In Vitro Activities of Two New Glycylcyclines, N,N-Dimethylglycylamido Derivatives of Minocycline and 6-Demethyl-6-Deoxytetracycline, against 339 Strains of Anaerobic Bacteria

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The in vitro activities of the N,N-dimethylglycylamido derivatives of minocycline (DMG-MINO) and 6-demethyl-6-deoxytetracycline (DMG-DMDOT) were compared with those of minocycline, tetracycline, clindamycin, and metronidazole by using the National Committee for Clinical Laboratory Standards-approved Wadsworth agar dilution method. The MICs of DMG-MINO, DMG-DMDOT, and metronidazole at which 90% of the strains were susceptible (0.5, 1, and 1 μ g/ml, respectively) were lower than those for clindamycin, minocycline, and tetracycline (4, 8, and 32 μ g/ml, respectively). All of the strains of anaerobes tested, except one strain of *Bacteroides ovatus* (MIC, 16 μ g/ml), were susceptible to DMG-MINO and DMG-DMDOT at 8 μ g/ml.

Two new antimicrobial agents, N,N-dimethylglycylamido derivatives of minocycline (DMG-MINO) and 6-demethyl-6deoxytetracycline (DMG-DMDOT), have been synthesized by American Cyanamid, Inc. (5). Data from the manufacturer indicate that these compounds are active against gram-positive and gram-negative aerobic and anaerobic bacteria, including those organisms carrying the most common tetracycline resistance determinants (3, 5). The purpose of this study was to evaluate the in vitro activities of these compounds against a large group of fresh clinical isolates of anaerobic bacteria.

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Antimicrobial agents were obtained as powders from the following sources: DMG-MINO, DMG-DMDOT, and minocycline were from American Cyanamid Inc., Pearl River, N.Y.; clindamycin was from Upjohn, Kalamazoo, Mich.; and metronidazole and tetracycline were from Sigma, St. Louis, Mo. All bacteria were randomly selected recent clinical isolates from the Veterans Administration Wadsworth Medical Center, Los Angeles, Calif. Bacteria were identified in accordance with established procedures (1, 4). MICs were determined by an agar dilution technique described previously by using an inoculum of 10⁵ CFU (as specified in the National Committee for Clinical Laboratory Standards guidelines [2]) and brucella base-laked blood agar. Bacteroides gracilis strains were tested on brucella base-laked blood agar with fumarate and formate (each at 0.3%) added; Bilophila wadsworthia was tested on brucella base-laked blood agar with pyruvate (1%). Plates were incubated in an anaerobic chamber (Anaerobe Systems, San Jose, Calif.) for 48 h at 37° C. The MIC was defined, in accordance with National Committee for Clinical Laboratory Standards guidelines, as the lowest antimicrobial agent concentration producing a marked change from the growth control (2). Reference strains of *Bacteroides fragilis* (ATCC 25285) and *B. thetaiotaomicron* (ATCC 29741) were used as controls in each test.

The in vitro activities of the agents tested are listed in Table 1. No breakpoints have been established for the new glycylcycline compounds; the National Committee for Clinical Laboratory Standards-approved breakpoints for clindamycin, tetracycline, and metronidazole are 4, 8, and 16 μ g/ml, respectively. DMG-MINO was more active than minocycline. The MIC of DMG-MINO at which 90% of the strains were susceptible (MIC₉₀) was as much as 7 twofold dilutions lower than the MIC₉₀ of minocycline (for *Porphyromonas* species, 0.062 and 8 μ g/ml, respectively). The MIC₉₀ of DMG-MINO for all of the anaerobes tested was 0.5 μ g/ml, compared with 8 μ g/ml for minocycline.

DMG-DMDOT demonstrated much better activity than tetracycline against most groups of organisms. For all of the strains tested, the MIC₉₀s of DMG-DMDOT and tetracycline were 1.0 and 32 μ g/ml, respectively.

