

Susceptibilities of Anaerobic Bacteria to *N*-Formimidoyl Thienamycin (MK0787) and to Other Antibiotics

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The susceptibilities of 462 clinical anaerobic bacterial isolates to *N*-formimidoyl thienamycin and 16 other currently available and investigational antibiotics were determined by the agar dilution technique. *N*-Formimidoyl thienamycin was significantly more active than the reference antibiotics against most organisms tested, especially *Bacteroides* sp., including clindamycin-resistant strains. All 462 isolates were inhibited by 4 μ g of *N*-formimidoyl thienamycin per ml, and no resistant strains were found in the species tested. *N*-Formimidoyl thienamycin was less active (i.e., had a higher 50% minimal inhibitory concentration) against *Fusobacterium* sp. than clindamycin, SM-1652, and piperacillin, and less active against *Clostridium difficile* than metronidazole, but was equally active or more active than the other reference antibiotics tested.

N-Formimidoyl thienamycin (MK0787) is a stable derivative of the novel β -lactam antibiotic thienamycin having des-thio-carbapenem as its nucleus. Preliminary studies have suggested that *N*-formimidoyl thienamycin possesses potent, broad-spectrum activity against most clinically important bacteria, including *Pseudomonas aeruginosa* (1-7). The present study was undertaken to compare the in vitro susceptibilities of 462 clinical anaerobic isolates to *N*-formimidoyl thienamycin and other available antibiotics which have useful activity against anaerobic bacteria.

Organisms. A total of 462 clinical anaerobic isolates (175 gram-positive bacteria and 287 gram-negative bacteria) were tested. The isolates were identified by previously described criteria (8) in the Institute of Anaerobic Bacteriology, Gifu University School of Medicine. Organisms were maintained in tubes containing GAM semisolid medium (Nissui Seiyaku Co.) at room temperature and were subcultured periodically onto fresh medium until the time of susceptibility testing.

Antibiotics. Standard antibiotic powders were kindly provided by the following manufacturers: *N*-formimidoyl thienamycin and cefoxitin, Merck & Co., Inc., Rahway, N.J.; clindamycin, The Upjohn Co., Kalamazoo, Mich; metronidazole, May & Baker Laboratories, Dagenham, United Kingdom; cefmetazole, Sankyo Co., Tokyo, Japan; cefotetan, Yamanouchi Pharmaceutical Co., Tokyo, Japan; moxalactam, Shionogi & Co., Osaka, Japan; cefotaxime, Hoechst-Roussel Pharmaceutical Inc., Sommerville, N.J.; ceftizoxime and cefazolin, Fujisawa Phar-

maceutical Co., Osaka, Japan; cefmenoxime, Takeda Chemical Industries, Osaka, Japan; cefoperazone and piperacillin, Toyama Chemical Co., Osaka, Japan; cefamandole, Eli Lilly & Co., Indianapolis, Ind.; SM-1652 and apalcillin, Sumitomo Chemical Co., Osaka, Japan; and carbenicillin, Taito-Pfizer Co., Tokyo, Japan.

In vitro susceptibility tests. The minimal inhibitory concentrations of the antibiotics tested were determined by the agar dilution technique, as previously described (3). Overnight cultures of test organisms were diluted to a density of approximately 10^6 colony-forming units per ml with a 0.05% yeast extract solution. A final inoculum of 10^4 cells of each strain was deposited with a metal replicator (Microplanter; Sakuma Seisakusho, Ltd.) onto brucella agar (BBL Microbiology Systems, Cockeysville, Md.) supplemented with 5% sheep blood, 10 μ g of hemin per ml, and a serial twofold dilution of each of the antibiotics. The dilutions were prepared daily in 0.01 M phosphate buffer (pH 7.0). Results were determined after 48 h of incubation at 37°C under an 80% N_2 -10% H_2 -10% CO_2 atmosphere in an anaerobic chamber (Forma Scientific).

The minimal inhibitory concentration was defined as the lowest concentration of antibiotic that produced no growth, less than five discrete colonies, or a faint haze.

