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# Antimicrobial Activity of Cefmenoxime (SCE-1365)

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The in vitro activity of cefmenoxime (SCE-1365 or A-50912), a new semisynthetic cephalosporin antibiotic, was compared with those of cefazolin, cefoxitin, and cefamandole against a broad spectrum of 486 organisms and with that of cefotaxime against 114 organisms. Cefmenoxime and cefotaxime exhibited nearly equivalent activities against those organisms tested and were the most active of these cephalosporins against all aerobic and facultative organisms except *Staphylococcus aureus*. The minimum inhibitory concentration (MIC) of cefmenoxime required to inhibit at least 90% of strains tested ($MIC_{90}$) ranged from 0.06 to 8 μg/ml for the *Enterobacteriaceae*. The $MIC_{90}$s for gram-positive cocci were 0.015 and ≤0.008 μg/ml for *Streptococcus pneumoniae* and *Streptococcus pyogenes*, respectively, and 2 μg/ml for *S. aureus*. Group D streptococci were less susceptible. Cefmenoxime was very active against *Haemophilus influenzae*, *Neisseria gonorrhoeae*, and *Neisseria meningitidis* with $MIC_{90}$s ranging from ≤0.008 to 0.25 μg/ml. Cefmenoxime, at a concentration of 16 μg/ml, inhibited 78% and 73% of *Pseudomonas aeruginosa* and *Acinetobacter* spp., respectively. MICs for anaerobes ranged from 0.5 to >128 μg/ml with good activity against the gram-positive organisms. In addition, cefmenoxime activity was bactericidal and only slightly affected by differences in inoculum size. The combination of cefmenoxime and gentamicin was synergistic against 80% of the *Enterobacteriaceae* and 100% of *P. aeruginosa* strains tested. Development of resistance to cefmenoxime was slow or absent for organisms with low initial MICs but more rapid for those with higher initial MICs. Cefmenoxime exhibited good protective activity in mice infected with *Escherichia coli*, *Enterobacter cloacae*, *Proteus mirabilis*, *Proteus vulgaris*, or *S. aureus* but was less effective against *P. aeruginosa*.

Cefmenoxime (proposed international nonprietary name), also referred to as SCE-1365 or A-50912, is a new semisynthetic cephalosporin antibiotic which has excellent activity against a broad spectrum of microorganisms (8). The chemical structure of cefmenoxime, 7-β-[2-(2-aminothiazol-4-yl)-(*Z*)-2-methoxyiminoacetamido]-3-[(1-methyl-1H-tetrazol-5-yl)thiomethyl]-ceph-3-em-4-carboxylic acid, is shown in Fig. 1.

This paper reports the in vitro activity of cefmenoxime compared with those of cefotaxime, cefazolin, cefoxitin, and cefamandole and the in vivo activity compared with that of cefazolin in acute infections in mice.

## MATERIALS AND METHODS

**Organisms.** The majority of organisms studied were randomly selected recent isolates from clinical material and were obtained from several hospital and public health laboratories.

**Antibiotics.** Cefmenoxime, as the hemihydrochloride salt, was received from Takeda Chemical Industries, Osaka, Japan. Cefazolin sodium and cefamandole nafate were obtained from Eli Lilly & Co., Indianapolis, Ind. Cefotaxime sodium standard powder was supplied by Hoechst-Roussel Pharmaceuticals, Somerville, N.J. Cefoxitin sodium was supplied by Merck Sharp and Dohme, West Point, Pa. Solutions of the compounds were prepared fresh daily, and concentrations were expressed on the basis of labeled potency for each antibiotic.

