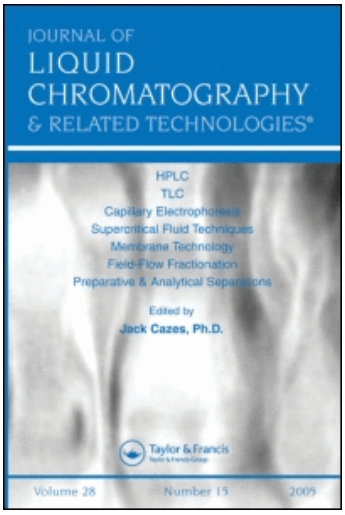

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Stability Indicating High Performance Liquid Chromatographic Method for the Assay of Diltiazem Hydrochloride in Tablets

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STABILITY INDICATING HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC METHOD FOR THE ASSAY OF DILTIAZEM HYDROCHLORIDE IN TABLETS

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ABSTRACT

A rapid high performance liquid chromatographic (HPLC) method for the determination of diltiazem hydrochloride, a calcium antagonist, is described. The stability indicating nature of the method was demonstrated by resolving diltiazem from products of decomposition. Reverse phase liquid chromatography was performed with an octadecyl silane-bonded silica column at ambient temperature, using UV detection at 240 nm. The mobile phase consisting of acetonitrile, methanol and 0.05 M monobasic potassium phosphate (25:20:55) was pumped at 2 ml/min. The internal standard was cyproheptadine hydrochloride. A percent RSD of < 1.5% and correlation coefficient 0.9996 were achieved over the concentration range studied (10-50 µg/ml.)

INTRODUCTION

Diltiazem hydrochloride is a calcium antagonist which has been shown to be useful in treatment of unstable angina. Chemically the drug is 3-(acetyloxy)-5-(2-[dimethylamino]ethyl) -2, 3-dihydro-2-(4-methoxyphenyl)-1, 5-benzothizepine-4-(5H) one. The drug and its tablet formulation are official in USP[1] wherein they are estimated by HPLC method using ion pair technique. The other methods for its estimation include GC[2-3] and HPLC[4-6]. In this report the development and validation of a HPLC method for the quantification of diltiazem in presence of decomposition product is described. The method is simple and sensitive.

EXPERIMENTAL

Materials :

All reagents used were of analytical grade, except acetonitrile, methanol and water which were of HPLC grade.

Chromatography :

The analysis were performed on a Shimadzu HPLC system LC-6A equipped with a variable wavelength detector SPD-6AV set at 240 nm, a Rexchrome ODS Column (25 cm x 4.6 mm i.d.). Sample injections were 50 ul. The mobile phase consisting of acetonitrile, methanol and 0.05 M monobasic potassium phosphate in the ratio of 25:20:55 was used at a flow rate of 2 ml/min.

Standard drug solution containing 25 mg of diltiazem hydrochloride was prepared in 50 ml methanol. Internal standard solution containing 25 mg of cyproheptadine hydrochloride in 50 ml

TABLE I - Results of diltiazem tablet analysis

Lot	Labelled amount mg/tablet	Found mg/tablet	% Recovery	RSD %
A	30	29.34	97.80	1.14
B	30	29.26	97.53	1.25
C	60	59.18	98.63	1.46
D	60	58.76	97.93	0.92

methanol was used. Into a series of 50 ml volumetric flasks, varying amounts of drug solution (1-5 ml) were pipetted out. To each flask 5 ml of internal standard solution was added and the volume was made upto the mark with water. The solutions were injected in triplicate and ratio of peak areas for diltiazem - internal standard were calculated. A plot of peak ratio against the drug concentration was linear in the range 10-50 µg/ml.

To 5 ml of filtered solution, 5 ml of internal standard solution was added and volume was made upto 50 ml with water and analysed. The amount of drug corresponding to the peak ratio was found from the calibration graph and the content of diltiazem hydrochloride in tablet was calculated using dilution factor. The results are given in Table I.