The two new glycylcycline compounds demonstrated excellent activity against anaerobes. DMG-MINO, DMG-DMDOT, metronidazole, and clindamycin inhibited all of the strains of *Prevotella* species tested at 8 µg/ml, compared with 82 and 64% for minocycline and tetracycline, respectively. All 9 strains of *B. gracilis*, 16 strains of *Fusobacterium nucleatum*, 12 strains of *F. mortiferum-F. varium*, and 30 strains of *Bilophila wadsworthia* tested were inhibited by all of the antimicrobial agents at 8 µg/ml, except for tetracycline. Ten *Clostridium difficile* strains were inhibited at 8 µg/ml by DMG-MINO, DMG-DMDOT, and metronidazole but only 50% were inhibited by clindamycin, minocycline, and tetracycline. All of the strains of *B. ovatus* tested but one (MIC,

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TABLE 1. Activities of antimicrobial agents against anaerobic organisms^a

| TABLE | 1-Continued |
|-------|-------------|
|-------|-------------|

| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | anaerobic organisms ⁴ | | | | Organism (no. of strains) and | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|----------------------------|-------------------|-------------------|----------------------------------------------|----------------------|-------------------|-------------------|
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Organism (no. of strains) and antimicrobial agent | MIC range | MIC ₅₀ | MIC ₉₀ | antimicrobial agent | MIC range | MIC ₅₀ | MIC ₉₀ |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | | | | | Other Fusobacterium species (8) | 0.0(0.0.05 | 0.070 | |
| | DMG MINO | 0.062 / | 0.5 | 1 | DMG-MINU DMG DMDOT | 0.062-0.25 | 0.062 | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-MINO | 0.002-4 | 0.5 | 2 | Clindamycin | 0.002 - 1 0.062 1 | 0.125 | |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | Clindamycin | 0.002-8 0.062->32 | 0.5 | 2 | Metronidazole | 0.002-1 | 0.002 | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Metronidazole | 0.002 - 2.52 | 1 | 1 | Minogycline | 0.125-0.25 | 0.125 | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Minocycline | 0.25-2 | 8 | 8 | Tetracycline | 0.125-8 | 0.125 | |
| | Tetracycline | 0.002-10 | 32 | 64 | Tetracycline | 0.125-0 | 0.5 | |
| | Tetracycline | 0.25 04 | 52 | 04 | Bilophila wadsworthia (30) | | | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Other B fracilia aroun analias $(74)^{b}$ | | | | DMG-MINO | 0.062-0.25 | 0.125 | 0.125 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | DMC MINO | 0.062.16 | 0.25 | 1 | DMG-DMDOT | 0.062-0.25 | 0.125 | 0.25 |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG DMDOT | 0.002 - 10 | 0.25 | 1 | Clindamycin | 0.062-4 | 0.25 | 0.5 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Clindomycin | 0.002 - 10 0.062 > 32 | 0.5 | 1 Q | Metronidazole | 0.062-0.25 | 0.125 | 0.125 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | Metropidazole | 0.002 - 2.52 | 2 | 0 | Minocycline | 0.125-4 | 0.5 | 1 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Minogycline | 0.002-2 0.062-32 | 1 | 8 | Tetracycline | 0.125–16 | 0.25 | 4 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Tetracycline | 0.002 = 52 0.125 =>64 | 16 | 32 | Clostridium difficile (10) | | | |
