Antimicrobial Characterization of CEM-101: Potential Application Against Species Causing Enteritis/Gastroenteritis

**RN JONES, HS SADER, TR FRITSCHE, DJ BIEDENBACH, M CASTANHEIRA**
JMI Laboratories, North Liberty, Iowa

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JMI Laboratories
North Liberty, IA, USA
319.665.3372, fax 319.665.3371
vonnah@jmi.com

**ABSTRACT**

Background: MLSL-resistant helicobacteria has been considered for targeting gastric enteritis disease pathogens (GDPs) such as *H. pylori* (HP) strains, and diarrheal illness associated with Campylobacter jejuni (CJ), Salmonella spp. (SAL), and Shigella spp. (SHG). CEM-101, a novel macrolide/ketolide, was tested against contemporary GDIs in broth and reported here.

Methods: SAL (20 strains, representing 11 serotypes) and SHG (40 strains) were tested by CLSI broth microdilution and Etest (AB BIODISK, Solna, Sweden). CJ (20 strains, HP [23] strains) were tested by Mueller-Hinton agar dilution method, supplemented with sheep blood, and CJ results were confirmed by Etest (AB BIODISK, Solna, Sweden). Helicobacter pylori AGA agents were tested against clarithromycin (CLA), clindamycin (CLA), levofloxacin (LEV), amoxicillin/clavulante (AC) and trimethoprim/sulfamethoxazole (TMSMX).

Results: CEM-101 demonstrated activity against food-borne GDIs, SAL (MIC range <0.06-256 μg/ml), SHG (MIC range, 0.06-256 μg/ml) and CJ (MIC range, 0.03%<256 μg/ml). This work was more comparable to clarithromycin (MIC90, 0.12 μg/ml). Testing the Enterobacteriaceae, CEM-101 MIC results for the clarithromycin-resistant (>16 μg/ml) strains were 2 or 4 μg/ml. Table 2 shows the CEM-101 MIC distributions for all tested strains (four species). CEM-101 MIC results for the HP were lowest (0.02-0.03 μg/ml), while MICs for the Enterobacteriaceae could range up to ≥16 μg/ml.

**RESULTS**

Conclusions: CEM-101 exhibited activity against GPD strains that are other macrolide/ketolide that have been applied for treatment (CLAS, LA), and this novel compound (CEM-101) should be studied alone in or combined with the clinical situation, especially versus CLA-Gastric disease.

**MATERIALS AND METHODS**

Susceptibility testing methods. For *C. jejuni*, *H. pylori* and *SHG*, CLSI-M100-A7 (2006) and M100-S2 (2010) agar dilution methods were used as follows:

- Mueller-Hinton (MH) agar with 5% sheep blood for *C. jejuni* and Campylobacter spp.
- MH broth
- Endotoxin read at 24 h (CJ) and 72 h (HP, CEM-101)
- Applied irradiation enrichment for appropriate species (e.g., *B. staphylococci*, etc.)

96-well-trimmed, waxed panels were also used, produced by JMI Laboratories and consisted of calcium-adjusted MH broth for testing the Enterobacteriaceae. Comparator agents were tested by Etest using manufacturer's package insert directions (AB BIODISK).

**CONCLUSIONS**

- CEM-101 was tested by the reference agar dilution method versus 20 strains of *C. jejuni* and compared to four other agents tested by the Elast procedure. The CEM-101 MIC90 (4 μg/ml) was equal to those of clarithromycin and erythromycin, and it was active against fluoroquinole-resistant isolates. **Table 1** summarizes CEM-101 activity against *H. pylori*. Eight strains were compared by testing five drugs, including CEM-101. Results showed that CEM-101 was slightly less active than clarithromycin or amoxicillin (MIC50, 0.015 μg/ml); however the comparator activity measurements were Elast results, not for the reference agar dilution method. In vitro data for clarithromycin (data not shown) exhibited a trend toward lower Elast results. CEM-101 MICs for the clarithromycin-resistant (>16 μg/ml) strains were ≤2 or 4 μg/ml. CEM-101 inhibited Gram-negative species associated with CA-RTI (e.g., *influenzae* [MIC50, ≤0.015 μg/ml], *lac него*, *penumococci* [MIC50, ≤0.015 μg/ml], and *methicillin-resistant S. aureus* (MIC50, 0.12 μg/ml); and in this report, *HP* (MIC50, 0.06 μg/ml), and various other gastrointestinal disease pathogens. **Table 2** demonstrates a comparison of CEM-101 against clarithromycin. In clinical studies should be considered for these pathogens, perhaps PK/PD findings in human subjects.

**REFERENCES**


