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Short Communication

EDTA reduces antimicrobial efficacy of thiomersal

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Some hard contact lens and most soft contact lens solutions are preserved with thiomersal, often in combination with EDTA. Information on the effect of EDTA on thiomersal have been conflicting with reports noting both increase (Bier and Lowther, 1977) and decrease (Richards and Reary, 1972) in preservative activity. The present report reevaluated the influence of EDTA on thiomersal efficacy.

Solutions containing thiomersal 0.004% with and without EDTA (0.1% and 0.05%) were autoclaved and 50 μ l introduced into wells cut out of agar pour plates. Twenty-four hour cultures of *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans* and *Pseudomonas aeruginosa* were used as test organisms in nutrient agar (except *C. albicans* in tryptone agar). EDTA containing thiomersal solution was introduced into half the wells on each plate with the remaining two wells containing thiomersal solution. The pour plates were incubated at 37°C for the bacteria and 32°C for *C. albicans*. Zones of inhibition were measured as the distance from the well edge to the edge of microbial growth.

EDTA in both concentrations significantly reduced antimicrobial efficacy of thiomersal against *E. coli*, *P. aeruginosa* and *C. albicans* with the higher EDTA concentration having the greater effect (Table 1). With *S. aureus* EDTA 0.05% caused a significant reduction in efficacy of thiomersal but at 0.1% did not significantly lower activity although the zones of inhibition were smaller (Table 1). EDTA has been shown to enhance antimicrobial efficacy of some preservatives (Richards, 1971; Richards and McBride, 1972) and the lack of significant inhibition of thiomersal activity with the 0.1% concentration may indicate that EDTA is capable of enhancing thiomersal activity. It is possible therefore, that EDTA is capable of influencing thiomersal activity in two ways—firstly by complexation resulting in a reduction in efficacy and secondly by enhancing activity of uncomplexed thiomersal which would account for the differences observed with *S. aureus* (Table 1).

Inhibition of activity can probably be attributed to EDTA complexation of thiomersal causing a reduction in available preservative. This was verified by obtaining UV spectrophotometric traces of thiomersal and EDTA separately and in

TABLE 1

ZONES OF INHIBITION (m/m) RESULTING FROM INCUBATION OF POUR PLATES WITH THIOMERSAL WITH AND WITHOUT EDTA

Results represent the mean of 20 values with standard error of the mean.

Thiomersal 0.004%	6.95 ± 0.30	10.90 ± 0.27	13.88 ± 0.30	3.38 ± 0.15
Thiomersal 0.004% with EDTA 0.05%	6.00 ± 0.25 **	10.23 ± 0.30 *	12.85 ± 0.30 **	1.45 ± 0.20 ****
Thiomersal 0.004%	8.33 ± 0.19	8.75 ± 0.31	6.70 ± 0.15	1.85 ± 0.07
Thiomersal 0.004% With EDTA 0.1%	7.00 ± 0.18 ****	8.35 ± 0.29	5.98 ± 0.18 ***	1.00 ± 0.11 ****

* $P = 0.05$; ** $P = 0.025$; *** $P = 0.005$; **** $P = 0.0005$.

combination. The summation of absorbances from the individual traces did not correspond with the trace from an EDTA–thiomersal combination suggesting that some interaction was occurring between the two compounds. This interaction can be assumed to be complexation between EDTA and the mercury of thiomersal.

It is apparent from these results that EDTA and thiomersal should not be used in combination and a large number of commercially available contact lens solutions are probably less effectively preserved than they would be if EDTA was omitted from the formulations.

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References

- Bier, N. and Lowther, G.E., Contact Lens Correction, Butterworths, London, 1977, p. 95.
- Richards, R.M.E., Inactivation of resistant *Pseudomonas aeruginosa* by antibacterial combinations. *J. Pharm. Pharmacol.*, 23 Suppl. (1971) 136S–140S
- Richards, R.M.E. and McBride, R.J., The preservation of ophthalmic solutions with antibacterial combinations. *J. Pharm. Pharmacol.*, 24 (1972) 145–148.
- Richards, R.M.E. and Reary, J.M.E., Changes in antibacterial activity of thiomersal and PMN on autoclaving with certain adjuvants. *J. Pharm. Pharmacol.*, 24 Suppl. (1972) 84P–89P