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NOTES

In Vitro Activity of Cinoxacin, an Organic Acid Antibacterial

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The activity of cinoxacin, a synthetic organic acid antimicrobial agent, was studied and found to have in vitro activity similar to that previously reported for nalidixic acid.

The present studies were performed to assess the in vitro antibacterial activity of cinoxacin (Lilly compound 64716), a new synthetic organic acid antibacterial agent (4).

Antibacterial activity was determined by antibiotic dilution methods performed in Nutrient (Difco) and Mueller-Hinton (Difco) agar and broth. Studies in agar were performed by use of a Steers replicator device (3). The methods for performing the agar and broth dilution tests were described previously by this laboratory (1, 2). A total of 150 isolates of *Enterobacteriaceae* and 30 strains of *Pseudomonas aeruginosa* were studied.

The cumulative percentage of 30 isolates each of *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Proteus mirabilis*, indole-positive *Proteus*, and *P. aeruginosa* susceptible to increasing concentrations of cinoxacin is shown in Fig. 1 and 2, which also summarize the effects of medium and inoculum size on the antibacterial activity of this compound in agar. The results of these studies performed in agar demonstrate that cinoxacin was active against most *Enterobacteriaceae* and, with the exception of some strains of *Enterobacter*, increasing the size of the inoculum 100-fold exerted little effect on the overall activity of cinoxacin in agar. Against all genera, cinoxacin was more active in Nutrient than in Mueller-Hinton agar. Although strains of *P. aeruginosa* were more resistant in agar to cinoxacin than were *Enterobacteriaceae*, approximately 80% of strains were inhibited by 100 μg or less of cinoxacin per ml when tested in Nutrient agar.

Figures 3 to 6 summarize the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) activity of cinoxacin against 150 *Enterobacteriaceae* and 30 isolates of *P. aeruginosa* tested in broth medium with two inoculum sizes of bacterial

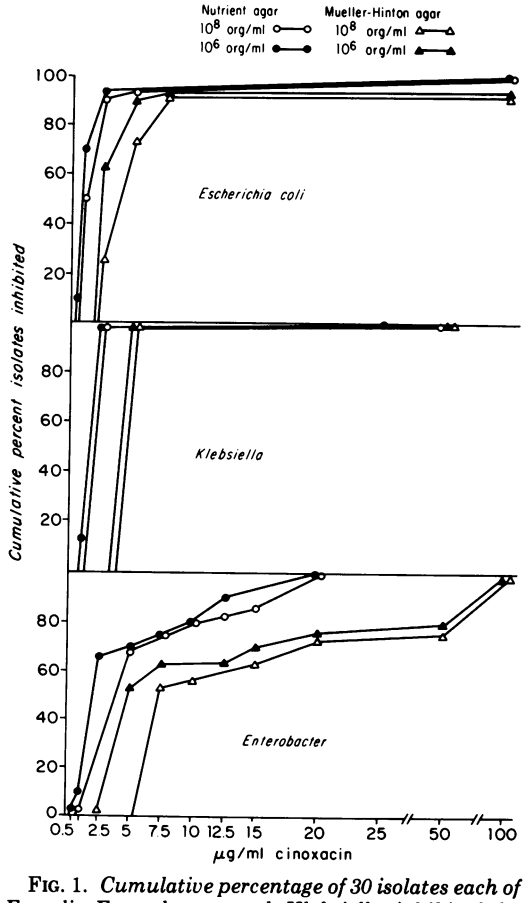

FIG. 1. *Cumulative percentage of 30 isolates each of E. coli, Enterobacter and Klebsiella inhibited by increasing concentrations of cinoxacin tested in agar medium with bacterial inocula of two different sizes.*

