

size distributions in penicillin treated cultures partially inhibited by these agents and in control cultures treated with penicillin alone were followed for periods of up to 3 h.

The cells in cultures of *E. coli* treated with isopropyl or benzyl alcohols and of *Ps. aeruginosa* treated with gentamycin all increased in size with time but at rates slower than in control cultures; the coefficients of variation of the size distributions remained virtually constant. These results indicate that these agents act by uniformly slowing the growth rates of all cells in cultures as reported for the action of phenol, chloramphenicol and tetracycline against *E. coli*, (Rye & Wiseman, 1968).

In penicillin treated cultures partially inhibited by the other agents studied, cell size distributions widened with time and each slowly resolved into a bimodal distribution corresponding to two populations of cells one having a mean size similar to that of the cells at the commencement of the experiment and the other similar to that of cultures treated with penicillin alone for an equivalent time. All these membrane active agents thus partially inhibit cultures by completely arresting the growth of some of the cells whilst allowing the remainder to grow at an unhindered rate in a manner analogous to that previously reported for cetyltrimethylammonium bromide (Rye & Wiseman, 1968).

REFERENCE

RYE, R. M. & WISEMAN, D. (1968). *J. Pharm. Pharmac.*, **20**, 697-703.

Enhancement of lincomycin activity against *E. coli* by alcohols

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Lincomycin is active against most Gram-positive and some Gram-negative organisms with a minimum inhibitory concentration (MIC) of about $3 \mu\text{g ml}^{-1}$ but not against *Escherichia coli* or *Pseudomonas aeruginosa*, because it cannot penetrate the cell envelope. Richards & McBride (1973) have shown that benzyl, 2-phenylethyl and 3-phenylpropyl alcohols enhance the activity of benzalkonium chloride and chlorhexidine acetate against *P. aeruginosa*.

The effect of various aliphatic and aromatic alcohols on *E. coli* was assessed by measurement of the growth rates of nutrient broth cultures containing subinhibitory concentrations of the alcohols and determination of the MIC as described by Richards & McBride (1973). The results obtained ranked the alcohols in order of effect as phenylpropyl > phenylethyl > benzyl > n-amyl > n-butyl > n-propyl > ethyl > methyl. Concentrations of lincomycin greater than $100 \mu\text{g ml}^{-1}$ had a significant effect on the growth rate of log phase cultures of *E. coli*, but the MIC could not be determined because growth occurred in medium containing $600 \mu\text{g ml}^{-1}$ (highest concentration used) of lincomycin.

The effects of combinations of the various alcohols and lincomycin were evaluated by determination of the growth rate of *E. coli* in media containing single chemicals as well as combinations. The effect of the chemical was measured as the percentage decrease in the growth rate of the organism in the presence of the chemical compared with that of the control culture containing no chemical. When the effects of the alcohols and lincomycin estimated as single chemicals were added, the sum was less than the effect of the combination determined experimentally, indicating that the combination had a greater than additive or synergistic effect. The difference between the experimental effect and the summed individual effects varied with the alcohol used in the combination in the same ranking order as for the MIC.

In summary, the enhancing effect of the aromatic alcohols on the activity of antibacterials is also shown by the aliphatic alcohols. The enhancement may be due to the antibacterial being able to penetrate the bacterial cell more readily in the presence of the alcohol.

REFERENCE

RICHARDS, R. M. E. & MCBRIDE, R. J. (1973). *J. pharm. Sci.*, **62**, 585-587.