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In Vitro Activity of Midecamycin, a New Macrolide Antibiotic

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Midecamycin, an acetoxy-substituted macrolide antibiotic, was tested against gram-positive and gram-negative bacteria. It inhibited the majority of streptococci, staphylococci, and strains of *Haemophilus* and *Listeria* at concentrations of <3.1 μg/ml. It was less active than erythromycin, and it failed to inhibit erythromycin-resistant isolates.

Interest in macrolide antibiotics has been rekindled by the new uses of the erythromycin for treatment of infections due to organisms such as *Legionella* spp. and *Campylobacter* spp. Erythromycin has a long history of successful use as an alternative to penicillin against many gram-positive bacteria. However, it does produce significant gastrointestinal discomfort in many adults. Midecamycin (Fig. 1) is a macrolide in which an acetoxy group is substituted on position 9 of the 16-member ring and on position 4 of the terminal sugar. It has been reported to act against some erythromycin- and josamycin-resistant bacteria (1). Midecamycin is alleged to have no bitter taste, and it can be administered orally with good absorption (1).

Midecamycin was a gift from the Central Research Laboratories of Mejii Seika Kaisha Ltd., Yokohama, Japan. Erythromycin was supplied by Abbott Laboratories, North Chicago, Ill. Methicillin and ampicillin were provided by Beecham Laboratories, Bristol, Tenn., and vancomycin was supplied by Lilly Research Laboratories, Indianapolis, Ind. All organisms had been cultured from patients hospitalized at the Columbia-Presbyterian Medical Center, New York, N.Y. Organisms had been identified by standard methods. Minimal inhibitory concentrations (MICs) of staphylococci and gram-negative species were determined with Mueller-Hinton agar by the spot inoculum method with an inoculum of 10^5 CFU. MICs of streptococci and *Listeria* sp. were determined on brain-heart agar which contained 5% sheep erythrocytes. Minimal bactericidal concentrations were determined in Mueller-Hinton broth with an inoculum of 10^5 CFU with 0.1 ml plated from clear tubes to sheep blood agar plates. The minimal bactericidal concentration was the concentration at which no growth was observed on the agar plates.

The overall activity of midecamycin is given in Table 1. It inhibited the majority of streptococci, staphylococci, and *Haemophilus influenzae* at concentrations of ≤3.1 μg/ml. *Streptococcus pneumoniae* was inhibited at concentrations of ≤0.2 μg/ml. Midecamycin also inhibited *Campylobacter jejuni* at 3.1 μg/ml. *Bacteroides fragilis* had a considerably higher MIC of 25 μg/ml, and all of the *Enterobacteriaceae* and *Pseudomonas* spp. were resistant, with MICs of >100 μg/ml. Midecamycin did not inhibit *Enterobacteriaceae* or *Pseudomonas* spp., even when the assays for the organisms shown were performed at pH 8. All five isolates of each of the following species had midecamycin MICs of >100 μg/ml: *Acinetobacter anitratum, Citrobacter diversus, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Morganella morganii, Providencia stuartii, Pseudomonas aeruginosa,* other *Pseudomonas* spp., *Serratia marcescens,* and *Shigella sonnei.*

Table 2 shows the comparative activities of midecamycin, erythromycin, and several other agents against *Listeria* spp. and staphylococci. Midecamycin was less active than erythromycin

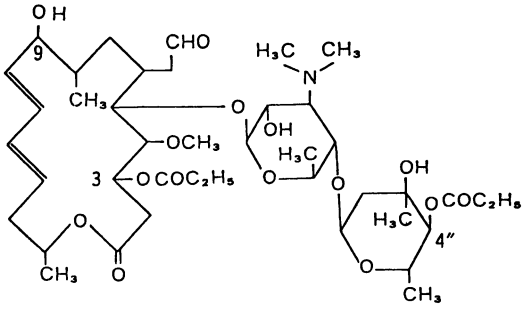

FIG. 1. Structure of midecamycin.

