ACTIVITY OF NITROFURANTOIN AND NIFURATEL AGAINST ANAEROBIC GRAM-NEGATIVE BACILLI

SIR,—Fusidic acid 1 and metronidazole 2 have, perhaps unexpectedly, been found to be active in vitro against non-sporing gram-negative anaerobic bacteria. However, it is becoming more widely appreciated that demonstrating in-vitro activity is only the first step in clinical application of new antimicrobial agents. Subsequent work must show not only that blood-levels exceed the minimum inhibitory concentration (M.I.C.) for the organism being tested but also that adequate concentration can be achieved at the site of infection.

Metronidazole has been very successful in protozoal infections, and in view of the close similarity between the nitroimidazoles (of which metronidazole is the most familiar example) and the nitrofurans, we thought it would be worth testing the activity of two nitrofurans against a representative selection of the more commonly encountered gram-negative anaerobic bacilli.

73 strains were tested; 24 were reference strains, the remainder were clinical isolates. All were either Bacteroides spp. or Fusobacterium spp. Strains were incubated for 22 hours at 37°C in liquid thiglycollate medium (B.B.L.; supplemented with yeast extract (1%), haemin (5 μg. per ml.) and menadione (0-5 ng. per ml.). Such cultures were diluted 1/500 in sodium phosphate buffer (0-06M, pH 7) containing 0-03% cysteine hydrochloride, and these dilutions used as inoculum. Nitrofurantoin (sodium salt) was dissolved in water, and nifuratel (' Magmilor ') was dissolved in dimethyl sulphoxide; various amounts of each solution were added to plates to give the desired dilutions. The medium used was brucella agar (B.B.L.) supplemented with lysed horse blood (5%), haemin (5 g. per ml.) and menadione (0-5 μg. per ml.). 3 μl. volumes of inoculum were placed on each plate by means of a multiple inoculating device.3 Plates were incubated for 42 hours at 37°C using the 'Gaspak' system (B.B.L.; 90% hydrogen and 10% carbon dioxide), and the remainder were cultured with over 90% of these organisms tested in the laboratory.

Our results are shown in the accompanying table. Mean M.I.C.s were: nitrofurantoin 7-7 (μg. per ml.), nifuratel ≤0-28 (μg. per ml.). Thus, it is clear that nifuratel is much more active than nitrofurantoin against anaerobic gram-negative bacilli. A similar observation has been made for aerobic bacteria.4 The only other report we have seen on the activity of nitrofurans against anaerobic organisms is that by Schoutens et al.,5 who found that nitrofurantoin was inhibitory at 6-26 (μg. per ml.) to several strains of Staphylococcus aureus, and to some strains of Proteus mirabilis and E. coli. This in-vitro effect has been reported in Germany, Japan, and France 1-3 with nalidixic acid but not as far as we are aware with oxolinic acid. Although antagonism may not occur in vivo, it would seem inadvisable to treat Proteus, klebsiella, and non-lactose-fermenting coliform urinary-tract infections with oxolinic acid and nitrofurantoin concurrently, since the inhibitory effect has been observed with over 90% of these organisms tested in the laboratory.

---

**Table:**

<table>
<thead>
<tr>
<th>No. of strains inhibited by indicated concentration (μg. per ml.)</th>
<th>≤0-25</th>
<th>0·5</th>
<th>1·0</th>
<th>2·0</th>
<th>4·0</th>
<th>8·0</th>
<th>16·0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifuratel</td>
<td>63</td>
<td>8</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Nitrofurantoin (N) inhibiting action of oxolinic acid (O) on Proteus mirabilis.

---

**References:**