| | Tetracycline | 0.125 > 04 | 10 | 52 | DMG-MINO | 0.062-0.5 | 0 125 | 0.25 |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | \mathbf{P} | | | | DMG-DMDOT | 0.125-1 | 0.25 | 1 |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | Bacierolaes gracuis (9) | 0.062.0.062 | 0.062 | | Clindamycin | 2->32 | 4 2 | >32 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-MINO | 0.062-0.062 | 0.002 | | Metronidazole | 0.125-1 | 0.25 | 0.25 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Clindomusin | 0.002-0.002 | 0.002 | | Minocycline | 0.125-16 | 1 | 16 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Metronidazole | 0.002 - 0.123 | 0.123 | | Tetracycline | 0.125->64 | 4 | 64 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Minocycline | 0.002-0.5 | 0.002 | | | | | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Tetracycline | 0.002-0.25 | 0.002 | | Clostridium perfringens (10) | | ~ - | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Tetracyenne | 0.002-0.5 | 0.125 | | DMG-MINO | 0.125-4 | 0.5 | 4 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | | | | | DMG-DMDOT | 0.125-4 | 0.5 | 4 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | Other Bacteroides species (12) ^c | 0.040.1 | 0.040 | 0 1 9 5 | Clindamycin | 0.062-4 | 0.25 | 2 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-MINO | 0.062-1 | 0.062 | 0.125 | Metronidazole | 0.25-2 | 0.5 | 1 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | DMG-DMDOT | 0.062-0.5 | 0.125 | 0.25 | Minocycline Tatus malin a | 0.125-32 | 0.25 | 10 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Clindamycin | 0.062-0.5 | 0.002 | 0.25 | Tetracycline | 0.125-32 | 8 | 32 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Minegraline | 0.125-4 | 0.125 | 1 | Clostridium ramosum (10) | | | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Tatragueline | 0.123 - 10 | 0.5 | 32 | DMG-MINO | 0.125-0.25 | 0.125 | 0.25 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Tetracycline | 0.23-04 | 0.5 | 52 | DMG-DMDOT | 0.125-0.5 | 0.25 | 0.5 |
| | | | | | Clindamycin | 2->32 | 4 > | >32 |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$ | Porphyromonas species (11) ^a | 0.0(0.000 | 0.0/2 | 0.0(2 | Metronidazole | 0.5–2 | 0.5 | 1 |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-MINU | 0.062-0.062 | 0.062 | 0.062 | Minocycline | 0.125-16 | 0.125 | 16 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-DMDOI Clindomusin | 0.062 - 0.125 | 0.062 | 0.125 | Tetracycline | 0.5-64 | 0.5 | 64 |
| Minocycline 0.002-0.125 0.125 0.125 DMG-MINO 0.062-0.062 0.062 Prevotella species (32)* 0.125-16 0.5 16 DMG-DMDOT 0.062-0.062 0.062 DMG-MINO 0.062-1 0.125 0.5 16 DMG-DMDOT 0.062-2 0.5 DMG-MINO 0.062-1 0.125 0.5 Minocycline 0.125-2 0.125 DMG-DMDOT 0.062-4 0.25 2 Tetracycline 0.125-2 0.125 Clindamycin 0.062-0.062 0.062 0.062 Petrostreptococcus species (25)* Minocycline 0.062-0.25 0.125 0.125 0.5 Minocycline 0.062-16 0.5 16 DMG-MINO 0.062-0.25 0.125 0.5 Tetracycline 0.125->64 1 64 Clindamycin 0.062-0.25 0.125 0.5 Minocycline 0.062-0.125 0.062 0.125 0.55 Tetracycline 0.125-64 4 32 DMG-MINO 0.062-0.125 0.125< | Metropidazale | 0.002 - 2.52 | 0.002 | 0.125 | Other Clostridium species $(5)^h$ | | | |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $ | Minocycline | 0.002-0.125 | 0.125 | 8 | DMG-MINO | 0.062_0.062 | 0.062 | |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | Tetracycline | 0.002-0 | 0.125 | 16 | DMG-DMDOT | 0.062-0.062 | 0.002 | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | Tetracycline | 0.125 10 | 0.5 | 10 | Clindamycin | 0.062-2 | 0.002 | |
