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# Determination of felodipine in bulk drug and in tablets by high performance liquid chromatography

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**A rapid assay procedure based on high-performance liquid chromatography (HPLC) has been developed for the specific determination of antihypertensive drug felodipine in pharmaceutical formulations (tablets). The HPLC determination was carried out on a reversed-phase $C_{18}$ (250×4.6 mm i.d) column using a mobile phase consisting of acetonitrile- 20 mM aqueous ammonium acetate buffer of pH 4.5 (80+20) at a flow rate of 1.0 mL $min^{-1}$ with UV defection at 236 nm. Calibration graph was linear from 2.49 to 99.60 μg $mL^{-1}$. The method has been validated according to current guidelines including the assay of pharmacopoeial standard tablets. Recoveries ranged from 97.80 to 102.10%. The excipient present in the tablets did not interfere in the method. The described HPLC method is comparable in terms of accuracy and precision with that of a reported method.**

Felodipine (FLD), chemically, ethyl methyl-4(2,3-dichlorophenyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridine dicarboxylic acid-3-ethyl-5-methylester, is a calcium antagonist widely used in the treatment of hypertension, heart failure and angina pectoris[1]. Various techniques have been used for the assay of FLD in pharmaceuticals and body fluids. The drug has been determined in human plasma by capillary gas chromatography[2], high-selectivity gas chromatography[3] and high performance liquid chromatography (HPLC)[4,5], and in urine by liquid chromatography (LC)[6]. The drug metabolites in plasma have been determined by HPLC[7], LC[8], gas chromatography (GC)[9] and capillary GC[10]. Many methods have been described for the determination of FLD in formulations based on different techniques such as LC[11,12], GC[13], HPLC[14,15], reversed-phase HPLC[16], cyclic voltammetry[17] nuclear magnetic resonance spectroscopy[18] and visible spectrophotometry[19]. Many of the reported methods suffer from one or the other disadvantage. In the LC method[11], the accelerated extraction technique is performed at 50 and 100°C, the GC procedure[13] is less sensitive (18-500 μg $mL^{-1}$) whereas the HPLC[14,16] and spectrophotometric[19] methods have narrow range of determination. The aim of this paper was to develop a rapid, sensitive, accurate and precise method for the determination of FLD in pharmaceutical formulations based on the use of HPLC.

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## Experimental Procedure

### *Reagents and materials*

Analytical grade ammonium acetate (Thomas Baker, England), HPLC grade acetonitrile (RANKEM, India), AR grade acetic acid (S.d. Fine Chem., India) and distilled water filtered through a 0.45 μm filter (Millipore) were used. A 20 mM ammonium acetate was prepared by dissolving 3.08 g in 2 L of water, the pH was adjusted to 4.5 with acetic acid, and filtered through 0.45 μm filter. The diluent solution was prepared by mixing acetonitrile and water in the ratio 60:40. The solvent system used for chromatography consisted of acetonitrile-ammonium acetate buffer (80:20). Pharmaceutical grade FLD was kindly provided by Cipla India Ltd., Mumbai, India as gift and was used as received. A stock standard solution of FLD (249 μg $mL^{-1}$) was prepared in the diluent solution.

### *Apparatus*

A HPLC (Agilent 1100 series) equipped with an inbuilt solvent degasser, quarternary pump, photodiode array detector with variable injector and autosampler and reversed-phase column (Hypersil ODS $C_{18}$ 25 cm long and 4.6 mm i.d Thermosil) were employed.

### *Chromatographic conditions*

Chromatographic separation was achieved at ambient temperature on a reversed phase ODS $C_{18}$ column using mobile phase consisting of acetonitirle-

20 mM ammonium acetate buffer (80+20) at a flow rate of 1.0 mL $min^{-1}$. The UV detector was set at 236 nm.

### *Calibration graph*

Working standard solutions containing 2.49-99.60 μg $mL^{-1}$ of FLD were prepared by transferring 0.5-20 mL of stock standard solution (249 μg $mL^{-1}$) into separate 50 mL volumetric flasks and diluting to volume with the diluent solution. 20 μL volume was injected automatically into the chromatograph in duplicate and chromatograms were recorded. Calibration graph was constructed by plotting the mean peak area against FLD concentration.

### *Procedure for tablets*

Felogard ER-10 and plendil tablets each labelled to contain 2.5, 5.0 or 10.0 mg FLD were procured from local commercial sources. Five or ten tablets depending on the labelled amount were weighed accurately and ground into a fine powder with agate pestle and mortar. An amount of the powdered tablets equivalent to 10 mg of FLD was dissolved in the diluent solution and the resulting mixture was transferred quantitatively into a 50 mL calibrated flask and made up to volume with the diluent solution through thorough mixing. A small portion of this solution (~10 mL) was withdrawn and filtered through a 0.2 μm filter to ensure the absence of particulate matter. This filtered solution was appropriately diluted to get the final solution for analysis.