TABLE 1. In vitro activity of midecamycin against various microorganisms

Organism (no. of isolates)	MIC (μg/ml)[a]		
	Range	50%	90%
Bacteroides fragilis (35)	1.6–25	12.5	25
Campylobacter spp. (4)	0.8–3.1	1.6	3.1
Haemophilus influenzae (4)	0.8–3.1	1.6	3.1
Listeria monocytogenes (25)	1.6–>100	1.6	1.6
Staphylococcus aureus (48)	0.4–>100	1.6	1.6
Staphylococcus epidermidis (32)	0.4–>100	0.8	>100
Streptococcus agalactiae (5)	0.4–0.8	0.4	0.8
Streptococcus bovis (5)	0.1–0.4	0.1	0.4
Streptococcus faecalis (19)	0.8–>100	1.6	3.1
Streptococcus faecium (3)	0.8		0.8
Streptococcus mitis (3)	0.05–25	0.4	25
Streptococcus MG-intermedius (1)	0.5		
Streptococcus pneumoniae (4)	0.1–0.4	0.2	0.2
Streptococcus pyogenes (21)	0.1–1.6	0.4	1.6

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

TABLE 2. Comparative in vitro activities of midecamycin and other agents

Organism (no. of isolates)	Agent	MIC (μg/ml)[a]		
		Range	50%	90%
Listeria monocytogenes (25)	Midecamycin	0.4–>100	1.6	1.6
	Erythromycin	1.6–>100	0.2	0.2
	Ampicillin	0.8–6.3	1.6	3.1
Staphylococcus aureus (48)[b]	Midecamycin	0.4–>100	1.6	1.6
	Erythromycin	0.2–>100	0.4	1.6
	Nafcillin	0.2–>100	1.6	12.5
	Vancomycin	<0.1–6.3	1.6	3.1
Staphylococcus epidermidis (32)[b]	Midecamycin	0.4–>100	0.8	>100
	Erythromycin	0.05–>100	0.4	>100
	Nafcillin	0.1–>100	0.8	50
	Vancomycin	<0.1–6.3	1.6	6.3

[a] 50% and 90%, MIC at which 50 and 90% of the isolates, respectively, were inhibited.
[b] All strains were β-lactamase positive, and 10 *S. aureus* and 10 *S. epidermidis* strains were methicillin resistant.

against all the species. Furthermore, staphylococci and *Streptococcus faecalis* resistant to erythromycin were not inhibited by midecamycin. Erythromycin usually was two- to fourfold more active against most, but not all, isolates of staphylococci, streptococci, *H. influenzae*, and *S. pneumoniae*.

MICs were only slightly affected by increasing the inoculum size from 10^3, 10^5, and 10^7 CFU when testing either *Staphylococcus aureus* or *Staphylococcus epidermidis*. For example, MICs of 0.1 and 0.8 μg/ml at 10^3 CFU became 0.2 and either 0.8 or 1.6 μg/ml at 10^7 CFU. However, the minimal bactericidal concentrations increased from 1.6 and 3.1 μg/ml at 10^3 CFU to 100 and >100 μg/ml at 10^7 CFU.

Although midecamycin has activity similar to erythromycin against most gram-positive bacteria, in general it was less active than erythromycin in vitro in this study. We also did not find that the drug would inhibit staphylococci, streptococci, or *Listeria* spp. resistant to erythromycin, as has been reported (1). However, midecamycin has proved to be as effective as erythromycin and more protective than josamycin in mouse protection studies in which *S. aureus* was the pathogen (1). Clearly, further studies of the efficacy of midecamycin in treating human infections would be of value.

LITERATURE CITED

1. Kawajarjo, K., Y. Sekizawa, and I. Matsuhisa. 1981. The in vitro and in vivo antibacterial activity of 9,3″-di-0-acetyl midecamycin (MOM), a new macrolide antibiotic. Antibiotics 34:436–442.