| Prevoluta species (32)* 0.062-1 0.125 0.5 Minocycline 0.125-02 0.125 DMG-DMDOT 0.062-4 0.25 2 Tetracycline 0.125-32 0.125 Clindamycin 0.062-0.062 0.062 0.062 Peptostreptococcus species (25)* 0.062-0.5 0.125 0.5 Minocycline 0.062-16 0.5 16 DMG-MINO 0.062-0.5 0.125 0.5 Tetracycline 0.125->64 1 64 Clindamycin 0.062-2.32 0.125 2 Minocycline 0.062-0.125 0.062 0.125 0.25 Minocycline 0.125-64 4 32 DMG-MINO 0.062-0.125 0.062 0.125 Tetracycline 0.125-64 4 32 DMG-MINO 0.062-0.125 0.062 0.125 Tetracycline 0.125-64 4 32 DMG-DMDOT 0.062-0.125 0.062 0.125 Gram-positive rods (non-spore 6/minocycline 0.125-0.5 0.5 Tetracycline 0.125-128 4 >128 Minocycline 0.062-0.25 0.125 0.25 | D (1) (20) | | | | Metronidazole | 0.125-0.5 | 0.25 | |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$ | Prevotella species (32) | 0.0(2.1 | 0 1 2 5 | 0.5 | Minocycline | 0.125-2 | 0.125 | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-MINO | 0.062 - 1 | 0.125 | 0.5 | Tetracycline | 0.125-32 | 0.125 | |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | DMG-DMDOI Clindomusin | 0.062-4 | 0.25 | 2 | | 0.120 02 | 0.1120 | |
| Metronidazole $0.002-5$ 0.5 2 DMG-MINO $0.062-0.25$ Minocycline $0.125->64$ 164DMG-DMDOT $0.062-0.5$ 0.125 0.5 Fusobacterium nucleatum (16) $Metronidazole$ $0.062-0.125$ 0.062 0.125 1 DMG-MINO $0.062-0.125$ 0.062 0.125 0.062 0.125 0.125 0.5 DMG-MINO $0.062-0.125$ 0.125 0.25 $0.125-16$ 0.5 8 DMG-DMDOT $0.062-0.125$ 0.125 0.25 $0.125-64$ 4 32 DMG-DMDOT $0.062-0.125$ 0.125 0.25 0.125 $0.125-64$ 4 32 DMG-MINO $0.062-0.125$ 0.125 0.25 0.125 0.125 0.125 0.25 Minocycline $0.062-0.125$ 0.125 0.25 0.125 0.25 0.125 0.25 Minocycline $0.062-0.25$ 0.125 0.25 $0.062-0.5$ 0.125 0.25 Tetracycline $0.125-1$ 0.5 1 $0.062-0.25$ 0.125 0.25 DMG-MINO $0.062-0.25$ 0.125 0.25 $0.125-128$ 4 >128 DMG-MINO $0.062-0.25$ 0.125 0.25 $0.125-128$ 4 >128 DMG-MINO $0.062-0.5$ $0.125-0.5$ 0.5 $0.125-8$ $0.125-8$ $0.125-8$ DMG-MINO $0.062-0.5$ 0.5 0.5 0.5 $0.125-8$ $0.125-8$ $0.125-8$ DMG-DMDOT $0.062-0.5$ 0.5 < | Matranidazala | 0.062-0.002 | 0.002 | 0.002 | Peptostreptococcus species (25) ⁱ | | | |
| Minocycline $0.02-10$ 0.05 10 DMG-DMDOT $0.062-0.5$ 0.125 0.5 Tetracycline $0.125->64$ 164Clindamycin $0.062->32$ 0.125 2Fusobacterium nucleatum (16)Minocycline $0.062-0.125$ 0.062 0.125 1DMG-DMDOT $0.062-0.125$ 0.062 0.125 0.062 0.125 0.062 Clindamycin $0.062-0.125$ 0.062 0.125 0.125 $0.125-64$ 4 32 DMG-DMDOT $0.062-0.125$ 0.062 0.125 0.125 $0.125-64$ 4 32 Clindamycin $0.062-0.125$ 0.125 0.25 0.125 $0.062-0.5$ 0.125 0.125 $0.062-0.5$ 0.125 $0.062-0.5$ 0.125 $0.062-0.5$ 0.125 0.25 Tetracycline $0.062-0.25$ 0.125 0.25 DMG-MINO $0.062-0.5$ 0.125 0.5 $0.125-0.5$ 0.5 $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.062-0.5$ $0.125-0.5$ $0.062-0.5$ $0.125-0.5$ $0.062-0.5$ $0.125-0.5$ $0.125-0.5$ $0.062-0.6$ $0.125-0.5$ $0.125-0.5$ $0.125-0.5$ $0.062-0.6$ $0.125-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.062-0.5$ $0.052-0.5$ <td< td=""><td>Minogycline</td><td>0.002-8</td><td>0.5</td><td>16</td><td>DMG-MINO</td><td>0.062-0.25</td><td></td><td></td></td<> | Minogycline | 0.002-8 | 0.5 | 16 | DMG-MINO | 0.062-0.25 | | |
