# THE MODE OF ACTION OF TETRADECYLTRIMETHYL AMMONIUM BROMIDE (CTAB) ON STAPHYLOCOCCUS AUREUS

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The antimicrobial effect of cationic surface active agents has been attributed to a change in membrane permeability causing leakage of essential small molecular weight metabolites (Salton, 1951; Lambert and Hammand, 1973).

Mitchell's chemiosmotic hypothesis (Mitchell, 1966) has done much to illuminate the vital metabolic function of the membrane at the molecular level. It states that, during respiration or adenosine triphosphate (ATP) hydrolysis, protons are extruded across the $H^+$-impermeable membrane producing a proton gradient. The electrochemical potential $\bar{\mu}_{H^+}$ of the proton then powers the process of active transport and completes the coupling of respiration to energy-dependant uptake.

It seemed worthwhile, therefore, to investigate the effect of membrane active substances on $\bar{\mu}_{H^+}$.

$\bar{\mu}_{H^+}/F$, the electrochemical potential in electrical units ($\Delta p$ or proton motive force in Mitchell's nomenclature) is resolvable into two components, one osmotic, $-Z\Delta pH$, and one electrical, $\Delta\Psi$ (Nernst or membrane potential), and $\Delta p = \Delta\Psi - Z\Delta pH$

Using S. aureus, $4 \times 10^9$ cells $ml^{-1}$, the effect of CTAB on the membrane permeability to protons was investigated by the method of Gilby and Few (1958), when it was shown that the pH gradient, artificially induced by adding a pulse of protons to the suspending fluid, was discharged at a CTAB concentration of 18 $\mu g\ ml^{-1}$. This concentration also caused maximum leakage of 260 nm - absorbing material, the complete hydrolysis of ATP reserves, and was the minimum inhibitory concentration for growth. Maximum inhibition of glucose oxidation, as measured using the Warburg respirometer, occurred at a concentration of 10 $\mu g\ ml^{-1}$

The organism is able to withstand the assault of lower concentrations, 7.5 $\mu g\ ml^{-1}$, of the drug for, although the permeability of the membrane to protons suffers some increase, the organism is still able, at this concentration of CTAB, to hydrolyse ATP to maintain its proton gradient and thereby continue its metabolic activity. With increasing inhibition of glucose oxidation, however, ATP reserves are soon exhausted with the subsequent collapse of the pH gradient. Higher concentrations i.e. $<18\ \mu g\ ml^{-1}$ of CTAB, produce rapid death probably as a result of precipitation of cytoplasmic constituents.

It is suggested that cationic surface active agents can induce a prime metabolic lesion, the collapse of the proton motive force, by a mechanism similar in effect if not in nature to that of the classical uncoupling agents and the loss of cell constituents and some glucose oxidising activity are secondary consequences of this lesion.

F = Faraday constant; Z = 2.303 RT/F

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