## Results and Discussion

The conditions used, gave well-resolved peak (Fig. 1). A mobile phase consisting of acetonitrile and 20 mM aqueous ammonium acetate (80+20) was chosen after several trials with acetonitrile-water, methanol-water, acetonitrile potassium dihydrogen phosphate and methanol-potassium dihydrogen phosphate. The described chromatographic system gave the peak in a reasonable time of ~5 min. For quantitative determinations a linear calibration graph ($y = -11.35 + 55.06x$; $r = 0.9996$; $n = 6$, where $y$ and $x$ are mean peak area and concentration in μg $mL^{-1}$, respectively) was obtained over the working concentration range of 2.49-99.60 μg $mL^{-1}$. The limit of detection and the limit of qualification were 0.60 and 1.60 μg $mL^{-1}$, respectively.

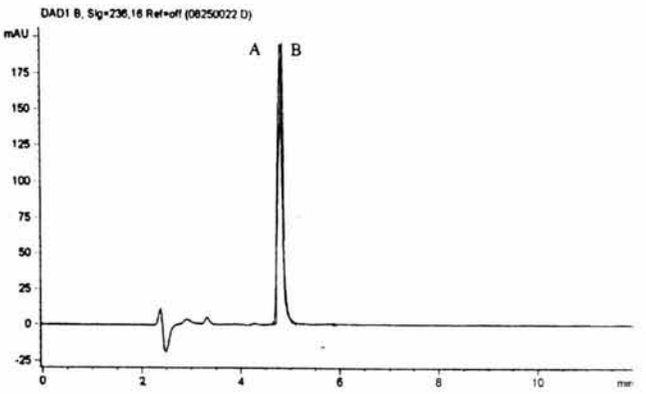


Fig. 1—Chromatogram of tablet solution

### *Precision*

The within-day precision of the method was determined for both peak area and retention time by repeat analyses (seven identical injections) of the standard solution containing the drug at three different concentration levels. The RSD for retention time ranged from 0.14 to 0.30% and that for peak area ranged from 0.36 and 0.68%. The day-to-day precision was established by performing the analysis over a five-day period on solution prepared freshly each day. The low RSD values (<1%) indicate the ruggedness of the method.

### *Accuracy*

Accuracy of the proposed method for the determination of FLD was established by assaying the solution of known concentration as done for determining the within-day precision. Low percent error values (<2%) indicate the high accuracy of the method.

### *Application to tablets*

The developed method was applied to the determination of FLD in commercially available tablets. The results obtained are presented in Table 1. Determination of FLD content of six samples of FLD tablets gave values between 97.80 and 102.10 and were in agreement with the labelled amount. No significant differences were found between the results obtained by the HPLC and those obtained by reported method[19] for the same batch at the 95% confidence level.

In order to demonstrate the validity and applicability of the method, recovery studies were performed via standard-addition technique. Tablets were spiked with pure FLD at three different levels and the total was found by the proposed method. The

Table 1— Results of assay of felodipine tablets by the proposed HPLC method

| Brand name of tablet | Label claim, mg/tablet | Found (mg±SD) | | Student's t-value (2.78) | F-value (6.39) |
|---|---|---|---|---|---|
| | | Proposed method | Reported method | | |
| Fellogard[a] EF | 2.50 | 2.45±0.25 | 2.40±0.62 | 0.18 | 6.15 |
| | 5.00 | 5.10±0.65 | 5.18±1.41 | 1.60 | 4.70 |
| | 10.00 | 9.98±0.85 | 9.81±1.59 | 0.22 | 3.49 |
| Plendil[b] | 2.50 | 2.51±0.45 | 2.59±0.91 | 0.19 | 4.09 |
| | 5.00 | 4.89±0.79 | 4.80±1.21 | 0.14 | 2.34 |
| | 10.00 | 10.21±0.81 | 9.89±1.32 | 0.30 | 2.65 |

Marketed by: a—Cipla India, b—Astra-IDH, India
*Mean value of five determinations

experiment at each level was repeated three times. The percent recoveries of the pure drug added, reveal that the commonly added excipients such as lactose, talc, starch, gum acacia, sodium alginate and magnesium stearate did not interfere in the assay method. This is amply demonstrated by a single peak due to FLD in the chromatogram of the tablet solution (Fig. 1).

## Conclusions

Thus, a method has been developed and appropriately validated for the assay of FLD in tablets for the purpose of product quality assessment. The method is rapid, selective, accurate and precise for FLD determination. A single chromatographic run took less than 5 min. The method does not require extensive sample treatment and involves a HPLC system employing an inexpensive mobile phase. The UV detection was linear for the concentrations studied. There was no interference from matrix sources. The proposed assay method is applicable over a wide concentration range compared to many chromatographic methods proposed earlier[14,16] and is more sensitive than the existing HPLC[13-16] and visible spectrophotometric[19] methods for pharmaceutical formulations. The method is suitable for regular determination of FLD and for checking the stability of its formulations.

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