| Tetracycline $0.125-04$ 1 04 Clindamycin Metronidazole $0.062-32$ 0.125 2 Fusobacterium nucleatum (16)Minocycline $0.062-0.125$ 0.062 0.125 1 Minocycline $0.125-16$ 0.5 8 DMG-DMDOT $0.062-0.125$ 0.062 0.125 0.25 Tetracycline $0.125-64$ 4 32 Clindamycin $0.062-0.125$ 0.062 0.125 0.25 $0.125-64$ 4 32 Metronidazole $0.062-0.125$ 0.062 0.125 0.125 0.125 0.25 Metronidazole $0.062-0.25$ 0.125 0.125 0.125 0.25 Minocycline $0.062-0.25$ 0.125 0.25 0.125 0.125 0.25 Tetracycline $0.125-1$ 0.5 1 $DMG-MDOT$ $0.062-0.5$ 0.125 0.25 Tetracycline $0.125-1$ 0.5 1 $DMG-MDOT$ $0.062-0.5$ 0.125 0.25 Tetracycline $0.125-0.5$ 0.5 0.5 0.5 $0.125-0.5$ 0.5 $0.125-0.5$ DMG-DMDOT $0.062-0.25$ 0.125 0.5 0.5 0.5 0.5 $0.62-0.25$ $0.125-0.5$ 0.5 DMG-DMDOT $0.062-0.5$ $0.125-0.5$ 0.5 0.5 0.5 0.5 $0.125-0.5$ 0.5 $0.125-0.5$ DMG-DMDOT $0.062-16$ $0.125-0.5$ 0.5 0.5 $0.62-0.5$ 0.5 $0.62-0.5$ $0.125-0.5$ DMG-DMDOT $0.062-16$ $0.125-0.$ | Tetracycline | 0.002 - 10 0.125 > 64 | 0.5 | 10 64 | DMG-DMDOT | 0.062-0.5 | 0.125 | 0.5 |
| Metronidazole $0.062-2$ 0.25 1Fusobacterium nucleatum (16)DMG-MINO $0.062-0.125$ 0.062 0.125 0.125 0.125 $0.125-16$ 0.5 8DMG-DMDOT $0.062-0.5$ 0.125 0.25 0.125 0.25 $0.125-64$ 4 32 DMG-DMDOT $0.062-0.125$ 0.062 0.125 0.25 $0.125-64$ 4 32 Minocycline $0.062-0.125$ 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 $0.062-0.5$ 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.5 $0.125-1$ 0.5 1 $Metronidazole$ $0.062-0.5$ 0.125 0.5 $0.125-1$ 0.5 1 $Metronidazole$ $0.125->128$ 4 >128 minocycline $0.062-0.25$ 0.125 0.25 0.25 $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-8$ $0.125-92$ 1 32 DMG-DMDOT $0.062-4$ $0.062-4$ 0.062 4 $0.062-16$ $0.125-92$ 1 32 DMG-DMDOT $0.062-16$ $0.125-0.5$ 0.5 $0.125-0.5$ 0.5 $0.125-0.5$ $0.62-16$ $0.25-11$ $0.55-11$ DMG-DMDOT 0 | Tetracycline | 0.125-204 | 1 | 04 | Clindamycin | 0.062->32 | 0.125 | 2 |
| <i>Pusobacterium nucleatum</i> (16) Minocycline 0.125–16 0.5 8 DMG-MINO 0.062–0.125 0.062 0.125 Tetracycline 0.125–64 4 32 DMG-DMDOT 0.062–0.125 0.062 0.125 0.25 Gram-positive rods (non-spore forming) (23) ⁱ Gram-positive rods (non-spore forming) (23) ⁱ DMG-DMDOT 0.062–0.5 0.125 0.25 DMG-DMDOT 0.062–0.5 0.125 0.5 1 Start and the positive rods (non-spore forming) (23) ⁱ DMG-DMDOT 0.062–0.5 0.125 0.5 0.125 0.5 1 DMG-DMDOT 0.062–0.5 0.125 0.5 1 Start and the positive rods (non-spore forming) (23) ⁱ Minocycline 0.062–0.25 0.125 0.25 DMG-DMDOT 0.062–1 0.25 0.5 1 <i>Fusobacterium mortiferum-F. varium</i> group (12) Image of the positive rode (12) Minocycline 0.125–0.5 0.5 0.5 1 Metronidazole 0.125–8 0.125 8 DMG-DMDOT 0.062–0.25 0.125 0.5 0.5 Total (339) 1 32 Clindamycin 0.062–4 0.062 4 | | | | | Metronidazole | 0.062-2 | 0.25 | 1 |
| DMG-MINO 0.062-0.125 0.062 0.125 1etracycline 0.125-64 4 32 DMG-DMDOT 0.062-0.125 0.062 0.125 1etracycline 0.125-64 4 32 Clindamycin 0.062-0.125 0.062 0.125 0.25 Gram-positive rods (non-spore forming) (23) ⁱ 5 0.125 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.5 1 MG-MINO 0.062-0.5 0.125 1 0.062-0.5 0.125 1 1 Metronidazole 0.125-8 0.125 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | Fusobacterium nucleatum (16) | 0.0(0.0.105 | 0.040 | 0 105 | Minocycline | 0.125-16 | 0.5 | 8 |
