INCOMPATIBILITY OF PHENYLMERCURIC ACETATE WITH SODIUM METABISULPHITE IN EYE DROP FORMULATIONS

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The British Pharmacopoeia (1980) allows the use of phenylmercuric acetate (PMA) or phenylmercuric nitrate (PMN), at a level of 0.002% w/v, as a preservative in some eye drop formulations. Sodium metabisulphite (SM) is also present in some of these formulations, at a level of 0.1% w/v, as an antioxidant.
Phenylmercury compounds have been determined by HPLC (Mehta et al 1976; MacCrehan et al 1977). In this laboratory, whilst developing a reversed phase method for PMA in eye drop formulations, which also contained SM, it was found that the PMA was lost on autoclaving at 115°C for 30 minutes.
Loss on autoclaving of 0.002% w/v PMN with 0.1% w/v SM has been reported by Richards and Reary (1972), using atomic absorption spectroscopy (AA).
In order to fully investigate the possible incompatibility of PMA with SM, a trial was set up using the B.P. amethocaine hydrochloride (AH) 0.25% w/v eye drop formulation. Four solutions were prepared; 0.002% w/v PMA alone, 0.002% w/v PMA with 0.1% w/v SM, 0.002% w/v PMA with 0.25% w/v AH and the B.P. formulation (0.002% w/v PMA with 0.1% w/v SM and 0.25% w/v AH). To eliminate any problems due to adsorption of PMA onto rubber seals in eye drop bottles (Sykes 1958) the solutions were sealed in 10ml glass ampoules before autoclaving at 115°C for 30 minutes. After autoclaving the solutions were assayed using HPLC and AA.
The conditions used for the HPLC method were :- flow-rate 2.0 ml/min of the solvent (0.005M heptane sulphonic acid sodium salt in 50% v/v methanol 50% v/v water, adjusted to pH 3.5 with glacial acetic acid), a μBondapak C18 reversed phase column and UV-detection at 210nm 0.08 AUFS. Linear response was found over the range 0 to 0.002% w/v PMA, using peak height measurements. Samples were assayed by direct 50μl loop injection. Relative standard deviation was ± 1.5%. Retention times for the PMA and AH were 5.8 and 15.0 minutes respectively.
The conditions used for the AA assay were :- fuel acetylene/air 20/30 mixture, burner height 15mm with 50mm slotted tube atom trap and impact bead, lamp current 5mA and wavelength 253.7nm. Linear response was found over the range 0.0001% w/v to 0.002% w/v PMA, with a RSD of ± 3%.

Table 1. HPLC and AA assay results for autoclaved PMA solutions

	0.002% PMA alone	0.002% PMA + 0.1% SM	0.002% PMA + 0.25% AH	0.002% PMA + 0.1% SM + 0.25% AH
HPLC	99.8%	0.0%	100.1%	0.0%
AA	102.6%	∠ 5.0%	105.0%	12.0%

Results given as % of original concentration of PMA

From the results in table 1 and work on other formulations carried out in this laboratory, it is clear that PMA is incompatible with SM. Preliminary microbiological investigations have shown that despite the losses of PMA from two of the solutions, they still exhibit antibacterial activity. This is probably due to the SM in the formulation which, as well as being an antioxidant, has been shown to exhibit antibacterial activity (Richards and Reary 1972).

Mehta, A.C. et al (1976) J. Clin. Pharmac. 1: 177-180
MacCrehan, W.A. et al (1977) Anal. Lett. 10: 1175
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