Table 1 shows the in vitro activities of *N*-formimidoyl thienamycin, clindamycin, metronidazole, cefoxitin, cefmetazole, moxalactam, cefotetan, cefotaxime, ceftizoxime, cefmenoxime, SM-1652, cefazolin, cefamandole, cefoperazone, carbenicillin, piperacillin, and apalcillin against 462 clinical anaerobic isolates. *N*-Formi-

TABLE 1. In vitro activities of *N*-formimidoyl thienamycin and 16 other antibiotics against clinical anaerobic isolates

Organism	No. of strains	Antibiotic	Minimal inhibitory concn (µg/ml)				
			Range	For 50% inhibition	For 90% inhibition		
<i>Clostridium perfringens</i>	10	<i>N</i> -F-thienamycin ^a	0.016–0.125	0.031	0.063		
		Clindamycin	0.016–1	0.031	0.063		
		Metronidazole	0.25–1	0.5	1		
		Cefoxitin	0.25–2	0.5	1		
		Cefmetazole	0.125–1	0.125	0.25		
		Moxalactam	0.063–1	0.125	1		
		Cefotetan	0.016–0.25	0.125	0.25		
		Cefotaxime	0.016–1	0.125	1		
		Ceftizoxime	0.125–1	0.25	1		
		Cefmenoxime	<0.016–2	0.063	1		
		SM-1652	0.016–1	0.031	1		
		Cefazolin	0.031–1	0.125	0.5		
		Cefamandole	0.016–1	0.125	1		
		Cefoperazone	0.031–2	0.125	1		
		Carbenicillin	0.125–0.5	0.25	1		
		Piperacillin	0.016–0.5	0.063	0.25		
		Apalcillin	0.016–0.63	0.031	0.063		
		<i>Clostridium difficile</i>	34	<i>N</i> -F-thienamycin	0.5–4	2	2
				Clindamycin	0.125–>128	4	>128
Metronidazole	0.125–>128			0.25	0.5		
Cefoxitin	32–128			128	128		
Cefmetazole	8–64			32	64		
Moxalactam	64–128			128	128		
Cefotetan	8–128			16	32		
Cefotaxime	32–128			64	128		
Ceftizoxime	128–>128			>128	>128		
Cefmenoxime	16–64			32	64		
SM-1652	8–64			16	32		
Cefazolin	8–32			16	16		
Cefamandole	8–32			16	16		
Cefoperazone	16–64			32	64		
Carbenicillin	8–64			16	32		
Piperacillin	2–8			4	8		
Apalcillin	2–8			4	4		
<i>Clostridium bifermentans</i>	21			<i>N</i> -F-thienamycin	0.031–1	0.25	1
				Clindamycin	0.008–32	0.063	4
		Metronidazole	0.031–0.5	0.25	0.5		
		Cefoxitin	0.125–4	2	4		
		Cefmetazole	0.125–16	2	4		
		Moxalactam	0.5–8	4	8		
		Cefotetan	0.125–8	2	4		
		Cefotaxime	0.063–16	0.25	8		
		Ceftizoxime	0.031–128	0.5	128		
		Cefmenoxime	0.125–16	0.25	8		
		SM-1652	0.063–16	2	8		
		Cefazolin	0.125–16	4	8		
		Cefamandole	0.25–32	2	8		
		Cefoperazone	0.25–16	4	8		
		Carbenicillin	0.25–16	1	2		
		Piperacillin	0.063–4	0.5	1		
		Apalcillin	0.063–8	0.5	1		
		<i>Clostridium botulinum</i>	16	<i>N</i> -F-thienamycin	<0.016–0.25	0.063	0.125
				Clindamycin	<0.016–0.125	0.031	0.063
Metronidazole	0.031–0.5			0.125	0.5		
Cefoxitin	0.25–1			0.5	1		
Cefmetazole	0.031–0.5			0.25	0.5		
Moxalactam	0.25–4			0.5	1		
Cefotetan	0.063–0.25			0.25	0.25		
Cefotaxime	0.031–4			2	2		
Ceftizoxime	2–64			32	32		
Cefmenoxime	0.5–2			1	2		