| DMG-DMDOT 0.002-0.5 0.125 0.25 Gram-positive rods (non-spore forming) (23) ⁱ Metronidazole 0.062-0.125 0.125 0.125 0.125 DMG-MINO Minocycline 0.062-0.25 0.125 0.25 DMG-MINO 0.062-0.5 0.125 0.25 Tetracycline 0.125-1 0.5 1 DMG-DMDOT 0.062-0.2 0.125 0.25 Fusobacterium mortiferum-F. varium group (12) 0.062-0.25 0.125 0.25 DMG-DMDOT 0.062-2 0.125 1 DMG-MINO 0.062-0.25 0.125 0.25 DMG-DMDOT 0.062-2 0.125 1 DMG-MINO 0.062-0.25 0.125 0.25 DS 1 Metronidazole 0.125-8 0.125 8 DMG-DMDOT 0.125-0.5 0.5 0.5 Total (339) 0.25-32 1 32 Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.5 5 DMG-MINO 0.062-16 0.25 1 Minocycline 0.062-8 </td <td>DMG-MINO</td> <td>0.062-0.125</td> <td>0.062</td> <td>0.125</td> <td>Tetracycline</td> <td>0.125-64</td> <td>4</td> <td>32</td> | DMG-MINO | 0.062-0.125 | 0.062 | 0.125 | Tetracycline | 0.125-64 | 4 | 32 |
| Metronidazole 0.062-0.125 0.062 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.062-0.5 0.125 0.25 0.062-0.5 0.125 0.25 0.062-0.125 0.062-0.25 0.125 0.062-0.25 0.125 0.05 1 0.062-0.25 0.125 0.05 0.062-0.25 0.125 0.062-0.25 0.125 0.062-0.25 0.125 0.062-0.25 0.125 0.125 0.062-0.25 0.125 0.125 0.062-0.25 0.125 0.125 0.062-0.25 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 | DMG-DMDOI Clindomusin | 0.062-0.5 | 0.125 | 0.25 | Gram-positive rods (non-spore | | | |
| Metronidazole 0.002-0.125 0.125 0.125 0.125 0.027 Minocycline 0.062-0.25 0.125 0.25 DMG-DMDOT 0.062-0.5 0.125 0.25 Tetracycline 0.125-1 0.5 1 DMG-DMDOT 0.062-2 0.125 0.5 1 Fusobacterium mortiferum-F. varium group (12) Metronidazole 0.125-8 0.125 8 0.125 0.5 1 Metronidazole 0.125-8 0.125 8 DMG-DMDOT 0.062-0.25 0.125 0.5 0.5 Tetracycline 0.125-8 0.125 8 DMG-DMDOT 0.125-0.5 0.5 0.5 Total (339) 0.062-16 0.125 0.5 Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.5 5 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.5 0.5 DMG-MINO 0.062-16 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062 | Matranidagala | 0.062 - 0.125 | 0.002 | 0.125 | forming) (23) | | | |
| Tetracycline 0.002-0.25 0.125 0.25 DMG-DMDOT 0.062-1 0.25 0.5 1 Tetracycline 0.125-1 0.5 1 DMG-DMDOT 0.062-2 0.125 1 Fusobacterium mortiferum-F. varium group (12) Minocycline 0.125->128 4 >128 DMG-MINO 0.062-0.25 0.125 0.25 Tetracycline 0.125-8 0.125 8 DMG-DMDOT 0.125-0.5 0.5 0.5 Total (339) 0.062-16 0.125 0.5 Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.5 0.5 Total (339) 0.062-16 0.125 0.5 Minocycline 0.062-4 0.062 4 DMG-DMDOT 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.25 0.5 DMG-DMDOT 0.062-16 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062-32 0.25 1 Minocycline 0.062-8 0. | Minocycline | 0.002 - 0.123 | 0.125 | 0.125 | DMG-MINO | 0.062-0.5 | 0.125 | 0.25 |
| Function 0.125-1 0.13 1 Clindamycin 0.062-2 0.125 1 Fusobacterium mortiferum-F. varium group (12) Minocycline 0.125->128 4 >128 DMG-MINO 0.062-0.25 0.125 0.25 Tetracycline 0.125-8 0.125 8 DMG-DMDOT 0.125-0.5 0.5 0.5 Total (339) Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.5 0.5 Total (339) Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.25 0.5 DMG-DMDOT 0.062-16 0.125 0.5 Minocycline 0.062-8 0.125 8 Clindamycin 0.062-32 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062-32 0.25 1 Minocycline 0.062-16 0.5 16 Metronidazole 0.062-32 0.5 1 | Tetracycline | 0.002-0.25 | 0.125 | 0.25 | DMG-DMDOT | 0.062-1 | 0.25 | 0.5 |
