UNIQUE BACTERICIDAL RESPONSE OF *PSEUDOMONAS AERUGINOSA* TO DR-3355, THE *S*-(-)ISOMER OF OFLOXACIN

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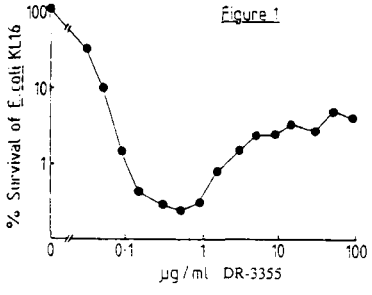
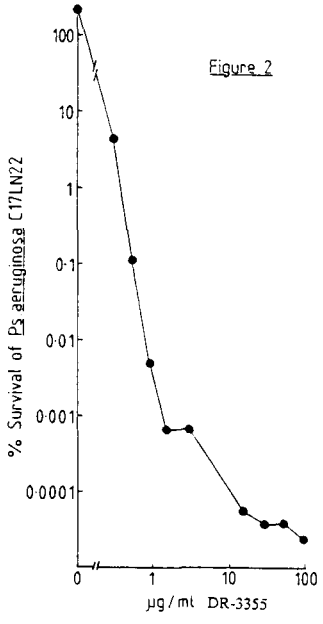
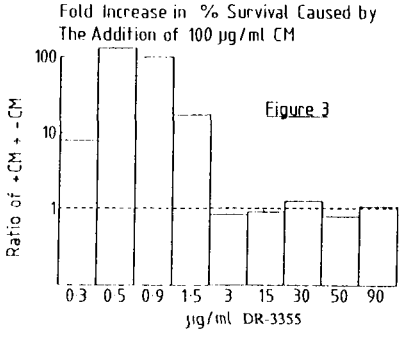
All quinolones possess a bactericidal mechanism termed A, which requires active RNA and protein synthesis for its activity. Some quinolones possess an additional mechanism, termed B, which requires neither RNA nor protein synthesis for its activity. Therefore it is possible to abolish mechanism A by inhibiting RNA or protein synthesis. Bacteria treated in nutrient broth (NB) with quinolones until now have displayed a paradoxical biphasic response (Smith 1984), which occurs because these drugs at high concentrations commence to inhibit RNA and protein synthesis (Crumplin, Smith 1975) thereby antagonising their own mechanism A. An example of this response is shown in Fig.1, where E.coli at an initial inoculum size of about 10^7 bacteria mL^{-1} was treated with a range of DR-3355 [S-(-)ofloxacin] concentrations for 1h at 37°C in NB.







When DR-3355 was tested against Ps.aeruginosa at an initial inoculum size of about 10^7 bacteria mL^{-1} in NB for 1h at 37°C (Fig.2) much more death occurred than that seen with E.coli. In addition, very surprisingly, a biphasic response was absent with the Pseudomonas (Fig.2). This peculiar behaviour was investigated by repeating the experiment in the presence of a bacteriostatic concentration of chloramphenicol (CM) and much less kill was seen up to about 1.5µg mL^{-1} DR-3355 than observed in NB alone (Fig.3). However, at concentrations above 1.5µg mL^{-1} there was no significant difference in % survival with or without CM. Therefore below about 1.5µg mL^{-1} DR-3355 exhibited both mechanisms A and B, but mechanism A was absent at higher concentrations. These findings explain why a biphasic response did not occur with Ps.aeruginosa treated with DR-3355 because only mechanism B was present at high concentrations with this species. This conclusion may explain why high concentrations of DR-3355 were much more bactericidal against Ps.aeruginosa than against E.coli.

Crumplin G.C., Smith J.T. (1975) Antimicrob. Agents Chemother. 8:251-261
Smith J.T. (1984) Pharm. J. 233:299-304.