**Susceptibility tests.** Antimicrobial activity was measured by agar or broth dilution methods as noted. A single lot of Mueller-Hinton agar or broth (BBL Microbiology Systems, Cockeysville, Md.) was used for all studies. Minimum inhibitory concentrations (MICs) were determined in agar by applying an inoculum of approximately $5 \times 10^4$ colony-forming units (CFU) to the surface with a Steers replicating device. Sheep blood (5%) was added for testing *Streptococcus* spp., and supplement C (Difco Laboratories, Detroit, Mich.) was added (1%) for testing of *Haemophilus* and *Neisseria* spp. with incubation in 3% $CO_2$. Broth studies were done by microdilution with an inoculum of approximately $5 \times 10^5$ CFU/ml. The effect of inoculum size on MICs was determined by broth dilution with inocula of $10^7$, $10^5$, and $10^3$ CFU/ml. Plates or microdilution trays were incubated at 35°C for 18 h. The MIC was defined as the lowest concentration of antibiotic that inhibited development of visible growth. A slight haze or fewer than three colonies was ignored. The minimal bactericidal concentration was determined by plating 0.02 ml from clear microdilution wells to brain heart infusion agar (BBL) and incubating for 24 h at 35°C. The minimal bactericidal concentration was the lowest antibiotic concentration in

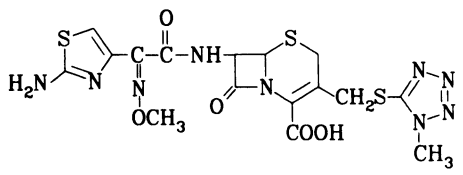

FIG. 1. *Chemical structure of cefmenoxime.*

which there was a 99.9% or greater reduction in count from the inoculum level. Susceptibility of anaerobes was determined by the agar dilution method described above, using Mueller-Hinton agar plus 5% sheep blood and an inoculum of $5 \times 10^5$ CFU/ml. Incubation of anaerobic cultures was at 35°C for 48 h in GasPak jars (BBL).

**Synergy.** Synergy of cefmenoxime with gentamicin was determined by the checkerboard technique with microdilution procedures in Mueller-Hinton broth supplemented with 60 μg of calcium and 20 μg of magnesium per ml. The inoculum was added by calibrated dropper to give a final count of approximately $5 \times 10^5$ CFU/ml. Plates were incubated at 35°C for 18 h. The fractional inhibitory concentration index was calculated for each antibiotic combination (4). Synergy was indicated by a fractional inhibitory concentration index of <0.6.

**Development of resistance in vitro.** Resistance was developed by using broth dilution with incubation at 35°C for 48 h. Successive transfers were made every 48 h, using as inoculum a $10^{-3}$ dilution from the well with the highest concentration of antibiotic showing growth approximating that in the control well. This procedure was repeated until either the antibiotic MIC reached >512 μg/ml or 14 transfers were made. Culture purity and identity were checked after every transfer.

**In vivo efficacy.** Female Swiss albino mice, weighing 18 to 20 g, were infected intraperitoneally with approximately 100 times the number of organisms needed to kill 50% of the untreated animals. The bacterial suspensions used to infect mice consisted of appropriate dilutions in brain heart infusion broth containing 5% aqueous hog gastric mucin (American Laboratories, Inc.). Serial twofold dilutions of the test substances were administered by the subcutaneous route to groups of 10 mice at 1 and 6 h postinfection. The animals were observed for 7 days, and mortality was recorded. The amount of antibiotic which protected 50% of the infected animals and the 95% confidence limits were calculated by the trimmed Spearman-Karber method (1).

## RESULTS

**Comparative antimicrobial activities.** The antimicrobial activity of cefmenoxime was compared with those of cefazolin, cefoxitin, and cefamandole against a broad spectrum of 486 organisms and with that of cefotaxime against 114 organisms. Results of these comparisons are shown in Table 1. Cefmenoxime and cefotaxime were considerably more active than the other cephalosporins against all organisms tested except *Staphylococcus aureus*. The cefmenoxime MIC which inhibited 90% of strains ($MIC_{90}$) was less than 1 μg/ml for most organisms and less than 16 μg/ml for all organisms except *Pseudomonas aeruginosa*, group D streptococci, and *Acinetobacter* spp.

Against the *Enterobacteriaceae*, cefmenoxime was highly active. Cefmenoxime $MIC_{90}$s were 2 μg/ml or less for all of this group of organisms except for *Serratia marcescens*, which had a cefmenoxime $MIC_{90}$ of 8 μg/ml. Cefmenoxime and cefotaxime showed nearly equal antimicrobial activity against the *Enterobacteriaceae*.

