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Susceptibility of *Campylobacter pyloridis* to Three Macrolide Antibiotics (Erythromycin, Roxithromycin [RU 28965], and CP 62,993) and Rifampin

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The presence of *Campylobacter pyloridis* in the gastric mucosa was recently linked to peptic ulcer disease. This study compared the inhibitory activity of three macrolide compounds (erythromycin, roxithromycin [RU 28965], and CP 62,993) and rifampin against 10 clinical isolates of *C. pyloridis*. The macrolides were equally effective against the test strains, with MICs ranging from 0.06 to 0.5 μg/ml; rifampin was less active, with MICs ranging from 0.25 to >1 μg/ml. Erythromycin and the two new macrolide derivatives are potentially useful agents in the treatment of infections caused by *C. pyloridis*.

Warren and Marshall were the first to isolate *Campylobacter pyloridis* from the gastrointestinal mucosa of patients with peptic ulcer disease, a phenomenon that has been confirmed by other investigators (7, 9, 11–13). Attention has subsequently focused on the susceptibility of *C. pyloridis* isolates to antimicrobial agents. Flores et al. determined the susceptibility to 20 antimicrobial agents of 50 isolates of *Campylobacter* species recovered from the gastrointestinal tracts of male homosexuals (2). Although half of the isolates were susceptible to less than 0.06 μg of erythromycin per ml, drug concentrations exceeding 128 μg/ml were required to inhibit 90% of the isolates. Rifampin was the most active of the drugs tested. McNulty and colleagues determined the susceptibility of 70 *C. pyloridis* isolates to 11 antimicrobial agents (8). Of the isolates, 90% were inhibited by 0.12 μg of erythromycin per ml, and all of the strains were inhibited by 0.5 μg/ml. Kasper and Dickgiesser noted similar results (6).

Roxithromycin (RU 28965) and CP 62,993 are two new macrolide derivatives. Preliminary studies demonstrated comparable in vitro activity between roxithromycin and erythromycin against *Campylobacter* species (1). Goossens et al. reported that erythromycin was significantly more active than roxithromycin against *Campylobacter jejuni* and *Campylobacter coli* (4). There are no available data on the activity of CP 62,993 against *Campylobacter* species. The purpose of the present study was to compare the activities of the three macrolides (erythromycin, roxithromycin, and CP 62,993) and rifampin against 10 clinical isolates of *C. pyloridis*.

Fresh gastric mucosal biopsy material obtained at gastroscopy from pediatric and adult patients with gastritis was plated onto Columbia agar containing 5% sheep blood and incubated at 37°C under microaerophilic conditions (Gas Generating Kit; Oxoid Ltd., London, England) for 4 days. Two isolates were kindly provided by M. A. Karmali, Hospital for Sick Children, Toronto, Ontario, Canada. All isolates were identified as *C. pyloridis* based on colony morphology, Gram stain, and the production of urease, catalase, and oxidase (3, 5, 7, 10). Reference strains of *Staphylococcus aureus* (ATCC 25923 and ATCC 29213) and *Streptococcus faecalis* (ATCC 29212) were used as controls.

Susceptibility determinations were performed in Mueller-Hinton agar supplemented with 7% sheep blood and containing erythromycin, roxithromycin (Hoechst-Roussel Pharmaceuticals Inc., Somerville, N.J.), or CP 62,993 (Pfizer Central Research, Groton, Conn.) in twofold dilutions ranging from 0.03 to 1 μg/ml. The test strains were inoculated onto Columbia agar containing 5% sheep blood, incubated under microaerophilic conditions, and recovered in saline. The agar plates were inoculated with a Steers replicator and a final inoculum of 2×10^6 to 5×10^7 CFU per spot and incubated at 37°C microaerophilically for 3 days. The MIC was defined as the lowest concentration of drug which totally inhibited growth.

