

THE ANTIBACTERIAL ACTION OF A SERIES OF 4-N-ALKYLPHENOLS

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Phenols are known to interact with the bacterial cytoplasmic membrane and promote cytoplasm leakage (Judis 1962; Kaye and Proudfoot 1971). More recent studies into the role of the bacterial membrane in energy generation (development of a proton motive force and ATP synthesis) and the effect of antimicrobial agents thereon (Hugo 1976) have provided us with a focus for the closer scrutiny of the mode of action of phenols, perhaps with the opportunity to determine their prime site of action.

In this communication we report the action of phenol and some 4-n-alkylphenols on energy generation and coupling within the bacterial cell.

Following evidence that 4-ethylphenol could increase the permeability of the bacterial membrane to protons (Hugo and Bowen 1973) initial studies using *S. aureus*, 4×10^9 cells ml⁻¹, were undertaken to compare the effect of phenol, 4-ethylphenol and 4-n-propylphenol on the trans-membrane proton flux. The results are tabulated below.

Table. The effect of three phenols on proton flux across the membrane.

Compound \ Effect	Minimum growth inhibitory conc.	Proton translocation rate (ng ion H ⁺ /min/4x10 ⁹ cells)
Phenol	50.00 mM	9.25
4-ethylphenol	8.30 mM	12.00
4-n-propylphenol	2.64 mM	17.50

As seen from this table, proton translocation was found to be most marked with 4-n-propylphenol which also stimulated respiration, inhibited ATP synthesis and stopped active transport. Work has been further extended to examine the response of *E. coli* to an homologous series of 4-n-alkylphenols (C₁ - C₆) using the same experimental systems.

An overall appraisal of all the results so far obtained point to a common site of action for the 4-n-alkylphenols, namely the collapse of the proton motive force by the inward drug-induced translocation of protons, the final manifestation of which is the onset of bacteriostasis.

Judis, J. (1962) *J. Pharm. Sci.* 51 261-265

Kaye, R.C. and Proudfoot, S.G. (1971) *J. Pharm. Pharmac.* 23, 223S

Hugo, W.B. (1976) *Symp. Soc. Gen. Microbiol.* 26, 383-413

Hugo, W.B. and Bowen, J.G. (1973) *Microbios* 8, 189-197