Activity of cefmenoxime against *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae* was particularly noteworthy. A concentration of 0.25 μg/ml inhibited all strains of these organisms, with most being inhibited by much lower concentrations. Cefazolin and cefamandole were approximately twofold more active, and cefoxitin was twofold less active than cefmenoxime against *S. aureus*. None of the four cephalosporins showed good activity against group D streptococci; however, cefmenoxime was most active, inhibiting 89% of strains at 16 μg/ml.

Against *P. aeruginosa*, cefmenoxime and cefotaxime exhibited identical activities, with the $MIC_{50}$ and $MIC_{90}$ being 16 and 32 μg/ml, respectively. Cefmenoxime was slightly less active than cefotaxime against *Acinetobacter* spp. Cefazolin, cefoxitin, and cefamandole showed little or no activity against these two organisms.

The in vitro comparative activities of cefmenoxime, cefotaxime, cefazolin, cefoxitin, and cefamandole against anaerobes are shown in Table 2. Cefoxitin showed the best overall activity, with the other compounds showing good activity against the gram-positive organisms and weak or no activity against *Bacteroides fragilis* and the other gram-negative bacilli.

The antibacterial activity of cefmenoxime was found to be primarily bactericidal. The minimal bactericidal concentration was the same as or twofold higher than the MIC for 87% of a broad spectrum of 31 gram-negative organisms.

Increasing the inoculum level from $10^3$ to $10^5$ CFU/ml had little or no effect on cefmenoxime MICs of 10 organisms tested. An increase in inoculum from $10^5$ to $10^7$ CFU/ml resulted in MIC increases of fourfold or less for 80% of the organisms tested.

The activity of cefmenoxime and gentamicin in combination is shown in Table 3. This combination was synergistic against 8 of 10 *Enterobacteriaceae* and all 9 *P. aeruginosa* strains. Concentrations of cefmenoxime in the most ef-

TABLE 1. *Activities of cefmenoxime, cefotaxime, cefazolin, cefoxitin, and cefamandole against various bacteria*

