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Application of orthogonal functions to the determination of naphazoline

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A rapid method for the determination of naphazoline in antazoline-naphazoline drops is discussed. The method depends upon precipitating antazoline by a solution of sodium carbonate. Naphazoline is determined in the filtrate using (i) the modified Vierordt method and (ii) Glenn's method of orthogonal functions to correct for the unprecipitated fraction of antazoline.

Imidazolines have been assayed colorimetrically using alkaline sodium nitroprusside (Slack & Mader, 1957). The reaction is specific for the intact imidazoline ring (Stern, 1958) and therefore gives a total imidazoline figure when applied to a mixture of antazoline and naphazoline. Gas-liquid chromatographic methods have been published for the separation and determination of imidazolines (Boon & Sudds, 1967; Molina & Poe, 1968).

Although gas-liquid chromatographic methods give satisfactory results in analysing naphazoline as a minor component in the mixture of naphazoline (0·025%)—antazoline (0·5%), the need was strongly felt for a spectrophotometric method, easy to automate for routine analysis.

The separation of antazoline-naphazoline was achieved by precipitating crystalline antazoline by means of a 5% w/v sodium carbonate solution (Clarke, 1969). The naphazoline content in the filtrate was determined using (i) the modified Vierordt method (Glenn, 1960) and (ii) the orthogonal function method (Glenn, 1963) to correct for the unprecipitated fraction of antazoline. The latter amounted to about 8% of the original concentration.

Absorption spectra of naphazoline nitrate and antazoline hydrochloride in 0·1N sulphuric acid were computed in different ways to obtain the optimum conditions for the application of the orthogonal function method (Wahbi, 1967; Abdine, Wahbi & Korany, 1971). Thus, by plotting convoluted absorption curves (Agwu & Glenn, 1967) it was found that over the wavelength range 270·5 to 300·5 nm at 6 nm intervals and using six-point orthogonal polynomials, the calculation of p_2, the coefficient of the quadratic polynomial, P_2, for a mixture of the two compounds is independent of the antazoline concentration (Fig. 1). Furthermore, according to Glenn's theory of comparative coefficients (see Wahbi, 1967), $|q_2|$ (where $q_2 = p_2.N_2^{\frac{1}{2}}$ and N is the normalizing factor) calculated at the finally chosen conditions for a solution of 0·0025% w/v naphazoline nitrate in 0·1N sulphuric acid was found to exceed 140×10^{-3}. In that case, the coefficient of variation of (p_2) can be considered to be less than 1 (see Abdine & others, 1971).

METHODS

Instrument. A Unicam SP 500 photoelectric spectrophotometer.

Assay. The nasal drops contained 500 mg antazoline hydrochloride, 25 mg

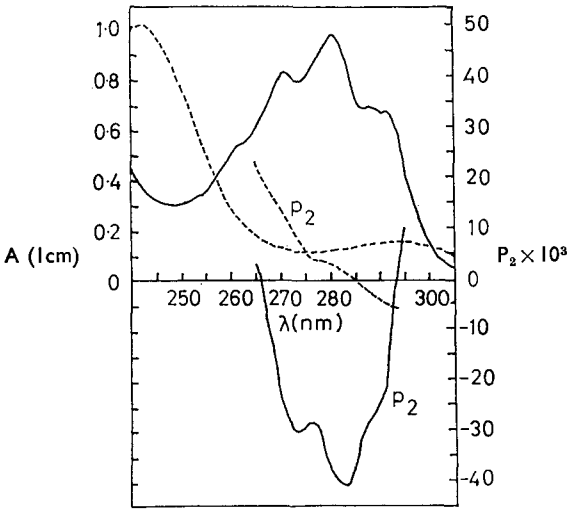

FIG. 1. ——— Absorption curve of 4 mg% w/v naphazoline nitrate in 0·1N sulphuric acid and its p_2-convoluted curve. - - - - - Absorption curve of 2 mg% w/v antazoline hydrochloride in 0·1N sulphuric acid and its p_2-convoluted curve.

naphazoline nitrate, 600 mg sodium chloride and 500 mg chlorbutol per 100 ml (Extra Pharmacopoeia). 5 ml of a 5% w/v aqueous solution of $Na_2CO_3.10\ H_2O$ were added slowly with continuous stirring to 10 ml of the nasal drops contained in a 50 ml beaker. The mixture was allowed to stand for 20 min and then filtered into a 100 ml volumetric flask. The beaker and precipitate were washed with 3 × 5 ml portions of the sodium carbonate solution. The combined filtrate and washings (30 ml) were acidified with 20 ml N sulphuric acid and made to volume using distilled water. The absorbances of 1 cm pathlength of the solution were measured against a blank, consisting of the same solvents and reagents, over the wavelength range 270·5 to 300·5 nm at 6 nm intervals and also at 281 and 305 nm. The quadratic coefficient, p_2, was calculated as follows: $p_2 = [(+5)\ A_0 + (-1)\ A_1 + (-4)\ A_2 + (-4)\ A_3 + (-1)\ A_4 + (+5)\ A_5]/84$ where the subscripts, 0, 1, . . . , 5 stand for 270·5, 276·5, . . . , 300·5 nm at 6 nm intervals, the numbers in brackets are given in standard works on numerical analysis (Milne, 1949; Fisher & Yates, 1953) and the divisor 84 is the normalizing factor. The concentration of naphazoline nitrate was obtained from the p_2 (1%, 1 cm) calculated for naphazoline nitrate in 0·1N sulphuric acid and by the modified Vierordt method ($\lambda_1 = 281$ nm and $\lambda_2 = 305$ nm).

RESULTS AND DISCUSSION

The results obtained for the determination of naphazoline nitrate in 9 samples at concentrations from 1·4–2·5 mg gave a % recovery for the orthogonal function method of 101·2 ± 1·1 and for the modified Vierordt method of 98·3 ± 0·9 ($P = 0·05$).

Errors in the orthogonal function method can be attributed to (i) wavelength setting errors which affect absorbances made on steep slopes in the absorption curves, (ii) the non-zero coefficient that may have been contributed by antazoline hydrochloride to the assay coefficient and (iii) overall shifts in the wavelength calibration which affect the coefficients sited on slopes in the convoluted absorption curves

(Agwu & Glenn, 1967). The latter is considered to be the most important source of error in this particular assay.

Although the modified Vierordt method gave satisfactory results, the presence of a linear irrelevant absorption, as may originate from differences between batches of the components of the mixture and the "reference" samples used to establish the assay coefficients would certainly lead to erroneous results. In these circumstances, the orthogonal function method would be superior to the modified Vierordt method (Glenn, 1963).

Antazoline hydrochloride was determined in the nasal drops by diluting 1 ml to 250 ml using 0·1N sulphuric acid and measuring the A (1 cm) at 242 nm after allowing for the naphazoline nitrate content in the blank cell. The mean percentage recovery for nine separate determinations was found to be 100·9 $\pm$ 0·8% ($P = 0{\cdot}05$).

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