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In Vitro Activity of Telithromycin (HMR3647), a New Ketolide, against Clinical Isolates of *Mycoplasma pneumoniae* in Japan

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The in vitro activity of telithromycin (HMR3647), a new ketolide, against *Mycoplasma pneumoniae* was determined by the broth microdilution test using 41 clinical isolates obtained in Japan, as compared with those of five macrolides (erythromycin, clarithromycin, roxithromycin, azithromycin, and josamycin), minocycline, and levofloxacin. Telithromycin was less potent than azithromycin, but it was more active than four other macrolides, minocycline, and levofloxacin; its MICs at which 50 and 90% of the isolates tested were inhibited were both 0.00097 μg/ml, justifying clinical studies to determine its efficacy for treatment of *M. pneumoniae*.

Mycoplasma pneumoniae is the common cause of community-acquired pneumonia; it was detected in 4.9% of patients with community-acquired pneumonia in a recent study in Japan (7). Macrolides and minocycline, a tetracycline, are the agents of first choice in the treatment of *M. pneumoniae* infections, but some strains are resistant to these antibiotics (10). Levofloxacin, a quinolone, is also known to be active against the organism. Antibacterial studies conducted outside Japan have already revealed that telithromycin (HMR3647), a new ketolide antibiotic, is highly effective against gram-positive organisms (e.g., *Streptococcus pneumoniae*), gram-negative organisms (e.g., *Haemophilus influenzae*, *Moraxella catarrharis*, and *Legionella pneumophila*), some enteric pathogens, and anaerobic bacteria (1, 2, 4, 5, 11, 13).

Bacteria, especially their clinical isolates, are known to differ from one country to another, but the efficacy of telithromycin against Japanese clinical isolates of *M. pneumoniae* has not been examined yet. This study was conducted to determine the in vitro activity of the antibiotic against 41 strains of the organism isolated in Japan, compared with those of five macrolides (erythromycin, clarithromycin, roxithromycin, azithromycin, and josamycin), minocycline, and levofloxacin.

Forty-one clinical isolates of *M. pneumoniae* were obtained from Nagasaki University Hospital and its affiliated medical facilities. Three standard strains used as controls were *M. pneumoniae* FH, Mac, and M129, which were kindly supplied by M. F. Barile, Food and Drug Administration, Bethesda, Md.

In vitro antimycoplasmal susceptibility tests have not been standardized; one was performed in this study by the broth microdilution method, which has been recently applied for several potent antibiotics for treatment of *M. pneumoniae* infections (6, 8, 9, 12, 14, 15). *M. pneumoniae* isolates were grown to a concentration of 10^8 CFU/ml in modified Chanock broth medium (3) consisting of 7 parts pleuropneumonia-like organism (PPLO) broth without crystal violet (Difco Laboratories, Detroit, Mich.), 2 parts uninactivated horse serum, and 1 part a mixture of 25% fresh yeast extract, 1% glucose, and 0.002% phenol red adjusted to a pH of 7.8 with 1 N sodium hydroxide. Drug concentrations were as follows: minocycline and levofloxacin, 0.0078 to 8 μg/ml; erythromycin, clarithromycin, roxithromycin, and josamycin, 0.00024 to 0.25 μg/ml; and azithromycin and telithromycin, 0.00003 to 0.031 μg/ml. The isolates were inoculated in microtiter plates containing telithromycin and reference antibiotics at a final concentration of 10^5 CFU/ml in the above broth medium. The inoculum numbers were confirmed by counting colonies grown on Chanock agar. The plates were sealed with a plate sealer and incubated at 37°C under atmospheric conditions for 3 to 6 days. In each case, when the color of the medium of the drug-free control changed from red to yellow, the minimal concentration of drug preventing the color change was defined as the MIC (6).

All plates were examined for prevention of the color change by each antibiotic once daily during the incubation. MIC_{50} and MIC_{90} were defined as the drug concentrations required to inhibit the growth of 50 and 90% of the total number of isolates tested, respectively (6, 8, 9, 12, 14, 15). As a control for potential interactions between antibiotics, medium components, and pH, which could potentially affect the observed MICs, the American Type Culture Collection bacterial reference strain *Staphylococcus aureus* ATCC 29213 was inoculated into microtiter plates containing Chanock broth.

The MIC range, MIC_{50}, and MIC_{90} of each antibiotic against *M. pneumoniae* isolates are shown in Table 1. Telithromycin was less potent than azithromycin, but it was more active than four other macrolides, minocycline, and levofloxacin; its MIC_{50} and MIC_{90} were both 0.00097 μg/ml.

TABLE 1. MICs of antimycoplasmal agents

Antimycoplasmal agent	Range (μg/ml) tested	MIC (μg/ml)		
		Range	50%	90%
Minocycline	0.0078–8	0.062–0.25	0.125	0.25
Erythromycin	0.00024–0.25	0.0019–0.0078	0.0039	0.0078
Clarithromycin	0.00024–0.25	0.00048–0.0039	0.0019	0.0019
Roxithromycin	0.00024–0.25	0.0019–0.0078	0.0039	0.0078
Azithromycin	0.00003–0.031	0.00006–0.00048	0.00024	0.00048
Josamycin	0.00024–0.25	0.0019–0.0313	0.0078	0.0156
Levofloxacin	0.0078–8	0.125–0.5	0.25	0.25
Telithromycin	0.00003–0.031	0.00024–0.0019	0.00097	0.00097

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The excellent in vitro activity of telithromycin against clinical isolates of *M. pneumoniae* justifies further studies to determine its clinical efficacy for treatment of community-acquired infections due to this organism.

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