

Application of orthogonal functions to spectrophotometric analysis of weakly absorbing compounds in tablets

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Glenn's method of orthogonal functions has been applied to correct for irrelevant absorption during the analysis of tablets of chlorpheniramine maleate, phenyltoloxamine dihydrogen citrate, diphenhydramine hydrochloride and ephedrine hydrochloride. The results suggest that the method can be used for routine analysis.

The need to correct for irrelevant absorption has occasioned many formulae ranging from the simple (Banes & Eby, 1946) to the highly sophisticated (Tunncliff, Rasmussen & Morse, 1949), depending upon the shape of the irrelevant absorption spectrum. The method developed by Ashton & Tootill (1956) for the assay of griseofulvin in fermentation samples depends upon the use of orthogonal polynomials. In 1963, Glenn outlined general procedures for the use of orthogonal functions to correct for irrelevant absorption in spectrophotometric analysis. The method is based upon the fact that a gross absorption curve $f(\lambda)$ can be expanded in terms of orthogonal functions as follows:

$$f(\lambda) = p_0P_0 + p_1P_1 + p_2P_2 + \dots + p_nP_n \quad \dots \quad (1)$$

where $f(\lambda)$ denotes the absorption of the sample at $(n + 1)$ wavelengths, P_j are the orthogonal polynomials given in standard works on numerical analysis (Milne, 1949; Fisher & Yates, 1953) and p_j are their respective coefficients. These coefficients are proportional to concentration (Glenn, 1963). Thus, $p_j = \alpha_j c_a$ where α_j is the coefficient of P_j for the A (1%, 1 cm) of the pure compound, a , c_a is the concentration. In the presence of irrelevant absorption, each observed coefficient is the sum of two terms; thus,

$$p_j = \alpha_j c_a + p_j(z) \quad \dots \quad (2)$$

where z denotes "contribution from irrelevant absorption". Equation (2) therefore contains two unknowns c_a and $p_j(z)$ and can only be used to evaluate c_a from p_j when there are good grounds for supposing $p_j(z)$ to be negligible relative to $\alpha_j c_a$. To minimize $p_j(z)$ to a negligible value, great care must be taken in choosing the polynomial and range, the number of wavelengths and the mean wavelength, all these choices being made with reference to the irrelevant absorption curve.

Glenn's method of orthogonal functions has been successfully applied to the assay of vitamin A in cod liver oil without saponification and atropine sulphate injections (Wahbi, 1967, 1970).

The present work represents an application of the method to the determination of a single substance in the presence of irrelevant absorption. The choice of polynomial, number of points, wavelength range and intervals is illustrated by the analysis of tablets containing a single, weakly-absorbing active constituent. These are: chlorpheniramine maleate (4 mg), phenyltoloxamine dihydrogen citrate (15 mg), diphenhydramine hydrochloride (25 mg) and ephedrine hydrochloride (30 mg) per tablet.

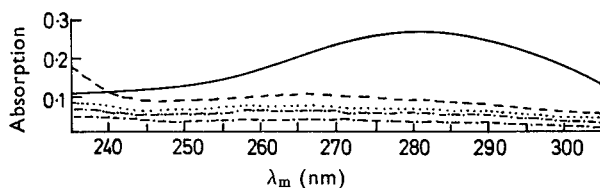


FIG. 1. Irrelevant absorption curves due to: — lactose, --- gelatin, . . . stearic acid, - - - - magnesium stearate, - - - - - starch.

Shapes of irrelevant absorption curves in tablets

Irrelevant absorption in spectra from tablets originates from the diluents, e.g., lactose, starch, sucrose, the moistening agents, e.g., acacia mucilage, gelatin, liquid glucose and the lubricants, e.g., talc, stearic acid and magnesium stearate. Different grades of these ingredients from different sources were separately investigated. Of the ingredients, lactose was found to be the main source of interference (Fig. 1). Furthermore, grade to grade differences were negligible.

