In Vitro Susceptibilities of Rapidly Growing Mycobacteria to Telithromycin (HMR 3647) and Seven Other Antimicrobials

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The antimicrobial activities of telithromycin (HMR 3647) and seven other antimicrobials against 94 strains of rapidly growing mycobacteria were determined. Telithromycin at a concentration of 1 μg/ml inhibited Mycobacterium peregrinum (100%), Mycobacterium chelonae (80%), Mycobacterium abscessus-Mycobacterium mucogenicum (44.4%), and Mycobacterium fortuitum (2.1%). All or most strains of M. peregrinum, M. fortuitum, and M. mucogenicum were inhibited by 2 μg of quinolones per ml.

Among the rapidly growing mycobacteria (RGM), the members of the Mycobacterium fortuitum complex are the species most often associated with human infections (11). Therapy of these infections is quite different from the treatment of tuberculosis and also from the treatment of disease caused by other, slowly growing mycobacteria (2). There are many differences in the susceptibility of the members of this group of mycobacteria in published studies, and several of them revealed that in vitro the susceptibility correlates with clinical response to therapy (10). Here we report a study of the in vitro susceptibility of these species to some antimicrobials, including newly developed ones.

A total of 94 (Mycobacterium fortuitum [48 strains], Mycobacterium chelonae [25 strains], Mycobacterium mucogenicum [3 strains], Mycobacterium peregrinum [12 strains], and Mycobacterium abscessus [6 strains]) strains of RGM isolated from clinical samples were tested. Prior to testing, strains were subcultured, checked for purity, and reidentified by standard techniques (5).

Telithromycin (HMR 3647), roxithromycin, clarithromycin, azithromycin, levofloxacin, and rifapentine were obtained from Hoechst-Marion-Roussel (Romainville, France); josamycin was obtained from ICN Biomedicals, Inc. (Aurora, Ohio); and ciprofloxacin was obtained from Bayer Corp. (Barcelona, Spain).

The MICs were determined by a broth microdilution technique (7). Mycobacteria were grown on blood agar and incubated at 35°C for 4 days in room air. After that, inoculum was prepared directly from blood agar plates in cation-supplemented Mueller-Hinton broth (Difco, Detroit, Mich.) with 0.02% Tween 80 (Difco). Double dilutions of antibiotics were prepared and added to the wells ranging from 64 to 0.03 μg/ml. The final volume was 0.1 ml. The medium used was cation-supplemented Mueller-Hinton broth without Tween 80. Plates were inoculated with a volume of 10 μl for a final concentration of 10^6 CFU/well; incubated at 35°C in room air; and read at 2, 3, and 4 days.

Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 29213, and Pseudomonas aeruginosa ATCC 27853 were used as controls. Type strains of M. fortuitum (ATCC 6841), M. chelonae (ATCC 35752), M. mucogenicum (ATCC 49650), M. peregrinum (ATCC 14467), and M. abscessus (ATCC 19977) were also studied.

Table 1 shows the MICs of the eight antimicrobials tested against five species of RGM. The better in vitro activity of the ketolide telithromycin was against M. peregrinum, M. chelonae, and M. abscessus-M. mucogenicum. Telithromycin is a new compound of this group of antimicrobials that has shown a good activity against some gram-positive microorganisms (6), but to our knowledge, there is no data about the activity of ketolides against RGM. In our study, the activity of telithromycin was in consonance with the activity of other macrolides. Except for M. fortuitum strains, telithromycin showed low MICs against a high percentage of isolates of the other species tested. By weight, it was more active than josamycin but slightly less active than clarithromycin, roxithromycin, and azithromycin.

In the macrolide group of antibiotics, clarithromycin was the most active in vitro compound, antimicrobial activities from the more to the less active compounds ranging from those of roxithromycin and azithromycin to that of josamycin, a finding which agrees with the previous publication by Brown et al. (1). These compounds were not very active in vitro against M. fortuitum strains; however, more than 75% of M. chelonae isolates were inhibited by a concentration lower than 2 μg/ml, and they yielded a good in vitro activity against isolates of M. peregrinum, M. abscessus, and M. mucogenicum.