| Metronidazole $0.125 > 128$ $4 > 128$ <i>Fusobacterium mortiferum-F. varium</i> Metronidazole $0.125 > 128$ $4 > 128$ group (12)DMG-MINO $0.062 - 0.25$ 0.125 0.25 DMG-DMDOT $0.125 - 0.5$ 0.5 0.5 Total (339)Clindamycin $0.062 - 4$ $0.062 - 4$ DMG-MINO $0.062 - 16$ 0.125 Metronidazole $0.125 - 0.5$ 0.25 0.5 DMG-DMDOT $0.062 - 16$ 0.125 Minocycline $0.062 - 8$ 0.125 0.5 DMG-DMDOT $0.062 - 16$ 0.25 1 Minocycline $0.062 - 8$ 0.125 8 Clindamycin $0.062 - 32$ 0.5 1 Minocycline $0.25 - 16$ 0.5 16 Metronidazole $0.062 - > 128$ 0.5 1 | Tetracycline | 0.125-1 | 0.5 | 1 | Clindamycin | 0.062-2 | 0.125 | 1 |
| Minocycline 0.125-8 0.125 8 DMG-MINO 0.062-0.25 0.125 0.25 0.25-32 1 32 DMG-DMDOT 0.125-0.5 0.5 0.5 Total (339) 0.062-16 0.125 0.5 0.5 Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.25 0.5 DMG-DMDOT 0.062-16 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062-16 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062-8 0.25 1 Tetracycline 0.25-16 0.5 16 Metronidazole 0.062->32 0.5 1 | Events a starium an artifum E annia | | | | Metronidazole | 0.125->128 | 4 > | 128 |
| group (12) Tetracycline 0.25-32 1 32 DMG-MINO 0.062-0.25 0.125 0.25 Total (339) 1 32 DMG-DMDOT 0.125-0.5 0.5 0.5 Total (339) 1 32 Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.25 0.5 DMG-DMDOT 0.062-16 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062-32 0.25 4 Tetracycline 0.25-16 0.5 16 Metronidazole 0.062->128 0.5 1 | rusouucierium monijerum-r. varium | | | | Minocycline | 0.125-8 | 0.125 | 8 |
| DMG-DMDOT 0.125 0.125 0.23 DMG-DMDOT 0.125-0.5 0.5 Total (339) Clindamycin 0.062-4 0.062 4 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.25 0.5 DMG-DMDOT 0.062-16 0.125 0.5 Minocycline 0.062-8 0.125 8 Clindamycin 0.062->32 0.25 4 Tetracycline 0.25-16 0.5 16 Metronidazole 0.062->128 0.5 1 | DMG-MINO | 0.062 0.25 | 0 125 | 0.25 | Tetracycline | 0.25-32 | 1 | 32 |
| Discription $0.122-0.5$ 0.5 0.5 10 (339)Clindamycin $0.062-4$ 0.062 4 DMG-MINO $0.062-16$ 0.125 0.5 Metronidazole $0.125-0.5$ 0.25 0.5 DMG-DMDOT $0.062-16$ 0.25 1 Minocycline $0.062-8$ 0.125 8 Clindamycin $0.062->32$ 0.25 4 Tetracycline $0.25-16$ 0.5 16 Metronidazole $0.062->128$ 0.5 1 | DMG-DMDOT | 0.002-0.23 | 0.125 | 0.23 | Tetal (220) | | | |
| Metronidazole 0.062-8 0.25 0.5 DMG-MINO 0.062-16 0.125 0.5 Metronidazole 0.125-0.5 0.25 0.5 DMG-DMDOT 0.062-16 0.25 1 Minocycline 0.062-8 0.125 8 Clindamycin 0.062->32 0.25 4 Tetracycline 0.25-16 0.5 16 Metronidazole 0.062->32 0.5 1 | Clindamycin | 0.123 - 0.3 0.062 - 4 | 0.5 | 4 | DMG MINO | 0.062.16 | 0 125 | 05 |
| Minocycline $0.062-8$ $0.125-8$ Clindanycin $0.062-32$ $0.25-4$ Tetracycline $0.25-16$ $0.5-16$ Metropidazole $0.062-32$ $0.5-14$ | Metronidazole | 0.125-0.5 | 0.002 | 05 | DMG-DMDOT | 0.062 16 | 0.125 | 0.5 |
| Tetracycline $0.25-16$ 0.5 $0.002-32$ $0.02-4$ Metropidazole $0.062-52$ 0.25 1 | Minocycline | 0.062-8 | 0.125 | 8 | Clindamycin | 0.002-10 | 0.25 | 1 |
| | Tetracycline | 0.25-16 | 0.5 | 16 | Metronidazole | 0.002-232 | 0.23 | 4 1 |