| Organism (no. of strains) | Drug | MIC range (μg/ml) | $MIC_{50}$ (μg/ml) | $MIC_{90}$ (μg/ml) |
|---|---|---|---|---|
| *E. coli* (62) | Cefmenoxime | 0.015–2 | 0.06 | 0.12 |
| | Cefotaxime[a] | 0.03–0.25 | 0.06 | 0.06 |
| | Cefazolin | 0.5–128 | 2 | 16 |
| | Cefoxitin | 1–64 | 4 | 8 |
| | Cefamandole | 0.12–64 | 1 | 16 |
| *K. pneumoniae* (38) | Cefmenoxime | 0.015–8 | 0.06 | 0.25 |
| | Cefotaxime[b] | 0.03–0.12 | ca. 0.06 | ca. 0.12 |
| | Cefazolin | 1–64 | 2 | 64 |
| | Cefoxitin | 1–128 | 2 | 16 |
| | Cefamandole | 0.012–128 | 1 | 128 |
| *Enterobacter cloacae* (37) | Cefmenoxime | 0.015–16 | 0.12 | 0.5 |
| | Cefotaxime[c] | 0.06–0.25 | ca. 0.12 | ca. 0.25 |
| | Cefazolin | 1–64 | 2 | 64 |
| | Cefoxitin | 2–128 | >128 | >128 |
| | Cefamandole | 0.5–128 | 8 | 64 |
| *Enterobacter aerogenes* (16) | Cefmenoxime | 0.06–4 | 0.12 | 2 |
| | Cefazolin | 8–>128 | 128 | >128 |
| | Cefoxitin | 64–>128 | >128 | >128 |
| | Cefamandole | 1–128 | 2 | 128 |
| *Enterobacter agglomerans* (5) | Cefmenoxime | 0.06–0.25 | ca. 0.12 | ca. 0.25 |
| | Cefazolin | 1–64 | ca. 4 | ca. 64 |
| | Cefoxitin | 2–64 | ca. 8 | ca. 64 |
| | Cefamandole | 0.5–2 | ca. 2 | ca. 2 |
| *Citrobacter* spp. (6) | Cefmenoxime | 0.015–2 | ca. 0.06 | ca. 0.12 |
| | Cefazolin | 0.5–>128 | ca. 4 | ca. >128 |
| | Cefoxitin | 1–64 | ca. 4 | ca. 8 |
| | Cefamandole | 0.12–64 | ca. 1 | ca. 16 |
| *S. marcescens* (34) | Cefmenoxime | 0.06–32 | 2 | 8 |
| | Cefotaxime[d] | 0.12–1 | ca. 0.5 | ca. 1 |
| | Cefazolin | 16–>128 | >128 | > 128 |
| | Cefoxitin | 8–>128 | >128 | >128 |
| | Cefamandole | 1–>128 | >128 | >128 |
| *Shigella* spp. (8) | Cefmenoxime | 0.06 | ca. 0.06 | ca. 0.06 |
| | Cefotaxime[d] | 0.03–0.06 | ca. 0.06 | ca. 0.06 |
| | Cefazolin | 2 | ca. 2 | ca. 2 |
| | Cefoxitin | 4–8 | ca. 4 | ca. 8 |
| | Cefamandole | 2 | ca. 2 | ca. 2 |
| *Salmonella* spp. (10) | Cefmenoxime | 0.06–0.25 | 0.12 | 0.25 |
| | Cefotaxime[d] | 0.12–0.25 | ca. 0.12 | ca. 0.25 |
| | Cefazolin | 1–4 | 1 | 2 |
| | Cefoxitin | 2–4 | 2 | 4 |
| | Cefamandole | 0.5–8 | 0.5 | 1 |
| *P. mirabilis* (41) | Cefmenoxime | 0.06–0.25 | 0.25 | 0.25 |
| | Cefotaxime[e] | 0.015–0.12 | 0.06 | 0.12 |
| | Cefazolin | 4–32 | 8 | 16 |
| | Cefoxitin | 2–16 | 8 | 16 |
| | Cefamandole | 1–16 | 4 | 8 |
| *Proteus* spp. (indole positive) (51) | Cefmenoxime | ≤0.008–8 | 0.06 | 2 |
| | Cefotaxime[f] | ≤0.008–8 | 0.12 | 8 |
| | Cefazolin | 0.25–>128 | >128 | >128 |
| | Cefoxitin | 1–>128 | 4 | 16 |
| | Cefamandole | 0.12–>128 | 4 | >128 |

