THE IMPLICATION OF STEARATE MOULD RELEASE AGENTS IN THE LOSS OF BENZALKONIUM CHLORIDE FROM OPHTHALMIC SOLUTIONS IN POLYETHYLENE BOTTLES

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0.001 - 0.01% Benzalkonium chloride is commonly used as a preservative in ophthalmic solutions. Being surface active, it is adsorbed onto the walls of containers and losses of up to 10% may occur from solutions in plastic and glass eye drop bottles. Typical data of this type are given in table 1 for the BAK content of a viscolysed pilopcarine formulation stored in polyethylene bottles type C, described by the fabricator as "additive free". However two different artificial tear formulations packaged in nominally the same bottles show serious and continuous loss of BAK during stability trials at 40°.

Formulation	Storage Time in Weeks								
	4	6	8	10	12	13	26	39	52
Pilocarpine, pH 5.2	90.0	-	92.5	-	-	92.5	-	94.5	94.5
SNPI Tears, pH 7.9	-	94.2	-	-	-	95.5	72.2	60.4	40.5
SNPII Tears, pH 8.4	96,8	-	-	81.9	73.4	-	-	-	-

Table 1. Percentage of initial BAK content (nominally 0.01%) for ophthalmic solutions stored in polyethylene bottles type C at 40°.

Initially it was considered possible that this was due to complexation with alkaline buffers in the tear formulations. However after finding that BAK loss could be rapidly accelerated by storage at 50-60°, further studies showed no significant loss from SNP II tears in neutral glass eye drop bottles (USP type I) closed with a polypropylene screw cap.

Examination of bottle batch records disclosed that the pilocarpine containers were from a different batch to those used for the tears and consequently further accelerated loss studies were carried out with a variety of polyethylene (PE), polypropylene (PP) and glass containers. Table 2 shows that the BAK loss from the tears is associated with the second batch of the PE type C bottles.

Container *, Type and Material	SNP II Tears pH 8.5 (50°)	Phosphate Buffer pH 7.9 (56°)
Neutral glass ampoules (BP)	-	96.9
Neutral glass (USP type I)	97.4	-
PP: ICI PXC 6804	96.6	93.4
PE type A: BASF Lupolen 1810D	95.5	98.6
PE type B: Bakelite DPX 527/1	-	96.9
PE type C: ICI Alkathene 45, batch I	-	93.6
PE type C: ICI Alkathene 45, batch II**	28.1	72.5

Table 2. Percentage of initial BAK content (nominally 0.01%) of Artificial Tears and Sorensen's phosphate buffer after 4 weeks storage. (* 10 ml capacity bottles unless otherwise stated: **batch with stearate additive).

Further discussions with the supplier revealed that stearate type mould release agents had been added to the Alkathene 45 granules prior to moulding and second batch of PE type C bottles. It is apparent that such practice can result in severe loss of BAK, presumably due to insoluble complex formation; SNP II tears showed both hazing and loss of antimicrobial activity.