TABLE 1—Continued

Organism	No. of strains	Antibiotic	Minimal inhibitory concn ($\mu\text{g/ml}$)				
			Range	For 50% inhibition	For 90% inhibition		
<i>Clostridium</i> spp. ^b	38	SM-1652	0.25-1	0.5	0.5		
		Cefazolin	<0.016-1	0.25	1		
		Cefamandole	0.25-0.5	0.5	0.5		
		Cefoperazone	0.125-2	1	1		
		Carbenicillin	0.125-0.5	0.5	0.5		
		Piperacillin	0.25-1	0.5	1		
		Apalcillin	0.031-0.5	0.25	0.5		
		N-F-thienamycin	<0.016-0.5	0.063	0.25		
		Clindamycin	<0.016->128	0.5	32		
		Metronidazole	0.016-2	0.25	1		
		Cefoxitin	0.125-16	0.5	4		
		Cefmetazole	<0.016-16	0.5	4		
		Moxalactam	0.063-16	2	8		
		Cefotetan	<0.016-16	0.25	2		
		Cefotaxime	<0.016-64	2	8		
		Ceftizoxime	<0.016->128	2	128		
		Cefmenoxime	<0.016-32	2	4		
		SM-1652	<0.016-32	0.5	4		
		Cefazolin	<0.016-32	0.25	1		
		Cefamandole	<0.016-64	0.5	2		
Cefoperazone	<0.016-16	1	2				
Carbenicillin	<0.016-8	0.5	4				
Piperacillin	<0.016->128	0.25	2				
Apalcillin	0.016->128	0.25	1				
<i>Peptococcus magnus</i>	18	N-F-thienamycin	<0.016-0.063	0.031	0.063		
		Clindamycin	0.063-2	0.5	0.125		
		Metronidazole	<0.016-4	0.5	1		
		Cefoxitin	0.063-2	0.5	2		
		Cefmetazole	0.063-2	1	1		
		Moxalactam	0.063-8	2	4		
		Cefotetan	0.125-4	1	2		
		Cefotaxime	0.063-8	2	4		
		Ceftizoxime	0.016-64	8	32		
		Cefmenoxime	0.031-4	1	2		
		SM-1652	0.031-8	2	8		
		Cefazolin	0.031-4	1	4		
		Cefamandole	<0.016-16	2	8		
		Cefoperazone	0.125-4	1	4		
		Carbenicillin	0.125-4	1	2		
		Piperacillin	0.031-0.5	0.25	0.5		
		Apalcillin	0.063-2	0.25	1		
		<i>Peptococcus</i> spp. ^c	21	N-F-thienamycin	<0.016-0.063	0.031	0.063
				Clindamycin	<0.016-0.5	0.063	0.125
				Metronidazole	0.125-16	0.5	2
Cefoxitin	0.031-16			0.5	8		
Cefmetazole	0.063-8			0.25	2		
Moxalactam	0.031-32			0.5	8		
Cefotetan	0.063-8			0.25	8		
Cefotaxime	0.016-4			0.5	2		
Ceftizoxime	<0.016-64			0.25	16		
Cefmenoxime	0.063-1			0.25	1		
SM-1652	<0.016-2			0.5	2		
Cefazolin	<0.016-32			0.25	1		
Cefamandole	0.031-8			0.25	4		
Cefoperazone	<0.016-8			0.5	2		
Carbenicillin	0.031-4			0.5	4		
Piperacillin	<0.016-0.5			0.125	0.5		
Apalcillin	<0.016-1			0.125	0.5		
<i>Peptostreptococcus</i> spp. ^d	17			N-F-thienamycin	<0.016-0.063	0.031	0.063
				Clindamycin	<0.016-0.25	0.063	0.25
				Metronidazole	0.125-4	0.5	4