TABLE 1—*Continued*

| Organism (no. of strains) | Drug | MIC range (μg/ml) | $MIC_{50}$ (μg/ml) | $MIC_{90}$ (μg/ml) |
|---|---|---|---|---|
| *Providencia* spp. (4) | Cefmenoxime | 0.12–1 | ca. 0.25 | ca. 1 |
| | Cefazolin | 8–128 | ca. 64 | ca. 128 |
| | Cefoxitin | 1–16 | ca. 4 | ca. 16 |
| | Cefamandole | 4–32 | ca. 8 | ca. 32 |
| *Acinetobacter* spp. (15) | Cefmenoxime | 8–64 | 16 | 32 |
| | Cefotaxime[d] | ca. 4–8 | ca. 8 | ca. 8 |
| | Cefazolin | 64–>128 | >128 | >128 |
| | Cefoxitin | 16–>128 | 64 | 128 |
| | Cefamandole | 16–>128 | 64 | 64 |
| *P. aeruginosa* (65) | Cefmenoxime | 0.25–128 | 16 | 32 |
| | Cefotaxime[g] | 0.5–>128 | 16 | 32 |
| | Cefazolin | >128 | >128 | >128 |
| | Cefoxitin | 64–>128 | >128 | >128 |
| | Cefamandole | 64–>128 | >128 | >128 |
| *H. influenzae* (15) | Cefmenoxime | ≤0.008–0.015 | ≤0.008 | ≤0.008 |
| | Cefazolin | 0.03–16 | 8 | 16 |
| | Cefoxitin | 0.5–8 | 2 | 2 |
| | Cefamandole | 0.06–0.25 | 0.12 | 0.25 |
| *N. gonorrhoeae* (8) | Cefmenoxime | ≤0.008–0.015 | ca. ≤0.008 | ca. 0.015 |
| *N. meningitidis* (9) | Cefmenoxime | ≤0.008–0.25 | ca. ≤0.008 | ca. 0.25 |
| | Cefazolin | 0.25–0.5 | ca. 0.5 | ca. 0.5 |
| | Cefoxitin | 0.06–1 | ca. 0.12 | ca. 1 |
| | Cefamandole | 0.03–0.25 | ca. 0.06 | ca. 0.25 |
| *S. aureus* (22) | Cefmenoxime | 0.5–32 | 1 | 2 |
| | Cefazolin | 0.25–32 | 0.5 | 1 |
| | Cefoxitin | 2–16 | 2 | 4 |
| | Cefamandole | 0.25–8 | 0.5 | 1 |
| *S. pyogenes* (21) | Cefmenoxime | ≤0.008–0.015 | ≤0.008 | ≤0.008 |
| | Cefazolin | 0.12 | 0.12 | 0.12 |
| | Cefoxitin | 0.5–1 | 0.5 | 1 |
| | Cefamandole | 0.03–0.06 | 0.06 | 0.06 |
| *S. pneumoniae* (12) | Cefmenoxime | ≤0.008–0.015 | ≤0.008 | 0.015 |
| | Cefazolin | 0.03–0.12 | 0.06 | 0.12 |
| | Cefoxitin | 0.25–1 | 1 | 1 |
| | Cefamandole | 0.015–0.12 | 0.06 | 0.12 |
| Group D streptococci (9) | Cefmenoxime | 0.06–>128 | ca. 8 | ca. 16 |
| | Cefazolin | 0.25–64 | ca. 32 | ca. 32 |
| | Cefoxitin | 1–>128 | ca. >128 | ca. >128 |
| | Cefamandole | 0.12–64 | ca. 32 | ca. 32 |

[a] Ten strains tested.
[b] Nine strains tested.
[c] Eight strains tested.
[d] Five strains tested.
[e] Eleven strains tested.
[f] Eighteen strains tested.
[g] Thirty-eight strains tested.

fective combination ranged from 0.001 to 0.25 μg/ml for the *Enterobacteriaceae* and 0.5 to 32 μg/ml for the *P. aeruginosa* strains.

The comparative in vitro development of resistance to cefmenoxime, cefotaxime, and cefazolin is shown in Table 4. Resistance development was similar for cefmenoxime and cefotaxime, i.e., slow or absent with *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *S. aureus* strains but rapid for *S. marcescens* and *P. aeruginosa* strains. The magnitude of resistance development was also similar for the

TABLE 2. *Activities of five cephalosporins against anaerobic bacteria*

| Organism | Strain no. | MIC (μg/ml) | | | | |
|---|---|---|---|---|---|---|
| | | Cefmenoxime | Cefotaxime | Cefazolin | Cefoxitin | Cefamandole |
| *B. fragilis* | 784 | 32 | 32 | 64 | 4 | 32 |
| | ATCC 25285 | 32 | 32 | 64 | 4 | 64 |
| | UC-2 | 32 | 16 | 16 | 8 | 32 |
| *Bacteroides thetaiotaomicron* | 3304 | 64 | 32 | 16 | 8 | 32 |
| *Fusobacterium mortiferum* | 789 | >128 | >128 | 128 | >128 | 0.5 |
| *Fusobacterium necrophorum* | 793 | 0.12 | 0.12 | 0.06 | 0.12 | 0.12 |
| *Eubacterium lentum* | 4 | 128 | 128 | 64 | 8 | 32 |
| *Clostridium perfringens* | 788 | 2 | 4 | 0.5 | 1 | 2 |
| | ATCC 13124 | 2 | 4 | 1 | 1 | 1 |
| *Clostridium ramosum* | 7 | 0.5 | 0.5 | 4 | 8 | 1 |
| *Peptococcus magnus* | 791 | 1 | 1 | 0.25 | 0.06 | 0.12 |
| *Peptococcus assaccharolyticus* | ATCC 29743 | 2 | 8 | 0.5 | 2 | 1 |