Choice of assay polynomial

Following the general rules collated by Wahbi (1967) for the choice of an assay polynomial, the results presented in Table 1 were obtained from the general shapes of the spectra of the compounds to be assayed (Figs 2 and 3).

Number of wavelengths

Eight-point orthogonal polynomials have been preferred for two reasons. Firstly, the irrelevant absorption curves were not too complex to require more than that

Table 1. Choice of assay polynomial.

| Compound | Segment | Polynomial |
|---|-----------|------------|
| Chlorpheniramine maleate | a b c | P_2 |
| Phenyltoloxamine dihydrogen citrate | d e f | P_2 |
| Diphenhydramine hydrochloride | g h i j | P_3 |
| Ephedrine hydrochloride | k l m n | P_4 |
| | o p q r s | P_6 |

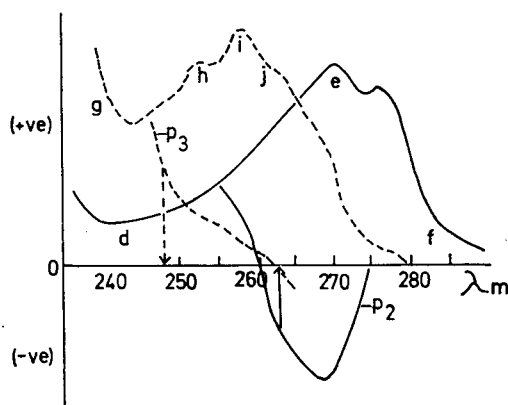


FIG. 2. — Absorption curve of 11 mg% w/v phenyltoloxamine dihydrogen citrate in 0.1N sulphuric acid and its p_2 -convoluted curve. - - - Absorption curve of 37 mg% w/v diphenhydramine hydrochloride in 0.1N sulphuric acid and its p_3 -convoluted curve.

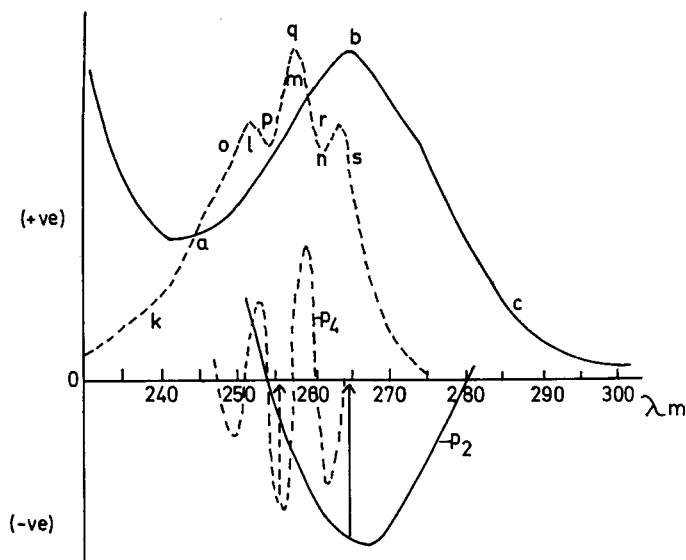


FIG. 3. ——— Absorption curve of 4 mg% w/v chlorpheniramine maleate in 0.1N sulphuric acid and its p_2 -convoluted curve. - - - - Absorption curve of 97 mg% w/v ephedrine hydrochloride in 0.1N sulphuric acid and its p_4 -convoluted curve.

number of points for their correction. Secondly, the calculation of any of the coefficients required no more than 5 min using a desk calculator. However, where the irrelevant absorption possessed high frequency components or its shape was completely unknown, more points needed to be used.

Choice of mean wavelength λ_m

λ_m , the mean of the set of wavelengths, was obtained by plotting convoluted absorption curves (Agwu & Glenn, 1967), i.e., p_j calculated at different intervals versus λ_m for both pure substance (Figs 2 and 3) and irrelevant absorption. The optimum wavelength range and intervals were finally selected to maximize p_j and minimize $p_j(z)$ to a negligible value (eqn 2).