TABLE 1—Continued

Organism	No. of strains	Antibiotic	Minimal inhibitory concn (µg/ml)				
			Range	For 50% inhibition	For 90% inhibition		
<i>B. fragilis</i>	146	Cefoxitin	0.125-1	0.5	1		
		Cefmetazole	0.063-2	0.5	2		
		Moxalactam	0.063-8	4	8		
		Cefotetan	0.063-2	2	2		
		Cefotaxime	0.063-1	0.125	1		
		Ceftizoxime	<0.016-1	0.063	1		
		Cefmenoxime	0.063-1	0.125	1		
		SM-1652	0.25-1	0.5	1		
		Cefazolin	0.25-0.5	0.5	0.5		
		Cefamandole	0.25-2	0.5	2		
		Cefoperazone	0.125-8	1	8		
		Carbenicillin	0.25-4	1	4		
		Piperacillin	0.031-0.5	0.125	0.5		
		Apalcillin	0.031-1	0.25	1		
		<i>N</i> -F-thienamycin	<0.016-0.5	0.031	0.25		
		Clindamycin	0.016->128	0.25	4		
		Metronidazole	0.25-4	0.5	1		
		Cefoxitin	2-16	4	8		
		Cefmetazole	1-128	4	16		
		Moxalactam	0.125-32	0.5	8		
		Cefotetan	0.5-64	2	4		
		Cefotaxime	0.5->128	4	64		
		Ceftizoxime	0.063-128	2	32		
		Cefmenoxime	0.125->128	4	128		
		SM-1652	1->128	8	>128		
		Cefazolin	0.5->128	16	>128		
		Cefamandole	4->128	32	>128		
		Cefoperazone	0.125->128	8	128		
		Carbenicillin	0.5->128	16	>128		
		Piperacillin	0.125->128	4	64		
		Apalcillin	2->128	16	>128		
		<i>Bacteroides thetaiotaomicron</i>	29	<i>N</i> -F-thienamycin	0.016-2	0.125	0.5
Clindamycin	0.125->128			4	>128		
Metronidazole	0.125-8			0.5	1		
Cefoxitin	8-128			16	64		
Cefmetazole	8-128			32	128		
Moxalactam	1->128			16	64		
Cefotetan	2->128			32	64		
Cefotaxime	0.5->128			32	64		
Ceftizoxime	0.5->128			16	128		
Cefmenoxime	4->128			64	128		
SM-1652	16->128			64	128		
Cefazolin	8->128			32	64		
Cefamandole	32->128			64	>128		
Cefoperazone	8->128			32	128		
Carbenicillin	16->128			32	128		
Piperacillin	4->128			16	>128		
Apalcillin	8->128			32	64		
<i>Bacteroides vulgatus</i>	15			<i>N</i> -F-thienamycin	0.016-0.5	0.063	0.5
				Clindamycin	0.125->128	0.25	>128
				Metronidazole	0.25-2	0.5	1
		Cefoxitin	0.5-8	8	8		
		Cefmetazole	2-16	8	8		
		Moxalactam	0.031-8	0.5	4		
		Cefotetan	0.25-4	4	4		
		Cefotaxime	0.016-128	2	128		
		Ceftizoxime	0.016->128	1	32		
		Cefmenoxime	0.25-128	2	64		
		SM-1652	1->128	8	128		
		Cefazolin	0.25->128	8	128		
		Cefamandole	2->128	16	>128		

TABLE 1—Continued

Organism	No. of strains	Antibiotic	Minimal inhibitory concn ($\mu\text{g/ml}$)				
			Range	For 50% inhibition	For 90% inhibition		
<i>Bacteroides ovatus</i>	11	Cefoperazone	0.25->128	8	>128		
		Carbenicillin	0.031->128	16	>128		
		Piperacillin	0.125->128	2	64		
		Apalcillin	1->128	8	>128		
		N-F-thienamycin	0.063-0.25	0.063	0.25		
		Clindamycin	0.5->128	1	>128		
		Metronidazole	0.125-2	0.5	2		
		Cefoxitin	8-32	16	32		
		Cefmetazole	64-128	128	128		
		Moxalactam	4-32	8	32		
		Cefotetan	32-64	32	64		
		Cefotaxime	16-128	32	128		
		Ceftizoxime	4-32	8	32		
		Cefmenoxime	16-64	32	64		
		SM-1652	32-128	64	128		
		Cefazolin	16-128	64	128		
		Cefamandole	64->128	128	>128		
		Cefoperazone	32-128	64	128		
		<i>Bacteroides distasonis</i>	10	Carbenicillin	32->128	64	>128
Piperacillin	8-32			8	32		
Apalcillin	16-64			16	64		
N-F-thienamycin	0.031-0.5			0.25	0.5		
Clindamycin	0.016->128			0.5	>128		
Metronidazole	0.5-1			1	1		
Cefoxitin	1-32			16	32		
Cefmetazole	2-128			16	128		
Moxalactam	0.5->128			32	>128		
Cefotetan	0.5->128			64	>128		
Cefotaxime	0.063-128			2	128		
Ceftizoxime	0.063-32			0.5	32		
Cefmenoxime	4->128			4	>128		
SM-1652	2->128			128	>128		
Cefazolin	0.5->128			16	>128		
Cefamandole	2->128			>128	>128		
Cefoperazone	2-128			16	128		
Carbenicillin	0.125->128			16	>128		
<i>Bacteroides uniformis</i>	10			Piperacillin	1->128	8	>128
		Apalcillin	1->128	16	>128		
		N-F-thienamycin	0.016-0.25	0.125	0.25		
		Clindamycin	0.125->128	2	>128		
		Metronidazole	0.25-1	1	1		
		Cefoxitin	4-16	16	16		
		Cefmetazole	8-128	32	128		
		Moxalactam	0.25-32	8	32		
		Cefotetan	2-64	32	64		
		Cefotaxime	4-64	32	64		
		Ceftizoxime	0.5-128	16	128		
		Cefmenoxime	8-64	32	64		
		SM-1652	8-64	32	64		
		Cefazolin	16-32	16	32		
		Cefamandole	32-128	64	128		
		Cefoperazone	8-64	32	64		
		Carbenicillin	8-64	32	64		
		<i>Bacteroides</i> spp. ^c	29	Piperacillin	2-32	16	32
				Apalcillin	8-64	16	64
N-F-thienamycin	<0.016-0.5			0.031	0.5		
Clindamycin	<0.016->128			0.031	4		
Metronidazole	0.125-64			1	8		
Cefoxitin	0.125-32			2	16		
Cefmetazole	0.031-64			2	16		
Moxalactam	0.125-64	2	32				