TABLE 3. *Activities of cefmenoxime and gentamicin alone and in combination*

| Organism | Strain no. | MIC (μg/ml) | | | | FIC[a] index |
|---|---|---|---|---|---|---|
| | | Antibiotic alone | | Most effective antibiotic combination | | |
| | | Cefmenoxime | Gentamicin | Cefmenoxime | Gentamicin | |
| *E. coli* | A-5070 | 0.12 | 2 | 0.03 | 0.25 | 0.37 |
| | A-5198 | 0.06 | 2 | 0.03 | 0.25 | 0.62 |
| *K. pneumoniae* | 8045 | 0.25 | 0.5 | 0.015 | 0.12 | 0.31 |
| | C-40 | 0.06 | 1 | 0.015 | 0.25 | 0.50 |
| | 13588 | 0.12 | 1 | 0.03 | 0.12 | 0.37 |
| | 13069 | 0.06 | 1 | 0.03 | 0.12 | 0.62 |
| *Enterobacter cloacae* | A-5141 | 0.12 | 1 | 0.008 | 0.5 | 0.56 |
| *S. marcescens* | A-5030 | 2 | 2 | 0.25 | 0.5 | 0.37 |
| *P. mirabilis* | 48575 | 0.03 | 16 | 0.008 | 1 | 0.31 |
| *Proteus rettgeri* | 47568-1 | 0.008 | 4 | 0.001 | 0.25 | 0.18 |
| *P. aeruginosa* | A-5000 | 64 | 1 | 8 | 0.12 | 0.25 |
| | A-5005 | 32 | 1 | 4 | 0.25 | 0.37 |
| | A-5007 | 4 | 4 | 1 | 0.5 | 0.37 |
| | VA-1316 | 2 | 4 | 0.5 | 0.5 | 0.37 |
| | A-5189 | 64 | 4 | 16 | 1 | 0.50 |
| | A-5178 | 256 | 4 | 32 | 0.5 | 0.25 |
| | 8764 | 128 | 2 | 32 | 0.5 | 0.50 |
| | A-5187 | 64 | 16 | 16 | 4 | 0.50 |
| | W19 | 4 | 128 | 1 | 16 | 0.37 |

[a] FIC, Fractional inhibitory concentration.

two compounds. Resistance to cefazolin developed slowly with *K. pneumoniae*, *P. mirabilis* and *S. aureus* and did not occur with *E. coli*. The *S. marcescens* and *P. aeruginosa* strains were initially resistant to cefazolin.

The in vivo efficacy of cefmenoxime compared with that of cefazolin against several *Enterobacteriaceae*, *S. aureus*, and *P. aeruginosa* strains is presented in Table 5. The protective effect of cefmenoxime was superior to that of cefazolin for all of the infections except that of *S. aureus*. More cefmenoxime was required to protect mice infected with *P. aeruginosa* than to protect against the other organisms, a result which is in agreement with the higher MICs observed for this organism in vitro.

## DISCUSSION

Cefmenoxime has been shown to have excellent activity against a broad spectrum of microorganisms. It was considerably more potent than the currently available cephalosporin antibiotics cefazolin, cefoxitin, and cefamandole against all of the *Enterobacteriaceae* and *P. aeruginosa*