Magnitude of coefficients

According to a theory contributed by Dr. A. L. Glenn (see Wahbi, 1967) the comparative coefficients, $|q_j|$ ($q_j = p_j \cdot N_j^{1/2}$; N_j is the normalizing factor) must exceed 140×10^{-3} if the coefficient of variation of p_j calculated at the optimum set of wavelengths is to be less than 1. This requirement was achieved by increasing the intervals of the set of points so that a greater coefficient was obtained. With the exception of ephedrine hydrochloride, observed values of $|q_j|$ were above the stated figure (Table 2).

Table 2. Comparative coefficients calculated at the optimum set of wavelengths

| Solution | A_{max} | j | $p_j \times 10^3$ | $ q_j \times 10^3$ |
|---|-----------|-----|-------------------|---------------------|
| Chlorpheniramine maleate | 0.840 | 2 | -42.530 | 551.2 |
| Phenyltoloxamine dihydrogen citrate | 0.583 | 2 | -28.208 | 365.6 |
| Diphenhydramine hydrochloride | 0.663 | 3 | +17.992 | 292.3 |
| Ephedrine hydrochloride | 0.578 | 4 | -2.125 | 52.7 |
| | | 5 | -2.056 | 96.1 |

Table 3. Assay results

| Tablets* | P _j | λ_m (nm) | Intervals (nm) | Mean % recovery (P = 0.05) |
|---|----------------|------------------|----------------|----------------------------|
| Chlorpheniramine maleate (5) | P ₁ | 264.5 | 6 | 99.2 ± 1.5 |
| Phenyltoloxamine dihydrogen citrate (10) .. | P ₂ | 263 | 6 | 98.5 ± 1.35 |
| Diphenhydramine hydrochloride (10) | P ₃ | 247.5 | 3 | 99.2 ± 1.8 |
| Ephedrine hydrochloride (10) | P ₄ | 249.5 | 3 | 99.8 ± 1.7 |
| | P ₅ | 256 | 2 | 101.0 ± 0.7 |

* Prepared separately using five different grades of lactose. Figures in parentheses indicate number of experiments (separate weighings).

For the reason that the three peaks of ephedrine hydrochloride occur within a narrow range of wavelengths (Fig. 3), it was found that by widening the wavelength intervals (more than 3 nm for p₄ and 2 nm for p₅), the magnitude of the coefficients and accordingly |q_j| decreased. Nevertheless, the assay of ephedrine hydrochloride tablets was made at the selected wavelength range and intervals given in Table 3 taking in consideration that the coefficient of variation (p_j) may exceed 1.0.

METHODS

Tablets. These were prepared to contain the previously specified doses per 0.30 g tablet powder. Five different grades of lactose were separately used for their preparation.

Assay. An accurately weighed quantity of the powdered tablets (0.2–0.5 g) was extracted with 0.1N sulphuric acid, filtered and suitably diluted for measurement by a Unicam SP 500 photoelectric spectrophotometer.

RESULTS AND DISCUSSION

Sources of error in the above results are due to (i) the non-zero coefficient which may have been contributed by the irrelevant absorption to the "tablet coefficient", (ii) wavelength setting errors which affect absorbances measured on steep slopes in the absorption curves and (iii) overall shifts in the spectrophotometer's wavelength calibration. The latter source of error affects mainly the coefficients sited on slopes in their respective convoluted absorption curves (Figs 2, 3) (Agwu & Glenn, 1967).

Glenn's method of orthogonal functions proved to be powerful in discounting irrelevant absorption contribution. Thus, the method can be applied for the routine analysis of tablets without separating the active constituent from the tablet fillers. Great care must be taken in the choice of the assay parameters.

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