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Susceptibilities of *Mycoplasma pneumoniae*, *Mycoplasma hominis*, and *Ureaplasma urealyticum* to a New Quinolone, Trovafloxacin (CP-99,219)

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The susceptibilities of mycoplasmas to a new quinolone, trovafloxacin (CP-99,219), were compared with those to sparfloxacin and ofloxacin. *Mycoplasma pneumoniae* was as susceptible to trovafloxacin (MIC = 0.25 μg/ml) as to sparfloxacin and fourfold less susceptible to ofloxacin. *Mycoplasma hominis* was highly susceptible to trovafloxacin (MIC = 0.06 μg/ml) and sparfloxacin (MIC = 0.03 μg/ml) and less susceptible to ofloxacin (MIC = 0.5 μg/ml). *Ureaplasma urealyticum* was most susceptible to trovafloxacin, with susceptibilities ranging from 0.06 to 0.5 μg/ml compared with 0.25 to 1.0 μg of sparfloxacin per ml and 1 to 4 μg of ofloxacin per ml.

The susceptibilities of *Mycoplasma pneumoniae* and *Mycoplasma hominis* to quinolones roughly parallel each other and the susceptibilities of gram-positive organisms such as *Staphylococcus aureus* (7). Susceptibilities of *Ureaplasma urealyticum* show less correlation with those of gram-positive bacteria. A new quinolone, trovafloxacin, 7-(3-azabicyclo[3.1.0]hexyl)naphthyridone (3), with known high activity against gram-positive organisms (2, 3) was tested for activity against *M. hominis*, *M. pneumoniae*, and *U. urealyticum* in comparison with ofloxacin and sparfloxacin.

(This work was presented in part at the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, Calif., 17 to 20 September 1995 [8].)

Mycoplasmas were tested by the agar dilution method using a Steers replicator as described previously (6, 9) with recent modifications (7). The inoculum was derived from actively growing cultures in broth medium supplemented with 20% serum and 10% fresh yeast extract as described elsewhere (5). Solid media contained 0.5% agarose. The pH of the agar media was 6.1 to 6.2 for *U. urealyticum* (U agar [5]), 7.1 to 7.2 for *M. pneumoniae* (H agar [5] in 2.5% CO_2 in air), and 7.5 to 7.6 for *M. hominis* (H agar incubated in air). The mycoplasmas included prototypic strains and clinical isolates (7). The *M. hominis* and *U. urealyticum* isolates were collected from 1963 to 1990, and the *M. pneumoniae* isolates were collected from 1963 to 1976. The MIC was the least amount of antimicrobial agent which completely prevented colony formation by an inoculum of 30 to 300 CFU per spot with a 4-day incubation period for *U. urealyticum*, a 5-day incubation for *M. hominis*, and a 14-day incubation for *M. pneumoniae* (6, 9). The new quinolone, trovafloxacin (CP-99,219 [3]), was obtained from Pfizer Inc., Groton, Conn.; ofloxacin was obtained from Ortho Pharmaceutical, Raritan, N.J.; and sparfloxacin was obtained from Parke-Davis, Ann Arbor, Mich. Quinolones were dissolved in water at 1 mg/ml (ofloxacin required a small amount of 0.2 N NaOH) and filtered through an 0.22-μm-pore-size filter (Millipore, Bedford, Mass.).

M. hominis was highly susceptible to trovafloxacin (MIC at which 50% of the strains tested were inhibited [MIC_{50}] = 0.06 μg/ml) (Table 1). Trovafloxacin was eightfold more active than ofloxacin and twofold less active than sparfloxacin. *M. pneumoniae* was fourfold more susceptible to trovafloxacin (MIC_{50} = 0.25 μg/ml) than to ofloxacin and was equally susceptible to sparfloxacin. Trovafloxacin was 2- to 4-fold more active against ureaplasmas (MIC_{50} = 0.125 μg/ml; MIC_{90} = 0.5 μg/ml) than sparfloxacin and 4- to 16-fold more active than ofloxacin. The control MICs of sparfloxacin and ofloxacin for the three organisms were the same as or within one twofold dilution of the results previously published (6, 7, 9). The MICs for strain G-37 (10) of *Mycoplasma genitalium* (0.5 μg of trovafloxacin per ml, 4 μg of ofloxacin per ml, and 0.5 μg of sparfloxacin per ml) were similar to those for *M. pneumoniae*. The pH of the agar had little effect on the susceptibility of *M. pneumoniae*, with MICs at pH 7.16 and 7.6 being the same for trovafloxacin with a small trend for greater activity at pH 7.6 by sparfloxacin and ofloxacin (one twofold dilution or less). Ureaplasmas were tested only at pH 6.2 since they grow poorly on agar at higher pH values. Tetracycline-resistant (because of Tet M) *M. hominis* and *U. urealyticum* strains were equally susceptible to trovafloxacin, sparfloxacin, and ofloxacin as tetracycline-susceptible strains, as noted previously for other quinolones (9). A derivative of *M. hominis* GX-55 selected on agar for resistance to ofloxacin (MIC = 32 μg/ml) showed increased resistance (>16-fold) to both trovafloxacin and sparfloxacin. In contrast, a derivative of GX-55 selected for resistance to streptomycin showed no change in susceptibility to quinolones.

For *M. pneumoniae*, the MICs of trovafloxacin were comparable to those of other recognized high-activity quinolones (7) such as sparfloxacin and grepafloxacin (OPC 17116) and fourfold lower than those of the moderately active quinolones such as ofloxacin and ciprofloxacin. Studies of treatment of Syrian hamsters infected with *M. pneumoniae* show that sparfloxacin (4) was more effective in eliminating both organisms and lesions than ofloxacin was, suggesting that higher in vitro susceptibility predicts better treatment success. A recent review (11) evaluated results for the moderately active quinolones for treatment of genital infections in humans with *M. hominis* and *U. urealyticum*. They concluded that sufficient information was available to support the use of ofloxacin in the treatment of nongonococcal urethritis and pelvic inflammatory disease.

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TABLE 1. Susceptibilities of *M. hominis*, *M. pneumoniae*, and *U. urealyticum* to trovafloxacin, sparfloxacin, and ofloxacin

Organism (no. of strains tested) and antimicrobial agent	MIC (μg/ml)[a]		
	Range	50%	90%
M. hominis (42)			
Trovafloxacin	0.03–0.06	0.06	0.06
Sparfloxacin	0.015–0.03	0.03	0.03
Ofloxacin	0.5–1.0	0.5	1.0
M. pneumoniae (40)			
Trovafloxacin	0.12–0.5	0.25	0.25
Sparfloxacin	0.06–0.5	0.25	0.25
Ofloxacin	0.5–2.0	1.0	1.0
U. urealyticum (46)			
Trovafloxacin	0.06–0.5	0.125	0.5
Sparfloxacin	0.25–1.0	0.5	1.0
Ofloxacin	1.0–4.0	2.0	2.0

[a] 50% and 90%, MIC_{50} and MIC_{90}, respectively.

Similar clinical data for the more active quinolones were not available and are needed.

Overall, trovafloxacin ranked with the best of the quinolones in terms of activity against *M. hominis* and *M. pneumoniae*. Its activity against ureaplasmas was excellent: with an MIC_{50} of 0.125 μg/ml, trovafloxacin was the most active compound recognized in our studies since WIN 57273 (9). The in vitro data indicate that trovafloxacin may have considerable promise for both genital and respiratory infections with mycoplasmas and ureaplasmas, but its clinical utility will depend upon its toxicity and pharmacokinetics (1).

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