s, 0.125 and 0.062 μg/ml, respectively). Temafloxacin, with an MIC_{90} of 0.25 μg/ml, was twofold more active than ofloxacin for *M. hominis*. In contrast, *U. urealyticum* was less susceptible to OPC 17116 and temafloxacin (MIC_{90}s, 2.0 and 4.0 μg/ml, respectively) than it was to sparfloxacin (MIC_{90}, 0.5 μg/ml). The data for sparfloxacin and ofloxacin were nearly identical to those presented in our previous publications (6, 7, 9), with the exception that the MIC_{50} of ofloxacin for *M. hominis* was twofold lower than that published previously.

A ranking summary of eight newer quinolones by their relative activities gives the same order for their activities against both *M. hominis* and *M. pneumoniae* (Table 2), an order that approximates that known for gram-positive bacteria, as exemplified by *Staphylococcus aureus* (Table 2). The ranking of quinolone activity against ureaplasmas was different. Temafloxacin and OPC 17116 were much less active than sparfloxacin (Table 1) and were no more active

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TABLE 1. Susceptibilities of *M. pneumoniae*, *M. hominis*, and *U. urealyticum* to OPC 17116 and temafloxacin

Organism and drug	MIC (μg/ml)		
	Range	50%	90%
M. pneumoniae (57)[a]			
OPC 17116	0.031–0.5	0.125	0.25
Temafloxacin	0.5–1.0	1.0	1.0
Sparfloxacin	0.062–0.5	0.125	0.25
Ofloxacin	0.5–2.0	1.0	2.0
M. hominis (49)			
OPC 17116	0.031–0.5	0.125	0.125
Temafloxacin	0.125–1.0	0.25	0.25
Sparfloxacin	<0.031–0.125	<0.031	0.062
Ofloxacin	<0.5–0.5	0.5	0.5
U. urealyticum (42)			
OPC 17116	0.5–2.0	1.0	2.0
Temafloxacin	1.0–4.0	2.0	4.0
Sparfloxacin	0.25–1.0	0.5	0.5
Ofloxacin	0.5–4.0	2.0	2.0

[a] Values in parentheses are number of strains tested.

than ofloxacin. Ureaplasmas were as much as 16-fold less susceptible to either temafloxacin or OPC 17116 than were *M. hominis* or *M. pneumoniae*. The MICs of temafloxacin were lower for *M. pneumoniae* (twofold) and *M. hominis* (eightfold) than those reported previously by Waites et al. (14), who used a broth dilution method, but were the same as those that they reported for *U. urealyticum*. Some of these differences may result from the difficulties in controlling inoculum size in the broth dilution test (8), whereas the inoculum is controlled at 30 to 300 CFU in the agar dilution method. The susceptibilities to quinolones of strains of *M. hominis* and *U. urealyticum* which contained Tet(M) were the same as those of tetracycline-susceptible strains.

Overall, the results show that OPC 17116 and temafloxacin are highly active quinolones for mycoplasmas, ranking third and fourth, respectively, in activity against *M. hominis* and *M. pneumoniae* when considering all of the quinolones that we tested (Table 2). However, the two compounds showed relatively poor activity against ureaplasmas, and their MIC_{90}s were the same as those of ofloxacin and were significantly lower than those of sparfloxacin.

TABLE 2. Comparative ranking of eight newer quinolones for activity against mycoplasmas, ureaplasmas, and *S. aureus*

Quinolone	MIC_{90} (μg/ml)			
	M. hominis[a]	*M. pneumoniae*[a]	*U. urealyticum*[a]	*S. aureus*[b]
WIN 57273	0.004	0.125	0.25	0.016
Sparfloxacin	0.062	0.25	0.5	0.125
OPC 17116[a]	**0.125**	**0.25**	**2.0**	0.25
Temafloxacin[a]	**0.25**	**1.0**	**4.0**	0.12
Ciprofloxacin	1.0	2.0	16.0	1.0
Ofloxacin	1.0	2.0	2.0	0.4
Fleroxacin	2.0	4.0	4.0	1.0
Lomefloxacin	2.0	4.0	4.0	2.0

[a] Results in boldface type are from the present study. Data in plain type are from our previous work (6, 7, 9). Quinolones are ranked with respect to their activities against *M. hominis*. Ranking of compounds with the same activity is alphabetical.

[b] Data for *S. aureus* were taken from the literature (1–4, 13).

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