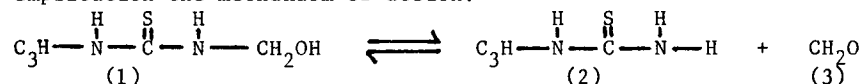


CLINICAL IMPLICATIONS OF THE MICROBIAL ANTI-ADHERENCE PROPERTIES OF NOXYTHIOLIN

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Noxythiolin is a broad spectrum antimicrobial compound available as a dry powder for reconstitution to form a 1% prophylactic or 2.5% therapeutic solution for irrigation of accessible body cavities and body surfaces. The mode of action of noxythiolin has not been clearly defined, but because of the slow release of formaldehyde on reconstitution of the powder, noxythiolin has been labelled a "masked formaldehyde compound" encompassing by implication the mechanism of action.



The release of formaldehyde (3) and N-methylthiourea (2) from noxythiolin solutions has been measured under a variety of conditions in an attempt to correlate this data with antimicrobial activity (McCafferty *et al* 1984 and Woolfson *et al*, in press). However, it has been shown that concentrations of formaldehyde equivalent to those in noxythiolin solutions possessed less antimicrobial activity. Furthermore, neither N-methylthiourea alone nor in combination with formaldehyde could explain this discrepancy in bactericidal action suggesting a more complex mode of action for noxythiolin than previously thought.

The initial stage of infection may be associated with adherence of the organism to epithelial surfaces (King *et al* 1980), thus the anti-adherence capacities of noxythiolin and formaldehyde were investigated. Buccal or uroepithelial cells (approx. 10^5 cells/ml) in PBS were incubated for 2 hrs at 37°C with the microorganism (10^7 cells/ml) pretreated with noxythiolin or formaldehyde. The number of adherent organisms per cell (min. cell count 150) was compared to a control and statistically evaluated using an unpaired t test. Noxythiolin (2.5% & 1%) significantly reduced adherence of the exponential phase blastospore of *Candida albicans* while 2.5% noxythiolin only was successful in significantly reducing the adherence of stationary phase cells. Formaldehyde solutions in equivalent concentrations to those found in noxythiolin solutions did not significantly reduce adherence. Similar results were obtained for 2.5% noxythiolin using urine isolates of *Escherichia coli* and *Staphylococcus saprophyticus*.

The secondary or invasive stage of infection with *Candida albicans* is associated with germination of the blastospore (Martin *et al* 1984). The percentage germination and extent of germ tube elongation was determined by light and electron microscopy. Incubation with noxythiolin (2.5%, 30 mins, 37°C) prevented germination whereas 1% noxythiolin allowed germination though germ tube elongation was restricted. Formaldehyde concentrations well in excess (x6) of those found in the 2.5% noxythiolin solution were required to prevent germination.

The data obtained from the adherence studies particularly in respect of exponential phase organisms indicates a useful role for the compound in prophylaxis. Furthermore the activity exhibited on germinating blastospores and germ tube elongation might explain, in combination with its known cidal effect, the efficacy of noxythiolin in clinical use.

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