The in vitro activity of rifapentine against RGM was very poor, and for only three isolates (one each of the following species: M. peregrinum, M. chelonae, and M. fortuitum) were there low MICs. To our knowledge, there is no published data dealing with the activity of rifapentine against RGM, but it is well known that the in vitro activity of rifampin, a related compound, against M. fortuitum complex is also very poor (4).

Levofloxacin and ciprofloxacin had the lowest MICs against M. peregrinum (MIC at which 90% of the isolates tested are inhibited [MIC90], 0.12 μg/ml) and M. fortuitum (MIC90, 0.25 μg/ml). Levofloxacin was slightly more active in vitro against M. mucogenicum than was ciprofloxacin (MIC90, 1 and 2 μg/ml, respectively), and both quinolones were not very active in vitro against M. chelonae (MIC90, 16 μg/ml). Our data shows a good activity of quinolones against M. fortuitum but a poor activity of these compounds against M. chelonae, a finding also previously reported (3, 12). These compounds also showed lower MICs against M. mucogenicum and M. peregrinum, but against M.
abscessus, their activity was very slight, this data being similar to that previously reported in the literature (8, 9).

Although the MICs were read at 48, 72, and 96 h, we present data from 72 h for \textit{M. fortuitum} and from 96 h for the other species tested. Before this time, the MICs were not clearly read, and for \textit{M. fortuitum} strains, there was no change in the MICs with a longer incubation.

The susceptibility of RGM varies widely. Some of the infections produced by these organisms could be treated with some oral antimicrobials, but our results show that any isolates of these species produced by these organisms could be treated with some oral antimicrobials, but our results show that any isolates of these species could be treated with some oral antimicrobials. The susceptibility patterns of sporadic isolates of the \textit{Mycobacterium chelonae}-like organism. J. Clin. Microbiol. 31:1231–1239.


### TABLE 1. In vitro activities of telithromycin and seven other antimicrobial agents against RGM

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>\textit{M. abscessus} (n = 6)</th>
<th>\textit{M. chelonae} (n = 25)</th>
<th>\textit{M. mucogenicum} (n = 3)</th>
<th>\textit{M. fortuitum} (n = 48)</th>
<th>\textit{M. peregrinum} (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>MIC&lt;sub&gt;90&lt;/sub&gt;</td>
<td>Range</td>
<td>MIC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>MIC&lt;sub&gt;90&lt;/sub&gt;</td>
</tr>
<tr>
<td>Telithromycin</td>
<td>0.12–64</td>
<td>0.25</td>
<td>4</td>
<td>0.03–32</td>
<td>0.03–2</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>0.06–64</td>
<td>0.12</td>
<td>0.5</td>
<td>0.03–1</td>
<td>0.03–0.12</td>
</tr>
<tr>
<td>Roxithromycin</td>
<td>0.25–64</td>
<td>0.25</td>
<td>2</td>
<td>0.12–16</td>
<td>0.03–0.5</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.5–64</td>
<td>0.5</td>
<td>2</td>
<td>0.25–4</td>
<td>0.12–1</td>
</tr>
<tr>
<td>Josamycin</td>
<td>8–64</td>
<td>8</td>
<td>&gt;64</td>
<td>2–&gt;64</td>
<td>1–2</td>
</tr>
<tr>
<td>Rifampentine</td>
<td>2–64</td>
<td>4</td>
<td>16</td>
<td>0.25–64</td>
<td>0.12–1</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1–64</td>
<td>2</td>
<td>16</td>
<td>0.25–64</td>
<td>0.12–2</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>16–64</td>
<td>32</td>
<td>64</td>
<td>0.25–&gt;64</td>
<td>2–32</td>
</tr>
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</table>

REFERENCES