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# Comparative Activity of Ciprofloxacin Against Anaerobic Bacteria

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**The in vitro activity of ciprofloxacin was assessed against 362 strains of anaerobic bacteria and compared with that of cefoxitin, clindamycin, metronidazole, and mezlocillin. Only 31% of the strains tested were susceptible to ciprofloxacin. The other agents were active against most of the strains tested.**

Ciprofloxacin (Bay o 9867), a new quinolone carboxylic acid compound, was tested for its in vitro activity against anaerobic bacteria in a comparative trial with cefoxitin, clindamycin, metronidazole, and mezlocillin. A total of 362 recent clinical isolates from the Wadsworth Anaerobic Bacteriology Laboratory were used in this study. The bacteria tested and numbers of isolates were as follows: *Bacteroides distasonis*, 15; *Bacteroides fragilis*, 57; *Bacteroides vulgatus*, 15; *Bacteroides ovatus*, 5; *Bacteroides thetaiotamicron*, 24; *Bacteroides uniformis*, 5; *B. fragilis* group (unidentified), 1; *Bacteroides bivius*, 4; *Bacteroides disiens*, 3; *Bacteroides melaninoganicus-Bacteroides intermedius* group, 14; *Bacteroides asaccharolyticus*, 9; *Bacteroides splanchnicus*, 3; *Bacteroides ureolyticus*, 2; *Bacteroides oralis*, 4; *Bacteroides veroralis*, 1; *Bacteroides oris-Bacteroides buccae* group, 5; *Bacteroides* spp., 6; *Fusobacterium necrophorum*, 2; *Fusobacterium nucleatum*, 13; *Fusobacterium* spp., 2; *Veillonella* spp., 3; *Peptostreptococcus* spp., 83; *Actinomyces* spp., 13; *Eubacterium* spp., 14; *Propionibacterium* spp., 5; *Lactobacillus* spp., 3; *Clostridium difficile*, 26; *Clostridium butyricum*, 1; *Clostridium cadaveris*, 1; *Clostridium clostriidiforme*, 3; *Clostridium innocuum*, 2; *Clostridium paraputrificum*, 3; *Clostridium perfringens*, 12; and *Clostridium ramosum*, 2.

MICs were determined by the tentative reference agar dilution procedure (4) with Wilkins-Chalgren agar. Laked sheep blood (5%) was added for the growth of *Bacteroides* spp. other than the *B. fragilis* group, *Fusobacterium* spp., anaerobic cocci, and the non-spore-forming gram-positive bacilli. The control strains, *B. fragilis* (ATCC 25285) and *B. thetaiotaomicron* (ATCC 29741), were included each time tests were run.

Table 1 gives the MICs at which 50% and 90% of the strains were inhibited by each of the antimicrobial agents. The three strains of *Veillonella* spp. were within the susceptible range for all antimicrobial agents tested. Tentative breakpoints for systemic therapy with ciprofloxacin are ≤1.0 μg/ml for susceptible isolates and >2.0 μg/ml for resistant isolates. Using these breakpoints only 31% of the strains tested were susceptible and 58% were resistant. All of the *C. difficile* and the *B. fragilis* group strains were resistant. Results with *C. difficile* are in agreement with those of Goodman and others (3), but the MICs obtained for the *B. fragilis* group are somewhat higher than those obtained by van Caekenberghe and Pattyn (7) and Wise and co-workers (8) and appreciably higher than those obtained by Chin and Neu (2) and Borobio and Perea (1). Variables such as medium, addition of blood, and inoculum density may be responsible for these differences, or there may be differences in the susceptibilities of the strains tested. van Caekenberghe and Pattyn and Chin and Neu used Mueller-Hinton agar, but van Caekenberghe and Pattyn added human blood and used an inoculum of $10^4$ organisms, whereas Chin and Neu added hemin and used an inoculum of $10^5$ organisms. The ranges of MICs obtained by each group were 4 to 32 and ≤0.01 to 0.8 μg/ml, respectively. Wise and co-workers used Iso-SensiTest agar (Oxoid) with lysed human blood and an inoculum of $10^4$ and obtained an MIC range of 2 to 16 μg/ml. They also observed that increasing inoculum density reduced susceptibility. Since Chin and Neu used a heavier inoculum, one would expect their MICs to be higher, unless the addition of blood was a factor. However, we found that addition of blood had no effect on the MICs of the control strains tested in the present study. Borobio and Perea used Wilkins-Chalgren agar and the same methodology as we did, and obtained an MIC range of 0.13 to 0.5 μg/ml. Therefore, we conclude that the differences observed are either due to strain differences or due to undetermined differences in methodology.

