THE ANTIBACTERIAL ACTIVITY OF DIMETHOXANE

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Dimethoxane, 6-acetoxy-2,4-dimethyl-1,3-dioxane, is a preservative used mainly in cosmetic formulations. It is claimed to remain concentrated in the aqueous phase of two-phase systems and to exert a broad-spectrum bactericidal action which is unaffected by such factors as pH of the system and the presence of non-ionic surfactants(Gump and Walter, 1964). Recently, commercial dimethoxane has been shown to consist largely of two 1,3-dioxane isomers, together with small amounts of aldehyde contaminants, acetaldehyde and crotonaldehyde(Woolfson and Woodside, 1976). In this study, the antibacterial activity of dimethoxane has been assessed with a view to its possible application to the preservation of pharmaceutical systems.

MIC values for dimethoxane against various organisms were determined by serial dilution in broth. Results are given in Table 1.

Organism	MIC $\mu g\ cm^{-3}$
P.aeruginosa NCTC 6750	500
E.coli 15TAU NCIB 10430	750
Staph. aureus NCTC 6571	1000

Time-survival studies with autoclaved dimethoxane(10^{-3} g cm^{-3}) against P.aeruginosa indicated a markedly slow bactericidal effect, a similar result being obtained with the other organisms.In general, a 99.9% kill required 160 minutes, reducing to about 100 minutes when the concentration of aqueous dimethoxane was increased to 10^{-2} g cm^{-3}. Solutions sterilised by filtration showed much weaker cidal activity, producing no effective kill within the time of the experiment. Although the activity of dimethoxane was found to be largely unaffected by change in pH or the presence of non-ionic surfactants, inactivation occurred in the presence of tris buffer(irrespective of pH), glutamate(0.5% w/v) and albumin(0.5% w/v).

Addition of dimethoxane to a log phase culture of P.aeruginosa resulted in an immediate cessation of growth, as indicated by turbidimetric measurements. This is in contrast to the result of Brown(1966), who reported a marked fall in the optical density of a P.aeruginosa suspension when treated with dimethoxane. This was attributed to dimethoxane-induced lysis. That lysis does not occur with dimethoxane was confirmed in this study by leakage experiments using tritiated glucose and by observations on the optical density of spheroplasts of E.coli. Thus, there is an apparent differentiation between the slow bactericidal and rapid bacteriostatic action of dimethoxane. An explanation for this behaviour may be found in the stability of dimethoxane in aqueous solution, where hydrolysis of the 1,3-dioxane ring results in an increase in the aldehyde concentration of the solution (Woolfson, A.D. Unpublished Data). The differential activity of dimethoxane may therefore result from the presence in aqueous solution of both aldehyde and 1,3-dioxane fractions.

Brown, M.R.W. (1966). J. Soc. Cosmet. Chem., 17, 185-195.
Gump, W.S. and Walter, G.R. (1964). German Patent 1, 171, 110.
Woolfson, A.D. and Woodside, W. (1976). J. Pharm. Pharmac., 28, 28P.