ETHYLENEDIAMINE MEASUREMENT IN AMINOPHYLLINE SUPPOSITORIES B.P.; A SPECTROPHOTOMETRIC METHOD

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Aminophylline Suppositories B.P. have been reported to be unstable (Pryce-Jones, Watt and Kraisintu 1979) and changes in the physical properties and dissolution rate attributed to the reaction of the ethylenediamine counter ion with the fatty acid triglyceride bases (Cieszynski 1975). However, it has been stated more recently that this reaction, which may result in the formation of fatty acid amides, only occurs on accelerated storage testing at above 80°C and that the fate of the ethylenediamine on storage at ambient temperatures is not known (Heers 1980). To investigate this latter statement further, a routine method of quantifying ethylenediamine in individual suppositories or sections thereof, is required.

The B.P. (1980) assay requires suppositories to be pooled and melted before titration of the ethylenediamine with sulphuric acid. It is time consuming and difficult to perform on individual suppositories or sections thereof. Ethylenediamine ($H_2N\text{-}CH_2\text{-}CH_2\text{-}NH_2$) is a simple molecule which does not absorb U.V. or visible light in the usual ranges needed for spectrophotometry, neither does it fluoresce. H.P.L.C. and G.L.C. would be possible but would require extraction and derivatisation in addition to the chromatography step. A spectrophotometric assay after extraction and derivatisation might be more suitable.

Primary and secondary amines will react with 4-dimethylaminobenzaldehyde in 2M HCl to form yellow Schiff's bases. The intensity of light absorption by these Schiff's bases differs from amine to amine. A method for several amines was developed from that of Spinkova (1971). A 4 ml sample of the amine solution was pipetted into a test tube and 4 ml of 2% $^{w}/_{v}$ 4-dimethylaminobenzaldehyde in 2M HCl was added and mixed. The absorbance was determined at the optimum wavelength for the amine under study (408nm for ethylenediamine). The reaction was complete in four minutes at ambient temperature and the colour was stable for at least twenty minutes. The A(1%, 1cm) for the Schiff's base of ethylenediamine was 9.62. Plots of absorbance against concentration showed good linearity and very good precision.

The ethylenediamine content of Aminophylline Suppositories was determined by extracting a known weight of suppository, dissolved in 10 ml $CHCl_3$, with 2 x 5 ml of 0.001M HCl for 2 minutes, pooling the HCl extracts and taking 4 ml aliquots for assay with 4-dimethylaminobenzaldehyde (as above).

A batch of freshly prepared Aminophylline Suppositories was assayed by this method and the B.P. assay. The percentage recovery was found to be 100.5%±1.19 (s.d.) of the values given by the B.P. method.

The new assay can measure down to 3.5 mg of ethylenediamine, equivalent to about 27mg of Aminophylline in whatever amount of suppository is used. This allows assays to be carried out on individual suppositories containing 50 mg of Aminophilline each and suitably sized sections of larger suppositories.

Although seemingly more complex than the B.P. assay the new method allows a number of assays to be performed at the same time (up to about 20) thus reducing the overall time required.

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