J. Pharm. Pharmacol. 1981, 33: 458–459
Communicated February 12, 1981

0022–3573/81/070458–02 $02.50/0

COMMUNICATIONS

The assay of procyclidine in tablets and injections by derivative spectrometry

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The official assay for procyclidine hydrochloride in tablets is 2-phase titration (British Pharmacopoeia 1980), using the indicator dimethyl yellow which is reported to be a carcinogen (IARC 1975). Non-aqueous titration, precipitation titration and fluorescence have also been proposed as assay methods (Chatten & Racz 1968; Campbell et al 1980; Gelbke 1976). Procyclidine contains an isolated phenyl group and the weak u.v. spectrum has the typical fine structure at 230–280 nm. This weak spectrum means that conventional u.v. spectrometric assay of procyclidine hydrochloride in formulated products is susceptible to interference from excipients. Derivative u.v. spectrometry minimizes interference from excipients which absorb or scatter the incident beam (O'Haver & Green 1976; Shibata et al 1976), and the sharpness of the bands in the u.v. spectrum means that derivative u.v. spectrometry can offer sufficient sensitivity for quantitative work.

Materials and methods

Hydrochloric acid (0·1 M). Type GF/F, 25 mm dia. glass fibre filter papers (Whatman Ltd). Swinnex filter holder (Millipore (UK) Ltd). Procyclidine hydrochloride B.P. Procyclidine 5 mg tablets B.P. Procyclidine injection (10 mg in 2 ml).

Two Perkin Elmer model 554 scanning u.v./visible spectrometers were used.

Assay of procyclidine hydrochloride in tablets

Standard solution. An accurately prepared solution containing about 0·025% w/v procyclidine hydrochloride in 0·1 M hydrochloric acid.

Test solution. Weigh and powder 20 tablets. Accurately weigh an amount of powder equivalent to about 25 mg of procyclidine hydrochloride into a 100 ml volumetric flask. Add about 80 ml of 0·1 M hydrochloric acid, shake well and place in an ultrasonic bath for 15 min. Cool and dilute to volume with 0·1 M hydrochloric acid. Filter through a 25 mm diameter type GF/F filter in a filter holder, applying air pressure if necessary to speed up filtration, and reject the first 5 ml of filtrate. The filtrate is the test solution.

Measurement of spectra. Record the second derivative of the u.v. spectrum of test and standard solutions in a 1 cm cell over the range 280 to 220 nm, using 0·1 M hydrochloric acid in the reference cell. The instrument settings should be optimized to produce a spectrum with about 80% full scale deflection and an acceptable noise level.

Suitable settings are: bandwidth 2 nm; scan speed 60 nm min^{-1}; chart speed 10 nm cm^{-1}; response time 3; recorder range −0·1 to +0·05.

Record each spectrum in triplicate (without refilling the cell) and measure the deflection from the largest peak at about 252 nm to the largest trough at about 255 nm (Fig. 1). Compare the mean measurements obtained for test and standard solutions and hence calculate the procyclidine content of the tablets.

Assay of procyclidine hydrochloride in injections. Dilute 5·0 ml of injection (equivalent to 25 mg of procyclidine hydrochloride) to 100 ml with 0·1 M hydrochloric acid. Follow the procedure for tablets.

Results and discussion

Choice of assay conditions. The bandwidth chosen is too large to measure the absorbance accurately at the maxima (Rogers 1959). This causes some distortion of the spectrum but improves the signal to noise ratio without affecting the linearity of the response (Cahill 1980). Filtration through a glass fibre filter paper removes turbidity caused by tablet excipients. Although derivative spectrometry will give accurate results for turbid solutions (Shibata et al 1976), it is better to clarify solutions before measurement.

The response was linear up to 150% of the assay concentration.

Assay specificity. Recovery experiments were carried out by adding the drug in solution to mixtures of the following pharmaceutical excipients in the appropriate quantities used in tablets and injections: lactose, starch, pregelatinized starch, sodium starch glycollate, lactic acid, polyvinylpyrrolidone, acacia gum, magnesium stearate. Per cent recoveries ranged from 98·5 to 101·1. Mixtures of excipients alone gave only a baseline spectrum.

Ruggedness. A ruggedness test was carried out by the procedure of the AOAC (Youden & Steiner 1975). The factors studied were the spectrometer (two similar models were used), bandwidth (2 nm or 1 nm), scan speed (60 or 30 nm min^{-1}), standard weight (100 or

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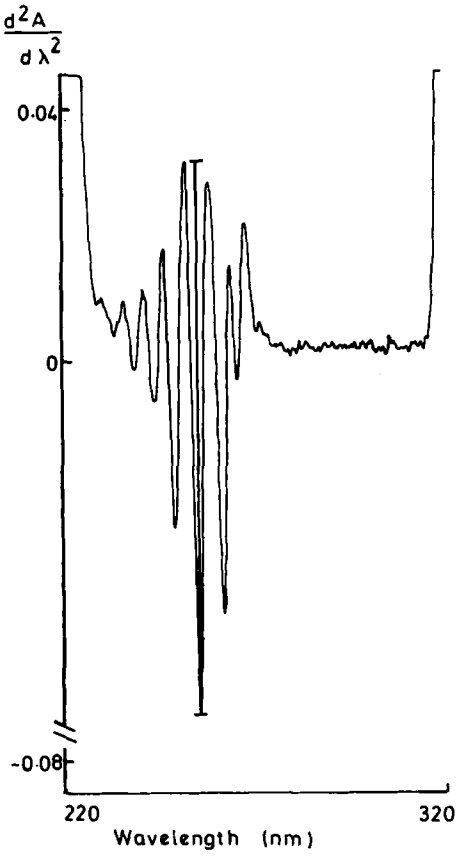

FIG. 1. A second derivative spectrum of procyclidine hydrochloride showing the method of measurement.

120 mg), test weight (equivalent of 25 or 30 mg of drug), acid strength (0·1 or 0·09 M) and time in the ultrasonic bath (15 or 10 min). Only one factor, the spectrometer, gave a significant difference at the 5% level. A second experiment was carried out to assess the difference between spectrometers. One batch of tablets and three batches of injection were assayed and the solutions measured on both spectrometers. There was no significant difference between the results from each instrument.

Precision of assay. Two operators each carried out four independent assays of a bulk of ground tablets. The mean (% of stated amount) was 99·5, s.d. 0·632 (n = 8). A single assay in this laboratory is expected to give a result within 2% of the mean result ($P = 0·95$).

Comparison with official method. Nine batches of tablets were examined by this method and by the official titration method (British Pharmacopoeia 1980). The mean response (% of stated amount) and standard deviations were:

derivative spectrometry 99·0 ± 0·98,

titration 101·0 ± 0·93

Both sets of results are well within the official limits of 90·0 to 110·0%. No official procedure is published for the injection, but three batches gave results of 98·7, 99·9 and 100·9% stated amount when assayed by second derivative u.v. spectrometry.

It is concluded that second derivative u.v. spectrometry is suitable as a rapid alternative to the official titration method for procyclidine tablets and may also be applied to the injection.

We wish to thank Mr T. W. P. Carter for skilled technical assistance and Mr P. H. Cobb for help with the manuscript.

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