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HPLC with electrochemical detection for the determination of dipyridamole in pharmaceuticals*

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Introduction

For many years dipyridamole has been used in the treatment of hypertension as a vasodilatator, however, recently it has been recognised as an anti-platelet aggregation agent. A great number of LC methods for the quantitative analysis of dipyridamole involving spectroscopic detection (UV or fluorescence) have been described [1–5].

Generally the best results are obtained with spectrofluorimetric detection, however all the spectroscopic methods require preliminary sample preparation and extraction. Previous studies have indicated that dipyridamole undergoes electrochemical oxidation in some organic solvents and aqueous media [6, 7]. Furthermore this detection method is found to be more selective than spectroscopic detection and free from interference by the degradation of dipyridamole or synthesis by-products. The present paper describes a method using HPLC and amperometric electrochemical detection for the determination of dipyridamole in pharmaceutical products.

Experimental

Apparatus

HPLC analyses were carried out using a Waters Ass. Model 6000A solvent delivery pump equipped with a Rheodyne injector (20 μl), a μBondapak C_{18} column (30 × 0.39 cm i.d.; particle size 10 μm) and a Metrohm 641VA detector with a Metrohm 656 cell. The signal from the detector was fed into an Omniscribe 10 mV chart recorder.

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Voltamperometric measurements were made on a PRG5 Tacussel potentiostat coupled with an EPL1 Tacussel recorder in conjunction with a three electrode thermostated cell (25°C) which consists of a rotating disk platinum electrode, a platinum wire auxiliary electrode and a SCE (standard calomel) reference electrode. A detection potential of +0.70 V (SCE) was used for the assay.

Reagents

Dipyridamole (pharmaceutical quality) was generously supplied by Nativelle Laboratory. Its purity was tested by thin-layer chromatography (methanol:strong ammonia solution; 100:1.5, $Rf = 0.68$) and found to be sufficiently pure for use as supplied.

The LC mobile phase which consisted of methanol and aqueous 0.1 M sodium acetate buffer (pH 4) (75:25, v/v) was filtered through a Millipore filter prior to use. A flow-rate of 1.0 cm^3 min^{-1} was used throughout the investigation.

Results and Discussion

Electrochemical study

In order to determine the optimum detection potential, a preliminary electrochemical study was undertaken using the mobile phase as solvent. In this medium the anodic behaviour of dipyridamole at the vitrous carbon electrode was very similar to that previously found in pure water [6]. Only one diffusion wave was recorded with a half-wave potential of +0.46 V (SCE). The measurements indicated a strict proportionality between current and concentration.

These results indicate that electrochemical detection is a valid method for HPLC analysis of dipyridamole. Furthermore, a potential of +0.70 V (SCE) was found to correspond to the maximum current intensity.

Precision and accuracy

Reproducibility. The studies were realised for four solutions of different concentrations; each solution was injected five times.

The peak areas were measured and analysed stastistically to yield a relative standard deviation maximum value of 0.9%, as summarised in Table 1.

Linearity. A strict proportionality between the peak area and the injected quantity of dipyridamole was found in the range 3–40 ng. With a detector sensitivity of 1 nA it was possible to determine quantities down to about 400 pg. Under these analytical conditions the dipyridamole retention time was 6.5 (+/−0.2) min and the limit of detection was 200 pg.

Table 1

Injected quantity	Area mean cm^2	Standard deviation	R.S.D. %
20.12 ng	0.65	0.006	0.908
50.3 ng	0.92	0.050	0.55
100.6 ng	1.96	0.011	0.56
150.9 ng	3.20	0.024	0.75

Area mean for 5 determinations.
R.S.D. = relative standard deviation.

Determination in pharmaceutical preparations

Calibration graphs of peak area (cm^2) against concentration were plotted over the range 20–400 ng of dipyridamole injected onto the column in the mobile phase: the response was linear in this range: ($n = 5$, $r = 0.999$): $y = 0.043X - 0.205$.

For calculations of the results evaluating the precision of the method, the following equations were used:

$$\bar{X} = (\Sigma_{i=1}^{n} X_i)/n$$

$$S = \sqrt{[\Sigma_{i=1}^{n} (X_i - \bar{X})^2]/n}$$

$$RSD = (S \times 100)/\bar{X}$$

The following pharmaceutical excipients which are commonly found in capsules and tablets did not interfere with the assay: lactose, saccharose, microcrystalline cellulose, magnesium and zinc stearates, PEG, *p*-hydroxybenzoates.

For the determination of dipyridamole in coloured tablets it was found necessary to eliminate the dyes prior to analysis.

A previous study of the qualitative and quantitative analysis of dyes by HPLC with electrochemical detection [8] has shown that synthetic dyes commonly used in pharmaceutical preparations, such as amaranth (E123), azorubin (E122), orange yellow S (E110), give rise to oxidative waves with half wave potentials of about +0,90 V (SCE) in aqueous methanol. For this reason when analysing coated tablets, it is necessary to eliminate the interfering dyes by dissolving the coating in water.

The results of the assay of dipyridamole capsules and tablets are summarised in Fig. 1

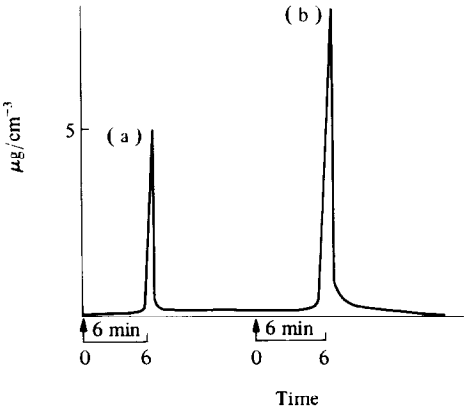

Figure 1
Chromatograms of dipyridamole solutions: (a) 5×10^{-3} mg ml^{-1}; (b) test sample.

Table 2
Assay of dipyridamole

	Stated amount	Average found*	Recovery %	R.S.D. %
Capsules	75 mg	73.5 mg	98.0%	0.29
Tablets	75 mg	74.1 mg	98.8%	0.30

*Average of 5 determinations.
R.S.D. = Relative standard deviation.

and Table 2. The averages agree well with the theory and standard error of the assays are less than 0.3%.

Conclusion

It is demonstrated that the electrochemical oxidation of dipyridamole may be used as the basis of the assay of pharmaceutical preparations.

This detection method coupled with HPLC results in a rapid, sensitive, specific and accurate assay which requires a minimum of sample preparation that is ideal for routine analysis.

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