THE ANALYSIS OF DIPHENHYDRAMINE HYDROCHLORIDE BY COMPUTER-AIDED MULTICHANNEL U.V.-SPECTROPHOTOMETRY

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The direct spectroscopic analysis of drugs in dosage forms is often complicated by interference due to the formulation matrix. For the quality control and routine analysis of diphenhydramine hydrochloride (DPH) in cough syrups, rapid and specific methods are required. In the present work, two techniques for the analysis of DPH preparations have been examined - second derivative spectroscopy and matrix deconvolution - using a computer-aided linear photodiode array spectrophotometer.

Second derivative spectra of DPH in aqueous solution generated digitally by a Hewlett-Packard 8450A multichannel spectrophotometer, display a series of sharp, negative minima, whose amplitudes are linearly related to concentration up to a concentration of 1 mg ml^{-1}. Whereas the coloured sucrose formulation matrix (Martindale, 1977) interferes strongly in the zero order spectrum, its amplitude is close to zero in the second derivative spectrum from 230-300 nm. In the mixture of DPH and matrix, diluted 1+3 with water, the peak amplitude at 268 nm, measured with respect to the satellite at 271 nm, varies linearly with DPH concentration, the confidence limits at 0.624 mg ml^{-1} being ± 0.006 mg ml^{-1} (p=0.95, n=8, 10 second measurement interval). Moreover, this peak amplitude for DPH is unaffected by variation in matrix concentration from 0-30% v/v in the diluted preparation. Comparison of the second derivative method with the USP XIX procedure (involving several extraction and back-extraction steps) applied to batches of DPH syrup (nominal strength 2.70 mg ml^{-1}) gave comparable percentage recoveries. The relative standard deviation (RSD) for the computer-aided method was 0.9% at 0.683 mg ml^{-1} (n=8).

The matrix deconvolution method, when all spectral information within a specified range is utilised, relies on the availability of stored spectral data for each component in a mixture. Zero order spectra for DPH and for the formulation matrix at concentrations equivalent to that in the dosage form after dilution (1+3) with water are used to generate the best fit to a test spectrum. The DPH assay values reported by this method for samples from 0.24 to 1.00 mg ml^{-1} yield a linear correlation (r=0.999, p=0.95, n=10) with respect to stoichiometric values. However, increasing the proportion of matrix at a constant DPH level reveals a small negative bias at high matrix concentration. This bias is almost eliminated when the deconvolution procedure is applied using second derivative spectra of DPH and matrix. The average DPH recovery relative to stoichiometric concentration for samples in the range 0.24 to 1.00 mg ml^{-1} was 98% (n=4).

These computer-aided methods based on the linear photodiode array UV Spectrophotometer offer a new approach for the routine quality control of DPH in its dosage forms. Such methods offer significant potential for increased selectivity when used in conjunction with high-pressure liquid chromatography (Fell, 1980).

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