In vitro activity of telithromycin (HMR 3647) against 502 strains of anaerobic bacteria

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Introduction

This report describes the activity of telithromycin (HMR 3647) against 502 strains of anaerobic bacteria, extending a previous study comparing the activity of HMR 3004 against these organisms. All bacteria tested in this study were randomly selected recent clinical isolates from the Wadsworth Anaerobic Bacteriology Laboratory, VA Greater Los Angeles Healthcare System in West Los Angeles. Bacteria were identified according to established procedures. MICs were determined by the NCCLS-approved Wadsworth agar dilution technique using an inoculum of 10^5 cfu/spot, and Brucella base-laked blood agar. Plates were incubated in an anaerobic chamber (Anaerobe Systems, San Jose, CA, USA) for 48 h at 37°C. MICs were determined by the NCCLS-approved Wadsworth agar dilution technique using an inoculum of 10^5 cfu/spot, and Brucella base-laked blood agar. Plates were incubated in an anaerobic chamber (Anaerobe Systems, San Jose, CA, USA) for 48 h at 37°C. MICs were determined as the lowest concentration of antimicrobial resulting in a marked change in the appearance of growth as compared with the control plate, as described in the NCCLS protocol. Reference strains of Bacteroides fragilis (ATCC 25285) and Bacteroides thetaiotaomicron (ATCC 29741) were used as controls in each test. Telithromycin was obtained from Hoechst-Marion-Roussel R&D (Romainville, France).

Results of this study are listed in Table I. For the comparative values of the agents tested the reader is referred to a previously published report. Results are listed as percent susceptible, intermediate and resistant using a breakpoint of 4 mg/L for inclusion in the intermediate category. Both B. fragilis and other B. fragilis group species were very resistant to telithromycin (5% and 10% inhibited, respectively, at 4 mg/L). As reported previously, of the macrolides tested, clarithromycin was the most active against the B. fragilis group (84% of B. fragilis and 71% of other B. fragilis group species, respectively, inhibited at 4 mg/L); azithromycin, erythromycin and roxithromycin were considerably less effective, inhibiting 5–29% of other B. fragilis group species.

Telithromycin inhibited 92% of other Bacteroides spp. Telithromycin was very active against Campylobacter gracilis (formerly Bacteroides gracilis), an organism that may be involved in severe, deep-seated infections, only one of 13 strains had an MIC of 8 mg/L (this strain was also resistant to the other macrolides tested previously). Bilophila wadsworthia was the third most common anaerobe isolated in cases of perforated or gangrenous appendicitis. Telithromycin had good activity against B. wadsworthia (85% inhibited at 4 mg/L) in contrast to the other macrolides reported previously, except for HMR 3004, which had similar activity to telithromycin. The other macrolides inhibited 4–33% of strains of B. wadsworthia.

Porphyromonas spp. were completely inhibited by...
Telithromycin was active against a Gram-negative anaerobe found in 81–93% of these strains at 2 mg/L. Telithromycin was somewhat active against *Prevotella nigrescens* at 2 mg/L; azithromycin, clarithromycin, erythromycin and roxithromycin, tested previously, were active against 66–83% of strains at 4 mg/L. Telithromycin inhibited approximately 90% of non-spore-forming Gram-positive bacilli at 2 mg/L. The macrolides tested previously had very similar activity against these strains.

It should be noted that testing methods, especially the inclusion of CO_{2} in the atmosphere, can vary affect the activity of some macrolides because of a pH effect. Goldstein et al. tested telithromycin and other ketolide and macrolide compounds against organisms involved in bite wound infections by the standard NCCLS approved agar disk method; however, this method is not approved for use with ketolides.

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC (mg/L)</th>
<th>%S</th>
<th>%I</th>
<th>%R</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>F. nucleatum</em></td>
<td>0.12–64</td>
<td>8</td>
<td>&gt;64</td>
<td>5</td>
</tr>
<tr>
<td>Other <em>F. nucleatum</em></td>
<td>0.25–&gt;64</td>
<td>4</td>
<td>&gt;64</td>
<td>40</td>
</tr>
<tr>
<td>Telithromycin</td>
<td></td>
<td>3%</td>
<td></td>
<td>97</td>
</tr>
</tbody>
</table>


*Includes* *Bacteroides ureolyticus* (1), *Bacteroides splanchicus* (7).

*Includes* *Porphyromonas asaccharolyticus* (4), *Porphyromonas gingivalis* (7) and *Porphyromonas spp.* (1).


*Includes* *Fusobacterium necrophorum* (3), *Fusobacterium necrogenes* (1) and *Fusobacterium spp.* (7).

*Includes* *Clostridium cadaveris* (1), *Clostridium innocuum* (5), *Clostridium spp.* (4) and *Clostridium sporogenes* (2).

*Includes* *Peptostreptococcus anaerobius* (6), *Peptostreptococcus asaccharolyticus* (7), *Peptostreptococcus magnus* (6), *Peptostreptococcus micros* (12), *Peptostreptococcus prevotii* (1), *Peptostreptococcus tetradius* (1) and *Peptostreptococcus spp.* (2).

Telithromycin against anaerobic bacteria
dilution method (as was done in this study). They found that telithromycin was active against *Bacteroides tectus, Bacteroides forsythus, Peptostreptococcus, Prevotella* and *Porphyromonas* spp. Five of 20 strains of *Fusobacterium* were resistant. In our study, telithromycin was also active against *Porphyromonas*, *Prevotella* (98%) and *Peptostreptococcus* spp. Ednie et al. tested 352 strains of anaerobes using Oxyrase and aerobic incubation for those strains not requiring CO2 and pH adjustment to a final pH of 7.1–7.2 and anaerobic incubation for those strains requiring CO2. The MIC ranges (approximately 0.5–64 mg/L) for the *B. fragilis* group were similar to those seen in our study (2–64 mg/L) as was the MIC50 (>64 mg/L), although the MIC50 (8 mg/L) was lower than ours (32 mg/L). Overall MIC50s and MIC90s were lower than found in this study.

Edlund and co-workers studied 342 clinical isolates of anaerobic bacteria by the agar dilution method and found the following ranges: anaerobic cocci, 0.016–0.125 mg/L; *C. difficile*, 0.125–256 mg/L; *B. fragilis*, 0.032–16 mg/L; *Bacteroides* and *Prevotella* spp., 0.016–4.0 mg/L; and *F. nucleatum*, 0.016–8.0 mg/L.

In summary, telithromycin showed good activity against certain groups of anaerobes. Further study into the clinical utility of this agent for specific infections involving certain anaerobes merits investigation.

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References

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