TABLE 1—Continued

Organism	No. of strains	Antibiotic	Minimal inhibitory concn ($\mu\text{g/ml}$)		
			Range	For 50% inhibition	For 90% inhibition
<i>Fusobacterium</i> spp. ^f	24	Cefotetan	0.016–64	2	32
		Cefotaxime	0.016–128	2	16
		Ceftizoxime	0.016–128	1	32
		Cefmenoxime	<0.016–128	2	16
		SM-1652	0.016–>128	2	64
		Cefazolin	0.016–>128	1	32
		Cefamandole	0.125–>128	8	128
		Cefoperazone	0.125–>128	2	64
		Carbenicillin	0.063–>128	2	64
		Piperacillin	0.063–>128	1	64
		Apalcillin	0.016–>128	8	<128
		<i>N</i> -F-thienamycin	<0.016–1	0.063	0.5
		Clindamycin	<0.016–4	0.031	1
		Metronidazole	<0.016–0.5	0.063	0.125
		Cefoxitin	<0.016–2	0.125	2
		Cefmetazole	0.016–32	0.063	1
		Moxalactam	0.016–8	1	4
		Cefotetan	<0.016–32	0.063	8
		Cefotaxime	<0.016–4	0.125	1
		Ceftizoxime	<0.016–4	0.125	4
		Cefmenoxime	<0.016–64	0.063	0.5
		SM-1652	<0.016–4	0.031	1
		Cefazolin	0.016–8	0.063	8
Cefamandole	0.016–8	0.125	4		
Cefoperazone	0.016–4	0.063	2		
Carbenicillin	0.016–32	0.125	2		
Piperacillin	<0.016–4	0.016	1		
Apalcillin	<0.016–16	0.063	4		
<i>Veillonella parvula</i>	13	<i>N</i> -F-thienamycin	<0.016–0.5	0.063	0.25
		Clindamycin	0.031–0.25	0.063	0.25
		Metronidazole	0.5–4	4	4
		Cefoxitin	0.063–16	8	16
		Cefmetazole	0.125–2	1	2
		Moxalactam	0.125–64	64	64
		Cefotetan	0.125–8	2	2
		Cefotaxime	0.031–4	0.5	4
		Ceftizoxime	0.031–4	2	4
		Cefmenoxime	0.016–1	0.5	1
		SM-1652	0.063–128	32	64
		Cefazolin	0.031–4	0.5	2
		Cefamandole	0.063–4	0.25	4
		Cefoperazone	0.016–64	16	64
		Carbenicillin	2–>128	16	128
		Piperacillin	4–>128	32	128
		Apalcillin	2–>128	128	>128

^a *N*-F-thienamycin, *N*-Formimidoyl thienamycin.

^b Includes *Clostridium sordellii* (five isolates), *Clostridium clostridioforme* (five isolates), *Clostridium sporogenes* (four isolates), *Clostridium tetani* (four isolates), *Clostridium barati* (four isolates), *Clostridium paraputrificum* (four isolates), *Clostridium novyi* (two isolates), *Clostridium subterminale* (two isolates), *Clostridium septicum* (one isolate), *Clostridium limosum* (one isolate), *Clostridium ramosum* (one isolate), and five isolates not identified more precisely than *Clostridium* sp.

^c Includes *Peptococcus prevotii* (ten isolates), *Peptococcus asaccharolyticus* (four isolates), *Peptococcus indolicus* (2 isolates), and 5 isolates not identified more precisely than *Peptococcus* sp.

^d Includes *Peptostreptococcus anaerobius* (six isolates), *Peptostreptococcus productus* (three isolates), and eight isolates not identified more precisely than *Peptostreptococcus* sp.