TABLE 4. *Development of resistance to cefmenoxime, cefotaxime, and cefazolin*

| Organism (strain no.) | Drug | MIC μg/ml | | Terminal/ initial ratio |
|---|---|---|---|---|
| | | Initial | Terminal (transfer no.) | |
| *E. coli* (A-5198) | Cefmenoxime | 0.06 | 1 (14) | 16 |
| | Cefotaxime | 0.03 | 0.5 (14) | 16 |
| | Cefazolin | 1 | 2 (14) | 2 |
| *K. pneumoniae* (C-40) | Cefmenoxime | 0.06 | 4 (14) | 64 |
| | Cefotaxime | 0.015 | 4 (14) | 256 |
| | Cefazolin | 1 | 128 (14) | 128 |
| *S. marcescens* (A-5030) | Cefmenoxime | 4 | >512 (2) | >128 |
| | Cefotaxime | 32 | >512 (5) | >16 |
| | Cefazolin | >512 | >512 (0) | 1 |
| *P. mirabilis* (C-42) | Cefmenoxime | 0.06 | 0.06 (14) | 1 |
| | Cefotaxime | 0.015 | 0.06 (14) | 4 |
| | Cefazolin | 4 | >512 (11) | >128 |
| *P. aeruginosa* (A-5000) | Cefmenoxime | 8 | >512 (6) | >64 |
| | Cefotaxime | 64 | >512 (2) | >8 |
| | Cefazolin | >512 | >512 (0) | 1 |
| *S. aureus* (Smith) | Cefmenoxime | 0.5 | 16 (14) | 32 |
| | Cefotaxime | 1 | 32 (14) | 32 |
| | Cefazolin | 0.25 | 16 (14) | 64 |

TABLE 5. *In vivo efficacy of cefmenoxime*

| Organism | Strain no. | MIC (μg/ml) | | $CD_{50}$ (mg/kg)[a] | |
|---|---|---|---|---|---|
| | | Cefmenoxime | Cefazolin | Cefmenoxime | Cefazolin |
| *E. coli* | Juhl | 0.12 | 1.6 | 0.5 (0.4–0.6) | 12.7 (10.3–15.6) |
| *Enterobacter cloacae* | A-5140 | 0.12 | >128 | 0.4 (0.3–0.5) | 145 (98–216) |
| | A-5053 | 0.12 | >128 | 0.5 (0.4–0.7) | 263 (198–349) |
| *P. mirabilis* | Fin. 9 | 0.25 | 50 | 4.1 (2.3–7.5) | 349 (335–364) |
| *P. vulgaris* | JJ | 0.06 | 50 | 0.4 (0.3–0.6) | 55 (42–73) |
| *P. aeruginosa* | A-5005 | 8 | >128 | 127 (91–176) | >500 |
| | A-5007 | 32 | >128 | 54 (31–93) | >500 |
| *S. aureus* | Smith | 1 | <0.2 | 4.1 (2.9–5.8) | 0.3 (0.2–0.4) |

[a] The 95% confidence limits are shown within parentheses; $CD_{50}$, 50% curative dose.

strains. Particularly noteworthy activity was demonstrated by cefmenoxime against *Neisseria* spp., *S. pyogenes*, *S. pneumoniae*, and *H. influenzae*. The activity of cefmenoxime was slightly poorer than those of cefazolin and cefamandole against *S. aureus* and slightly better against group D streptococci.

The excellent activity of cefmenoxime against the *Enterobacteriaceae* and good activity against *P. aeruginosa* are characteristics shared by some new cephalosporins such as cefotaxime (2, 5, 7). A limited comparison of cefmenoxime and cefotaxime showed the in vitro activities of the two compounds to be fairly similar.

The combination of a beta-lactam antibiotic and an aminoglycoside antibiotic is known to act synergistically against many organisms both in vitro and in vivo (6). In this study, cefmenoxime combined with gentamicin produced a synergistic effect against the large majority of *Enterobacteriaceae* and *P. aeruginosa* strains. The combinations of cefotaxime-gentamicin and cefotaxime-amikacin have also been reported (3, 5) to be synergistic, although against a somewhat smaller fraction of strains than the cefmenoxime-gentamicin combination.

The potent broad-spectrum activity of cefmenoxime and additional characteristics, such

as bactericidal activity, slow development of in vitro resistance, little inoculum effect on MICs, and demonstrated protective activity in vivo, mark this compound as a potentially useful therapeutic agent.

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