Continued

Continued on following page

TABLE 1—Continued

| Organism (no. of strains) and antimicrobial agent | MIC range | MIC ₅₀ | MIC ₉₀ |
|---------------------------------------------------|-----------|-------------------|-------------------|
| Minocycline | 0.062–32 | 0.5 | 8 |
| Tetracycline | 0.062–>64 | 4 | 32 |

^a All MICs are in micrograms per milliliter.

^b Includes 3 B. caccae, 11 B. distasonis, 1 B. eggerthii, 7 B. ovatus, 3 B. stercoris, 28 B. thetaiotaomicron, 8 B. uniformis, and 13 B. vulgatus strains.

^c Includes two *B. capillosus*, five *B. splanchnicus*, two *B. ureolyticus*, and two other *Bacteroides* species strains.

^d Includes four *Porphyromonas asaccharolytica*, two *P. endodontalis*, and four *P. gingivalis* strains and one other *Porphyromonas* species strain.

^e Includes four Prevotella bivia, one P. buccae, two P. corporis, two P. denticola, one P. disiens, eight P. intermedia, five P. loeschii, and five P. melaninogenica strains; one P. oralis, one P. oris, and one P. zoogleoformans strain; and one other Prevotella species strain.

^f Includes three F. necrophorum, one F. gonidiaformans, one F. necrogenes, and three other Fusobacterium species strains.

 ^{g}C . difficile is of interest primarily in relation to antimicrobial agent-induced pseudomembranous colitis. These data must be interpreted in the context of the level of the drug achieved in the colon and the impact of the agent on indigenous colonic flora.

^h Includes two C. innocuum strains and one C. bifermentans, one C. sordellii, and one other Clostridium species strain.

ⁱ Includes six Peptostreptococcus micros, five P. magnus, four P. prevotii, four P. asaccharolyticus, three P. anaerobius, and three other Peptostreptococcus species strains. ^j Includes three Actinomyces israelii, three A. odontolyticus, one other Actino-

myces species, one Eubacterium alactolyticum, three E. lentum, two E. limosum, one other Eubacterium species, two Lactobacillus catenaforme, two L. minutus, one other Lactobacillus species, and four Propionibacterium acnes strains. 16 µg/ml) were inhibited at ≤ 8 µg/ml by both DMG-MINO and DMG-DMDOT. The utility of these compounds for therapy of anaerobic infections merits further investigation.

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