^e Includes *Bacteroides ruminicola* (eight isolates), *Bacteroides adolescentis* (five isolates), *Bacteroides eggertii* (three isolates), *Bacteroides bifidum* (three isolates), *Bacteroides asaccharolyticus* (two isolates), *Bacteroides melaninogenicus* (two isolates), *Bacteroides oralis* (two isolates), *Bacteroides ochraceus* (one isolate), *Bacteroides bivius* (one isolate), *Bacteroides capillosus* (one isolate), and *Bacteroides succinogenes* (one isolate).

^f Includes *Fusobacterium nucleatum* (sixteen isolates), *Fusobacterium necrophorum* (four isolates), and *Fusobacterium varium* (four isolates).

midoyl thienamycin was the most active antibiotic against the great majority of the isolates tested. The minimal inhibitory concentrations of *N*-formimidoyl thienamycin ranged from <0.016 to 4 µg/ml; 90% of the isolates were inhibited at 0.5 µg/ml. At concentrations of 0.5 µg/ml, the other reference antibiotics inhibited the following percentages of the isolates: clindamycin, 66.7%; metronidazole, 64.2%; cefoxitin, 28.3%; cefmetazole, 29.5%; moxalactam, 35.4%; cefotetan, 30.2%; cefotaxime, 26.9%; ceftizoxime, 28.1%; cefmenoxime, 29.3%; SM-1652, 25.3%; cefazolin, 33.5%; cefamandole, 31.4%; cefoperazone, 22.2%; carbenicillin, 25.1%; piperacillin, 32.8%; and apalcillin, 33.7%.

Clindamycin and metronidazole were more active than the other reference β-lactam antibiotics (except *N*-formimidoyl thienamycin) against all of the isolates tested; the 90% minimal inhibitory concentrations of clindamycin and metronidazole ranged from 0.25 to >128 and from 0.125 to 4 µg/ml, respectively. Clindamycin-resistant strains (minimal inhibitory concentration, >128 µg/ml) occurred at rates of 9.5, 35.0, and 19.4% in *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, and *Clostridium difficile*, respectively.

Cephamecins, such as cefoxitin, cefmetazole, moxalactam, and cefotetan, inhibited 90% of the *B. fragilis* strains at concentrations of 4 to 16 µg/ml. Other *Bacteroides* sp. strains were also more susceptible to cephamecins than to the cephalosporins and penicillins tested.

Penicillins, such as carbenicillin, piperacillin, and apalcillin, as well as metronidazole, were the most active reference antibiotics against the gram-positive anaerobes tested. Minimal inhibitory concentrations ranged from 0.5 to 16 µg/ml, and 90% of the isolates were inhibited at a concentration of 2 µg/ml (the exception was *C. difficile*, which required 64 µg of carbenicillin per ml). At least 64 µg of each of the penicillins per ml was required to inhibit 90% of the gram-negative isolates tested, except *Fusobacterium* sp.

Our results demonstrate that *N*-formimidoyl thienamycin has significant in vitro activity against virtually all obligate anaerobes containing strains exhibiting resistance to clindamycin. This is in agreement with the results of previous studies (2). We also demonstrated the greater activity of clindamycin and metronidazole in most species compared with the activities of the currently available and investigational β-lactam

antibiotics, such as cefoxitin, cefmetazole, moxalactam, cefotetan, cefotaxime, ceftizoxime, cefmenoxime, SM-1652, cefazolin, cefamandole, cefoperazone, carbenicillin, piperacillin, and apalcillin, as well as the greater activity of *N*-formimidoyl thienamycin compared with the activities of all of the reference antibiotics. Of particular importance is the activity of *N*-formimidoyl thienamycin against isolates exhibiting resistance to other antibiotics, especially clindamycin. Cefoxitin, cefmetazole, moxalactam, and cefotetan were more active than the other β-lactam antibiotics tested, but there were some strains of *Bacteroides* which were not inhibited, even at concentrations of 64 to 128 µg/ml, as has been demonstrated previously (T. Kesado, K. Watanabe, Y. Asahi, M. Isono, and K. Ueno, Program Abstr. Int. Congr. Chemother. 12th, Florence, Italy, abstr. no. 999, 1981).

N-Formimidoyl thienamycin exhibits potent activity against a wide variety of clinically important bacteria, including *P. aeruginosa* and *B. fragilis*. The data in a previous report (2) and our data suggest that this drug can be used in the treatment of both pure anaerobic infections and mixed anaerobic-aerobic infections.

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