Cefoxitin remains active against most of the anaerobes, except *C. difficile*, with 88% of the *B. fragilis* group strains, 96% of *Clostridium* spp. (other than *C. difficile*), and all others susceptible to 32 μg or less per ml. Clindamycin continues to show good activity against most of the anaerobes previously susceptible to it. However, 12% of the recent *B. fragilis* group isolates, one unidentified strain of *Bacteroides* sp., and one unidentified *Fusobacterium* sp. had MICs ≥8 μg/ml. Metronidazole remains active against all anaerobes, except some *Peptostreptococcus* spp. and gram-positive bacilli. Mezlocillin exhibited good activity with all but 13% of the *B. fragilis* group, having MICs of ≤64 μg/ml. The results with cefoxitin, metronidazole, and mezlocillin are generally the same as those obtained with strains isolated in this institution approximately 10 years ago (5). Clindamycin-resistant strains have been noted previously (6).

Results with control strains were within the acceptable ranges with cefoxitin, clindamycin, and metronidazole. Mode MICs for *B. fragilis* (ATCC 25285) were 4 μg of ciprofloxacin per ml and 8 μg of mezlocillin per ml. For *B. thetaiotaomicron* (ATCC 29741) they were 16 μg of ciprofloxacin per ml and 32 μg of mezlocillin per ml. The addition of blood did not affect these mode values.

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TABLE 1. Comparative activity of ciprofloxacin and four other antimicrobial agents against anaerobic bacteria

| Bacteria | No. of strains | Antimicrobial agent | MIC (μg/ml)[a] | | |
|---|---|---|---|---|---|
| | | | Range | 50% | 90% |
| *Bacteroides fragilis* group | 122 | Ciprofloxacin | 4–256 | 8 | 32 |
| | | Cefoxitin | 2–256 | 16 | 64 |
| | | Clindamycin | ≤0.03–>128 | 1 | >128 |
| | | Metronidazole | 0.125–4 | 0.5 | 1 |
| | | Mezlocillin | 1–>256 | 16 | >128 |
| Other *Bacteroides* spp. | 52 | Ciprofloxacin | 0.125–32 | 1 | 16 |
| | | Cefoxitin | ≤0.03–32 | 1 | 4 |
| | | Clindamycin | ≤0.03–64 | ≤0.03 | 0.5 |
| | | Metronidazole | ≤0.03–4 | 1 | 4 |
| | | Mezlocillin | ≤0.125–>256 | 2 | 16 |
| *Fusobacterium* spp. | 17 | Ciprofloxacin | 0.06–16 | 2 | 8 |
| | | Cefoxitin | ≤0.03–4 | 0.5 | 2 |
| | | Clindamycin | ≤0.03–8 | 0.06 | 0.5 |
| | | Metronidazole | ≤0.03–0.5 | 0.06 | 0.25 |
| | | Mezlocillin | ≤0.125–>256 | ≤0.125 | 32 |
| *Peptostreptococcus* spp. | 83 | Ciprofloxacin | 0.25–16 | 1 | 8 |
| | | Cefoxitin | ≤0.03–8 | 0.25 | 1 |
| | | Clindamycin | ≤0.03–>128 | 0.125 | 2 |
| | | Metronidazole | 0.06–>128 | 0.5 | 1 |
| | | Mezlocillin | ≤0.125–16 | ≤0.125 | 1 |
| Gram-positive bacilli | 35 | Ciprofloxacin | 0.125–32 | 2 | 16 |
| | | Cefoxitin | ≤0.03–32 | 1 | 8 |
| | | Clindamycin | ≤0.03–>128 | 0.25 | 128 |
| | | Metronidazole | 0.125–>128 | 4 | >128 |
| | | Mezlocillin | ≤0.125–128 | 0.5 | 16 |
| *Clostridium difficile* | 26 | Ciprofloxacin | 4–16 | 8 | 16 |
| | | Cefoxitin | 64–256 | 128 | 128 |
| | | Clindamycin | 4–>128 | >128 | >128 |
| | | Metronidazole | 0.125–0.5 | 0.5 | 0.5 |
| | | Mezlocillin | 1–8 | 8 | 8 |
| Other *Clostridium* spp. | 24 | Ciprofloxacin | 0.25–64 | 1 | 64 |
| | | Cefoxitin | 0.25–128 | 1 | 16 |
| | | Clindamycin | 0.06–>128 | 0.5 | 4 |
| | | Metronidazole | 0.25–4 | 0.5 | 1 |
| | | Mezlocillin | ≤0.125–32 | 0.25 | 4 |

[a] 50% and 90%, MICs at which 50 and 90% of the strains were inhibited, respectively.

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