

## THE EFFECT OF UREA ON THE ACTIVITY OF SOME ANTIMICROBIAL COMPOUNDS

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Enhanced antibacterial activity of nitrofurantoin (Paul & others, 1967) and penicillin (Kalmanson & others, 1965) has been shown in the presence of urea. This present work was an investigation of other combinations of antimicrobials and urea with their application in topical preparations in mind.

Using a doubling dilution method with tryptone soya broth to determine bacteriostatic concentrations (M.I.C.) of compounds singly and in combination with urea, the presence of urea was found to enhance the antibacterial activity to differing extents with different compounds (Table 1).

Table 1. Activity of some antimicrobials alone and in combination with urea against Pseudomonas aeruginosa NCTC 7244 and Staphylococcus aureus NCTC 4163.

Compound	<u>Ps.aeruginosa</u>		<u>Staphylococcus aureus</u>	
	MIC w/out urea	MIC with 5% w/v urea	MIC w/out urea	MIC with 10% w/v urea
Benzalkonium chloride	$1.25 \times 10^{-2}\%$	$4.7 \times 10^{-3}\%$	$3.0 \times 10^{-4}\%$	$2.5 \times 10^{-5}\%$
Chlorhexidine gluconate	$1.0 \times 10^{-2}\%$	$2.5 \times 10^{-3}\%$	$1.57 \times 10^{-4}\%$	$7.9 \times 10^{-5}\%$
Polymixin	62.5u/ml	31.3u/ml	5000 u/ml	31.3u/ml
Neomycin sulphate	$1.0 \times 10^{-1}\%$	$4.0 \times 10^{-4}\%$	$3.13 \times 10^{-3}\%$	$7.5 \times 10^{-5}\%$
Tetracycline Hydrochloride	$5.0 \times 10^{-3}\%$	$5.0 \times 10^{-3}\%$	$2.0 \times 10^{-2}\%$	$7.9 \times 10^{-5}\%$
Urea	M.I.C. 8%w/v		M.I.C. 16%w/v	

The apparent enhanced activity seen from Table 1 could not be reproduced when combinations of urea and antimicrobial were tested by a cup plate diffusion method. This could have been due to lack of diffusion of the urea, which was unlikely; it is more probable that a very marked concentration gradient existed from the cup outwards and the concentration of urea in the agar fell almost immediately below the inhibitory concentration against the test organism. Thus an aqueous solution of 20% urea alone produced no inhibition against either Staph.aureus or Ps.aeruginosa. However, the potentiation could be seen if urea was included in the seeded agar. (Table 2).

Table 2. Neomycin Sulphate. Inhibition zones on agar plates, with and without urea, seeded with 0.3 ml. Ps.aeruginosa 24 hr broth culture

Antimicrobial soln.	Zones of inhibition	
	Agar without urea	Agar with 5% urea
Neomycin sulphate 0.05%	20.0 mm	42.0 mm

The apparent enhanced activity of antimicrobial in the presence of urea could be an additive effect of the activities of the urea and the other compound in the combination or perhaps synergism of one compound by the other. The use of urea with antimicrobials, as has been seen with urea/corticosteroid combinations, has potential in the topical field providing (a) sufficiently high concentrations of urea can be achieved in the immediate environment and (b) a suitable base can be employed to stabilise the urea in a non-stinging preparation (Laurberg 1975). Such stabilisation has been achieved using a matrix technique (B.P. 1 468 815). The presence of the urea would not only enhance the activity of the antimicrobial but should also aid its percutaneous penetration (Ayres, 1977) and therefore improve its efficacy against deep seated infections.

Ayres, P.J. Ichthyosis (1977), M.T.P. Press.

British Patent No. 1 468 815.

Kalmanson, G.M., Montgomerie, J.Z. Guze, L.B. (1965) Antimicrob. Ag. Chemother. p. 384-6.

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