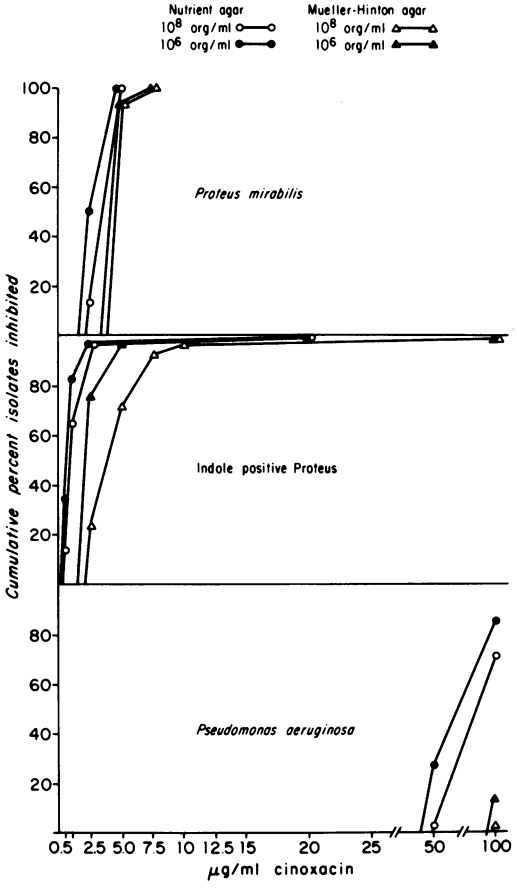

FIG. 2. *Cumulative percentage of 30 isolates each of indole-positive Proteus, P. mirabilis, and P. aeruginosa inhibited by increasing concentrations of cinoxacin tested in agar medium with bacterial inocula of two different sizes.*

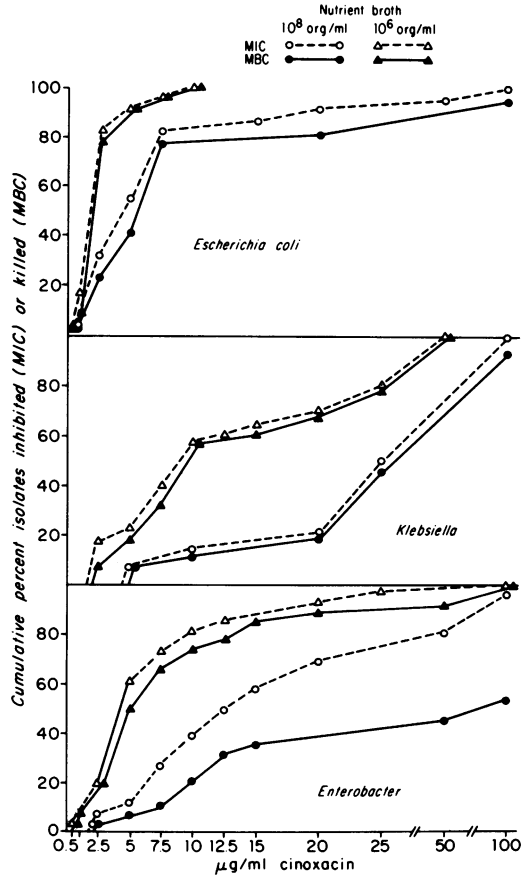

FIG. 3. *Cumulative percentage of 30 isolates each of E. coli, Enterobacter, and Klebsiella inhibited (MIC) or killed (MBC) by increasing concentrations of cinoxacin tested in Nutrient broth medium with bacterial inocula of two different sizes.*

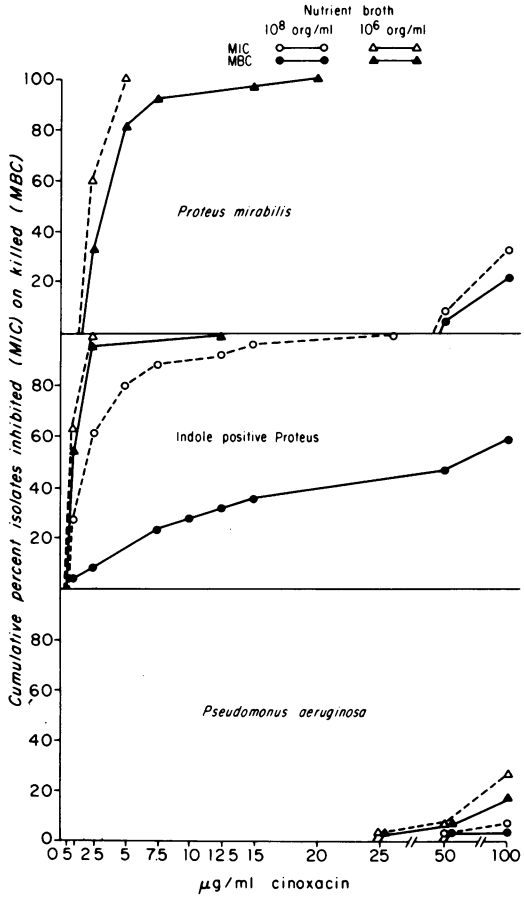

FIG. 4. *Cumulative percentage of 30 isolates each of indole-positive Proteus, P. mirabilis, and P. aeruginosa inhibited (MIC) or killed (MBC) by increasing concentrations of cinoxacin tested in Nutrient broth medium with bacterial inocula of two different sizes.*