The susceptibilities of the 10 test strains are shown in Table 1. The three macrolide derivatives were equally effective against all of the isolates. In most cases, the MICs of

TABLE 1. Susceptibility of *C. pyloridis* to erythromycin, roxithromycin, CP 62,993, and rifampin

Control organism or isolate no.	MIC (μg/ml)			
	Erythromycin	Roxithromycin	CP 62,993	Rifampin
S. aureus				
ATCC 25923	0.5	1	1	<0.06
ATCC 29213	0.5	1	0.5	<0.06
S. faecalis ATCC 29212	1	>1	>1	0.5
Pediatric isolates				
1	0.25	0.25	0.25	1
2	0.12	0.25	0.25	1
3	0.12	0.25	0.5	0.25
4	0.25	0.25	0.25	0.5
5	0.12	0.25	0.25	>1
Adult isolates				
1	0.06	0.25	0.25	1
2	0.06	0.25	0.25	1
3	0.06	0.25	0.12	1
Canadian isolates				
568	0.12	0.25	0.12	1
571	0.12	0.12	0.25	0.25

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rifampin were significantly higher than those of the macrolide derivatives.

In vitro, erythromycin, roxithromycin, and CP 62,993 had significant activities against *C. pyloridis* isolates, suggesting a use for the macrolide antibiotics in the treatment of gastrointestinal infections caused by this organism. The susceptibilities of the isolates to rifampin were less consistent. Because *C. pyloridis* infections typically localize to the mucosa of the upper gastrointestinal tract, the successful treatment of these infections depends on the development of effective mucosal drug concentrations (5, 11). Such studies are recommended before the initiation of clinical trials.

LITERATURE CITED

1. **Barlam, T., and H. C. Neu.** 1984. In vitro comparison of the activity of RU 28965, a new macrolide, with that of erythromycin against aerobic and anaerobic bacteria. Antimicrob. Agents Chemother. **25**:529–531.
2. **Flores, B. M., C. L. Fennell, K. K. Holmes, and W. E. Stamm.** 1985. In vitro susceptibilities of *Campylobacter*-like organisms to twenty antimicrobial agents. Antimicrob. Agents Chemother. **28**:188–191.
3. **Fricker, C. R., and R. W. A. Park.** 1985. Urease positive campylobacters. Lancet **i**:394.
4. **Goossens, H., P. De Mol, H. Coignau, J. Levy, O. Grados, G. Ghysels, H. Innocent, and J.-P. Butzler.** 1985. Comparative in vitro activities of aztreonam, ciprofloxain, norfloxacin, ofloxacin, HR 810 (a new cephalosporin), RU28965 (a new macrolide), and other agents against enteropathogens. Antimicrob. Agents Chemother. **27**:388–392.
5. **Jones, D. M., A. M. Lessels, and J. Eldridge.** 1984. Campylobacter-like organisms on the gastric mucosa: culture, histological and serological studies. J. Clin. Pathol. **37**:1002–1006.
6. **Kasper, G., and N. Dickgeisser.** 1985. Antibiotic sensitivity of "Campylobacter pylori." Eur. J. Clin. Microbiol. **3**:444.
7. **Marshall, B. J., and J. R. Warren.** 1984. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet **i**:1311–1314.
8. **McNulty, C. A. M., J. Dent, and R. Wise.** 1985. Susceptibility of clinical isolates of *Campylobacter pyloridis* to 11 antimicrobial agents. Antimicrob. Agents Chemother. **28**:837–838.
9. **McNulty, C. A. M., and D. M. Watson.** 1984. Spiral bacteria of the gastric antrum. Lancet **i**:1068–1069.
10. **Megraud, F., F. Bonnet, M. Garnier, and H. Lamouliatte.** 1985. Characterization of "*Campylobacter pyloridis*" by culture, enzymatic profile, and protein content. J. Clin. Microbiol. **22**:1007–1010.
11. **Price, A. B., J. Levi, J. M. Dolby, P. L. Dunscombe, A. Smith, J. Clark, and M. L. Stephenson.** 1985. *Campylobacter pyloridis* in peptic ulcer disease: microbiology, pathology, and scanning electron microscopy. Gut **26**:1183–1188.
12. **Rollason, P., J. Stone, and J. M. Rhodes.** 1984. Spiral organisms in endoscopic biopsies of the human stomach. J. Clin. Pathol. **37**:23–26.
13. **Warren, J. R., and B. J. Marshall.** 1983. Unidentified curved bacilli on gastric epithelium in chronic gastritis. Lancet **i**:1273–1275.