A stock solution containing 0.5 mg/ml of diltiazem hydrochloride was prepared in distilled water. Five ml of stock solution was mixed with either 5 ml 0.1N sodium hydroxide, 5 ml 0.1N hydrochloric acid or 2 ml of 30% hydrogen peroxide in 50 ml volumetric

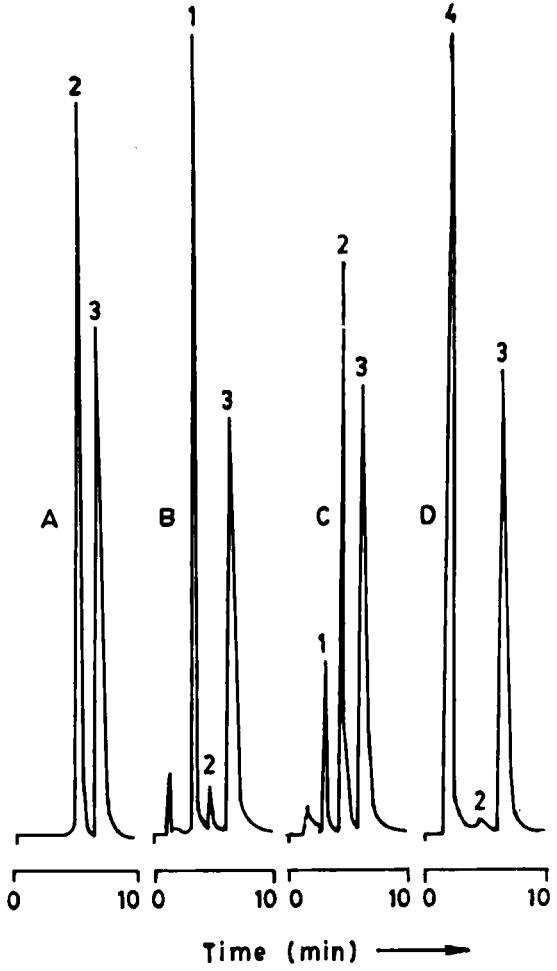

Figure 1 : Chromatograms of diltiazem hydrochloride solution boiled for 30 minutes in A, water pH 5.5 B, 0.1N NaOH C, 0.1N HCl D, 30% H_2O_2. Peak 1 - Desacetyl diltiazem hydrochloride 2 - Diltiazem hydrochloride 3 - Internal Standard. 4 - Unknown peak.

flasks. The flasks were kept in boiling water bath for 30 min. After cooling, the pH was adjusted to 5.5 with 0.1N HCl or 0.1N NaOH. To all the flasks 5 ml internal standard solution was added and the volume was made upto the mark with water and analysed.

RESULTS & DISCUSSION

The direct measurement of raw drug for diltiazem hydrochloride and the anticipated breakdown product is shown in Fig. 1. The limit of quantitation of diltiazem hydrochloride was 10 µg/ml under the operating conditions employed. The specificity of the HPLC method was tested with degraded diltiazem samples. No change in diltiazem concentration were seen in the boiled aqueous solution. After 30 minutes in boiling acid (0.1N HCl) or base (0.1N NaOH) diltiazem was partly or completely converted to desacetyl diltiazem as might be expected under these conditions. The drug solution upon boiling for 30 minutes in 30% hydrogen peroxide yielded several additional unidentified products. In each chromatogram, it can be seen that size of diltiazem peak decreases with degradation and that of degradation product increases. The practicality of the method was demonstrated by the analysis of diltiazem tablets. A percent RSD of < 1.5 % and correlation coefficient of 0.9996 for the calibration curves were obtained. The percent RSD values for a single sample were < 2 %.

In conclusion, the present HPLC method is rapid, precise and accurate for the determination of diltiazem hydrochloride in tablets.

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