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In Vitro Activities of New Oral β-Lactams and Macrolides against *Campylobacter pylori*

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The in vitro activities of amoxicillin, cefuroxime, ceftetrame, cefetamet, cefixime, tigemonam, erythromycin, roxithromycin, and dirithromycin against 30 clinical isolates of *Campylobacter pylori* were determined by an agar dilution technique. Roxithromycin and amoxicillin (MICs for 90% of isolates tested, 0.01 and 0.06 μg/ml, respectively) were the most active antibiotics tested, but all strains were susceptible to all antimicrobial agents tested.

Since Marshall and Warren detected and isolated *Campylobacter pylori* from gastric mucosa (9, 17), the role of this bacterium in the pathogenesis of gastroduodenal lesions has been controversial (7, 15).

It has been suggested that *C. pylori* colonization is secondary to damage of the gastroduodenal mucosa by other factors (W. L. Peterson, E. L. Lee, and M. Feldman, Gastroenterology **90**:1585, 1986), but several studies indicated a close association between both chronic gastritis and peptic ulcer and *C. pylori* (1, 4, 16). Clearance of microorganisms with amoxicillin or bismuth salts that leads to resolution of gastritis has been demonstrated (8; M. L. Langenberg, E. A. J. Rauws, M. E. I. Schipper, A. Widjojokosumo, G. N. J. Tytgat, P. J. G. M. Rietra, and H. C. Zanen, Proc. 3rd Int. Workshop Campylobacter Infections, p. 162–163, 1985), and the relapse rate of duodenal ulcers is much higher when eradication of *C. pylori* is not achieved.

In other in vitro studies, *C. pylori* was highly susceptible to β-lactams and macrolides (2, 3), which suggests in vivo efficacy. In this study, we report the in vitro susceptibilities of *C. pylori* to two new macrolides (dirithromycin and roxithromycin) and five oral β-lactams (cefuroxime, cefetamet, ceftetrame, cefixime, and tigemonam).

Thirty strains of *C. pylori* isolated from gastric biopsies and identified by accepted criteria (Gram stain and oxidase, catalase, and urease tests) were studied. Antibiotics were obtained as standard powders from Beecham Research Laboratories (amoxicillin), Glaxo Pharmaceuticals, Ltd. (cefuroxime), Roche (ceftetrame and cefetamet), Fujisawa Ltd. (cefixime), E. R. Squibb & Sons (tigemonam), Roussel (erythromycin and roxithromycin), and Eli Lilly & Co. (dirithromycin).

MICs were determined by the agar dilution method (National Committee for Clinical Laboratory Standards, 1985) by using Mueller-Hinton agar (Oxoid Ltd., Basingstoke, United Kingdom) supplemented with 7% sheep blood and containing antibiotics in concentrations ranging from 0.008 to 128 μg/ml. The inoculum was prepared in brain heart infusion broth with 10% horse serum and 0.25% yeast extract (5) from a 72-h culture in blood agar plates. The original inoculum was incubated for 15 h at 37°C in an atmosphere of 5% O_2, 10% CO_2, and 85% N_2 (GasPak; BBL Microbiology Systems, Cockeysville, Md.); adjusted to a McFarland no. 1 standard equivalent to approximately 5×10^8 CFU/ml; and applied to the plates with a Steers replicator capable of delivering 1-μl samples (5×10^5 CFU per spot). The plates were incubated at 37°C under microaerophilic conditions for 48 h.

Reference strains of *Staphylococcus aureus* (ATCC 25923) and *Escherichia coli* (ATCC 25922) were used as controls.

The range of MICs and the MICs for 50 and 90% of isolates tested are shown in Table 1. On the whole, the activities of β-lactams and macrolides were similar. Roxithromycin and amoxicillin were the most active antibiotics tested. No strain was resistant to any antibiotic tested.

Our results on the in vitro activities of macrolides (6) and β-lactams (10) are in agreement with results previously reported. *C. pylori* was susceptible to all macrolides and β-lactams tested.

Older macrolides, such as erythromycin ethylsuccinate, josamycin, and spiramycin, have been shown to be ineffective in clearing *C. pylori* from the gastric mucosa in clinical trials (12; H. Lamouliatte, F. Megraud, A. Mascarel, and A. Quinton, Proc. 4th Campylobacter Workshop, abstr. no. 190, p. 388–389, 1987), probably because of acid instability. Newer macrolides whose chemical modifications confer greater acid stability might have a higher correlation between in vitro and in vivo activities.

The β-lactams showed good activity. Cefetamet, ceftetrame, tigemonam, and cefixime, whose activities against *C. pylori* had not been tested until now, showed good activities against other gram-negative bacteria in previous studies (1a, 13, 14). These antibiotics had MICs under the break point for all strains of *C. pylori* tested. These β-lactams achieve high levels in blood and tissue after oral administration. On the other hand, McNulty et al. (11) recently demonstrated that β-lactams attain high concentrations in gastric mucosa, higher than those of macrolides and quinolones, although all the agents tested (amoxicillin, ampicillin, ciprofloxacin, and erythromycin) attained concentrations higher than the MICs for *C. pylori*. These facts, together with the high intrinsic activities of these new β-lactams, make them promising antibiotics against *C. pylori*. Despite the in vivo ineffectiveness of erythromycin, the acid stability and more favorable

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TABLE 1. In vitro activities of new β-lactams and macrolides against *C. pylori*

Antibiotic	MIC (μg/ml)[a]		
	50%	90%	Range
Amoxicillin	<0.008	0.06	<0.008–0.06
Cefuroxime	0.125	0.25	0.01–0.25
Cefetamet	2	4	1–8
Ceftetrame	0.5	2	0.03–2
Cefixime	0.06	0.25	0.008–0.25
Tigemonam	0.25	0.5	0.01–0.5
Erythromycin	0.01	0.03	0.01–0.125
Dirithromycin	0.25	0.25	0.125–0.5
Roxithromycin	<0.008	0.01	<0.008–0.03

[a] 50% and 90%, MIC for 50 and 90% of isolates tested, respectively.

pharmacokinetics of new macrolides might enhance their usefulness.

Clinical trials are obviously necessary to determine the true efficacy of these compounds for the treatment of *C. pylori*-related gastric diseases.

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