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Comparative in Vitro Activities of Cefmenoxime (SCE-1365) and Newer Cephalosporin Derivatives of Clinical Utility

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The minimal inhibitory concentrations of cefmenoxime (SCE-1365), cefotaxime, cefoperazone, and moxalactam against various species of aerobic bacteria were determined. The activities of cefmenoxime, cefotaxime, and moxalactam were generally similar and slightly higher than the activity of cefoperazone.

Cefmenoxime (SCE-1365), 7 β- [2-(2-aminothiazol-4-yl)-(*Z*)-2-methoxyiminoacetamido]-3-[(1-methyl-1*H*-tetrazol-5-yl)thiomethyl]-ceph-3-em-4-carboxylic acid (Fig. 1), is a new semisynthetic cephalosporin with a broad spectrum of antibacterial activity and β-lactamase stability (3). It is more active than cephalosporins of the first and second generations and some newer investigational cephalosporins (4, 5). We compared the activity of cefmenoxime with those of cefotaxime, cefoperazone, and moxalactam, new cephalosporin derivatives of promising clinical importance.

The test organisms consisted of 535 strains of bacteria representing recent clinical isolates from our hospitals and gifts from research laboratories. Organisms were identified by standard criteria (2).

The antimicrobial agents tested were cefmenoxime (Abbott Laboratories, North Chicago, Ill.), cefotaxime (Hoechst-Roussel Pharmaceuticals, Sommerville, N.J.), cefoperazone (Pfizer Inc., New York, N.Y.), moxalactam (Eli Lilly & Co., Indianapolis, Ind.), oxacillin (Beecham Laboratories, Bristol, Tenn.), and gentamicin (Schering Corp., Bloomfield, N.J.)

The minimal inhibitory concentrations (MICs) were determined by a broth microdilution method. Twofold serial dilutions of freshly prepared antibiotic solutions were distributed with an automatic dispenser (MIC 2000, Dynatech Laboratories Inc., Alexandria, Va.) into wells containing Mueller-Hinton broth supplemented with 10% laked blood for gram-positive bacteria. Overnight cultures of organisms (4-h culture for most gram-positive bacteria) in Mueller-Hinton broth were diluted and inoculated into antibiotic wells; the final concentration of bacteria was ca. 10^5 colony-forming units per ml. The MIC was the lowest antibiotic concentration that completely inhibited growth after 18 to 24 h of incubation.

The antibacterial activity of cefmenoxime compared with other antibiotics is shown in Table 1. Cefmenoxime had very good activity against most of the bacterial species tested. It inhibited 90% of all bacterial strains at a concentration of 1 μg/ml or less, with the exception of *Listeria monocytogenes*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, *Streptococcus faecalis*, and coagulase-negative staphylococci. The best activity was against *Neisseria gonorrhoeae*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*, with an MIC to inhibit 90% of strains (MIC_{90}) of 0.03 μg/ml. *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, and *Streptococcus agalactiae* also showed a high degree of susceptibility to cefmenoxime, with an MIC_{90} of 0.06 μg/ml.

Overall, the degree of activity of cefmenoxime was similar to that of cefotaxime; its MICs were generally only one dilution higher than those of cefotaxime. Moxalactam was less active than cefmenoxime and cefotaxime against *Yersinia enterocolitica*, *N. gonorrhoeae*, *Streptococcus* spp., and methicillin-susceptible *S. aureus*. Our results and those of Stamm et al. (4) and Tsuchiya et al. (5) show MICs generally within two dilutions for bacteria tested in common. The exceptions were *Haemophilus influenzae* and *S.*

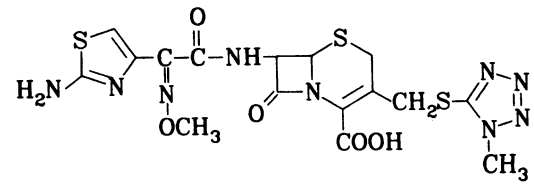

FIG. 1. Chemical structure of cefmenoxime.