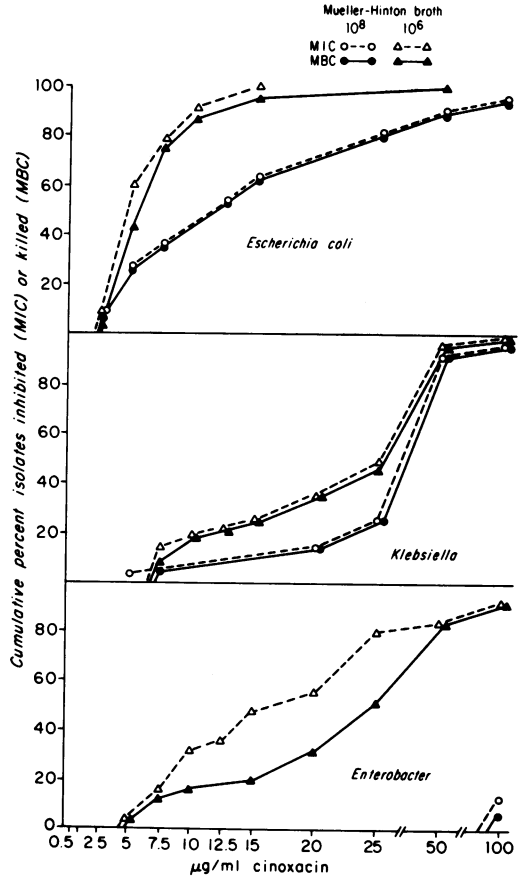

FIG. 5. *Cumulative percentage of 30 isolates each of E. coli, Enterobacter, and Klebsiella inhibited (MIC) or killed (MBC) by increasing concentrations of cinoxacin tested in Mueller-Hinton broth medium with bacterial inocula of two different sizes.*

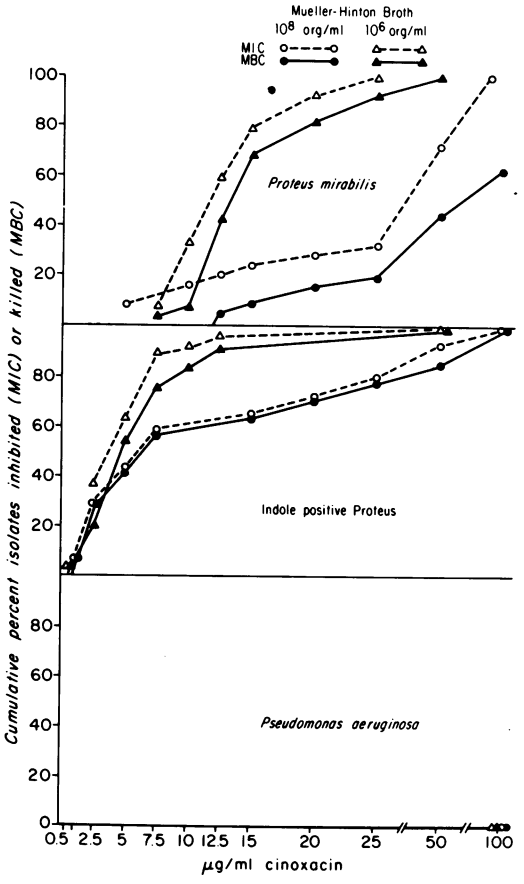

FIG. 6. *Cumulative percentage of 30 isolates each of indole-positive Proteus, P. mirabilis, and P. aeruginosa inhibited (MIC) or killed (MBC) by increasing concentrations of cinoxacin tested in Mueller-Hinton broth medium with bacterial inocula of two different sizes.*

cells. Against all genera, cinoxacin appeared less active in broth than in agar. This difference was most apparent with strains of *P. aeruginosa*, and most strains survived in 100 μg of cinoxacin per ml. In addition, studies of antibacterial activity performed in broth were influenced more by the size of the inoculum. This was most marked with isolates of *P. mirabilis* in Nutrient broth. For example, whereas 100% of isolates were inhibited by 5 μg or less of cinoxacin per ml when tested against an inoculum of 10^6 organisms per ml, less than 40% of these same strains were inhibited by 100 μg/ml when tested against 10^8 organisms per ml. In general, most strains were more susceptible to cinoxacin in Nutrient than in Mueller-Hinton broth, and there was close agreement between results of inhibitory (MIC) and bactericidal (MBC) tests of antibacterial activity. However, when tested against the larger inoculum size of bacterial cells, strains of *Proteus* appeared more susceptible in Mueller-Hinton broth.

The activity of cinoxacin mimics that reported previously from our laboratory with nalidixic acid (2). One of the problems with nalidixic acid is the appearance of resistant mutants when this compound is used to treat patients with bacteriuria. Controlled clinical studies with cinoxacin will be necessary to determine whether any therapeutic advantages will occur because of the increased levels of active drug reported in the urine with cinoxacin (4).

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