UNIFORMITY OF CHLORAMPHENICOL DISTRIBUTION WITHIN TUBES OF PROPRIETARY CHLORAMPHENICOL 1% EYE OINTMENT

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Chloramphenicol 1% eye ointment has been used for many years without our being aware of any problems. Complaints that one particular batch was so soft and runny that it came out of patients eyes led to an investigation. Physical examination confirmed the product to be very soft and chemical analysis showed the chloramphenicol content, when determined by the BP method, to be outside the limits of +/- 5% of stated content. To establish the extent of the problem, several tubes from this and other batches were examined. The results (Table 1) show that the consistency and chloramphenicol content varied.

The BP assay requires 1g, this limits the number of tests that can be carried out on an individual 4g tube. Since the normal dose is approximately 50 - 100 mg, a method of appropriate sensitivity would be desirable to permit detailed analysis of individual tubes. An HPLC method has been developed in which 100mg of the ointment is dissolved in toluene:methanol 90:10 containing an internal standard (nitrobenzene) and chromatographed on a C18 reversed phase column using methanol:water 62.5:37.5 at a flow rate of 1ml/min with detection at 278nm. A good separation (Fig 1) is obtained with a linear response over the range 0.01 - 2.0mg/ml.

Using this method more than 40 batches of chloramphenicol 1% eye ointment from three manufacturers have been examined. The results (Table 2) show a wide variation in measured chloramphenicol content. Product A showed the greatest variation, although not all batches were bad, Product B showed less variation and Product C was uniform. These results can be related to visual observations that a small, but variable quantity of a clear oil separates from the ointment mass. This oil was identified as liquid paraffin. Separation does not appear to occur to the same extent with every tube from the same batch and varies between products.

White and yellow soft paraffins are poorly defined mixtures of aliphatic hydrocarbons. They are normally mixed with liquid paraffin and/or lanolin to produce an eye ointment of suitable consistency. If the formulation is inadequate or unstable then, under adverse conditions, paraffin liquid can bleed out of the eye ointment base. The chloramphenicol will be concentrated in the remaining ointment and reduced in those parts of the ointment containing a high level of paraffin liquid. When this occurs the patient will not receive a consistent product.

The HPLC method developed allows chloramphenicol to be measured in samples of 100mg or less, equivalent to an individual dose. Variations in chloramphenicol content have been detected which could not be measured by the BP method. Two of the three products examined cannot be considered satisfactory in terms of chloramphenicol distribution when analysed by this method.

Table 1 Chloramphenicol content (BP)

Batch	%	Appearance
1A	0.80	very soft
2A	1.02	soft
3A	0.96	soft

Table 2 Chloramphenicol distribution

Batch	%			
1A	0.21	0.31	0.71	0.90
2A	1.01	0.82	1.10	0.71
3A	1.24	0.39	1.12	0.90
1B	1.02	0.61	1.02	0.76
1C	0.98	0.99	1.02	1.02

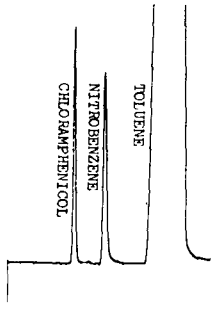

Fig 1.
Separation of Chloramphenicol by HPLC