TABLE 1. Susceptibility of aerobic bacteria to cefmenoxime

Organism (no. of strains tested)	Drug	MIC (μg/ml)		
		Range	MIC_{50}	MIC_{90}
Escherichia coli (40)	Cefmenoxime	≤0.01–0.125	0.03	0.06
	Cefotaxime	≤0.01–0.125	0.01	0.01
	Cefoperazone	0.01–4.0	0.06	2.0
	Moxalactam	0.03–0.25	0.06	0.125
Klebsiella pneumoniae (40)	Cefmenoxime	≤0.01–0.125	0.06	0.06
	Cefotaxime	≤0.01–0.06	0.01	0.03
	Cefoperazone	0.06–4.0	0.125	2.0
	Moxalactam	0.03–0.5	0.06	0.125
Enterobacter cloacae (40)	Cefmenoxime	0.03–2	0.125	1
	Cefotaxime	≤0.01–1	0.06	0.25
	Cefoperazone	0.125–8	0.125	0.5
	Moxalactam	0.03–2	0.5	2
Proteus mirabilis (40)	Cefmenoxime	0.03–0.125	0.03	0.06
	Cefotaxime	≤0.01–0.06	≤0.01	0.03
	Cefoperazone	0.125–0.5	0.25	0.5
	Moxalactam	0.03–0.25	0.06	0.125
P. stuartii (22)	Cefmenoxime	0.03–0.5	0.125	0.5
	Cefotaxime	≤0.01–0.5	0.06	0.25
	Cefoperazone	0.5–8.0	4.0	4.0
	Moxalactam	0.03–0.5	0.125	0.25
Pseudomonas aeruginosa (40)	Cefmenoxime	8–≥64	16	≥64
	Cefotaxime	8–≥64	16	≥64
	Cefoperazone	4–≥64	8	≥64
	Moxalactam	8–≥64	16	≥64
Serratia marcescens (40)	Cefmenoxime	0.06–2	0.25	1
	Cefotaxime	0.06–2	0.125	1
	Cefoperazone	0.5–64	2	32
	Moxalactam	0.125–2	0.25	2
Morganella morganii (40)	Cefmenoxime	0.06–0.125	0.06	0.125
	Cefotaxime	≤0.01–0.03	0.01	0.03
	Cefoperazone	0.25–8	1	8
	Moxalactam	0.06–0.5	0.125	0.25
Salmonella spp. (27)	Cefmenoxime	0.06–0.25	0.06	0.125
	Cefotaxime	≤0.01–0.03	0.01	0.03
	Cefoperazone	0.125–0.5	0.25	0.5
	Moxalactam	0.03–0.25	0.125	0.125
Shigella sonnei (13)	Cefmenoxime	0.06–0.125	0.06	0.125
	Cefotaxime	≤0.01–0.03	0.01	0.03
	Cefoperazone	0.25–≥16	≥16	≥16
	Moxalactam	0.06–0.125	0.125	0.125
Listeria monocytogenes (11)	Cefmenoxime	32–>64	32	>64
	Cefotaxime	8	8	8
	Cefoperazone	8–16	8	16
	Moxalactam	32–64	64	64
Yersinia enterocolitica (7)	Cefmenoxime	0.06–0.125	0.06	0.125
	Cefotaxime	≤0.01–0.06	0.01	0.06
	Moxalactam	0.125	0.125	0.125
	Gentamicin	0.5–1	1	1
Haemophilus influenzae (β-lactamase negative) (20)	Cefmenoxime	≤0.01–0.125	0.01	0.125
	Cefotaxime	≤0.01–0.125	0.01	0.125
	Moxalactam	0.03–0.5	0.25	0.5

TABLE 1—*Continued*

Organism (no. of strains tested)	Drug	MIC (μg/ml)		
		Range	MIC_{50}	MIC_{90}
Neisseria gonorrhoeae (5)	Cefmenoxime	≤0.01–0.03	≤0.01	0.03
	Cefotaxime	≤0.01–0.125	0.125	0.125
	Moxalactam	0.06–0.125	0.125	0.125
	Oxacillin	0.5–1	0.5	1
Staphylococcus aureus (20) (methicillin susceptible)	Cefmenoxime	0.25–2	1	2
	Cefotaxime	0.25–2	0.5	1
	Moxalactam	2–8	4	8
	Oxacillin	0.125–1	0.5	0.5
S. aureus (methicillin resistant) (32)	Cefmenoxime	8–≥64	8	≥64
	Cefotaxime	8–≥64	32	≥64
	Moxalactam	32–≥64	≥64	≥64
	Cefoperazone	32–≥64	≥64	≥64
Streptococcus pneumoniae (10)	Cefmenoxime	≤0.01–0.06	0.03	0.03
	Cefotaxime	≤0.01–0.06	0.03	0.03
	Moxalactam	0.125–1	0.25	0.5
	Oxacillin	0.03–0.125	0.125	0.125
S. pneumoniae (penicillin resistant) (10)	Cefmenoxime	0.5–1	0.1	1
	Cefotaxime	0.5–1	0.5	1
	Moxalactam	4–≥16	≥16	≥16
	Oxacillin	4–16	≥16	≥16
S. agalactiae (8)	Cefmenoxime	≤0.01–0.06	0.01	0.06
	Cefotaxime	≤0.01–0.06	0.03	0.06
	Moxalactam	1–4	2	4
	Oxacillin	0.03–0.06	0.03	0.06
S. pyogenes (11)	Cefmenoxime	≤0.01–0.06	≤0.01	0.03
	Cefotaxime	≤0.01–0.06	0.03	0.06
	Moxalactam	1–4	2	4
	Oxacillin	0.03–0.06	0.03	0.06
S. faecalis (29)	Cefmenoxime	4–≥64	≥64	≥64
	Cefotaxime	4–≥64	≥64	≥64
	Moxalactam	4–≥64	≥64	≥64
	Oxacillin	1–≥64	≥64	≥64
Staphylococcus spp. (coagulase negative) (30)	Cefmenoxime	0.125–≥64	0.25	≥64
	Cefotaxime	0.06–≥64	0.5	≥64
	Moxalactam	1–≥64	≥16	≥64
	Oxacillin	0.125–≥64	0.5	≥64

pyogenes, which were inhibited by much lower concentrations of cefmenoxime in the study by Stamm et al. than in our study.

Our results show that this novel cephalosporin compares favorably in antibacterial activity with two others recently licensed for clinical use (cefotaxime and moxalactam) and a third that is currently undergoing clinical trials (cefoperazone). Other attributes of cefmenoxime that have been reported (3) include β-lactamase stability (except *Proteus vulgaris* β-lactamase) and inhibition of β-lactamase production by bacterial species (except *S. aureus*, *P. aeruginosa*, and *E. coli*). Its relatively poor activity against *Pseudomonas* sp. (in comparison with other gram-negative bacilli) is a potential drawback which it shares with its third-generation cephalosporin predecessors, with the possible exception of cefoperazone (1; R. N. Jones and C. Thornberry, Rev. Infect. Dis., in press). In vivo studies are needed to determine the place of cefmenoxime in clinical usage. Its in vitro activity is promising.

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