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Quantitative Estimation of Felodipine by Zero and First Order Derivative Area under Curve Spectrophotometric Methods in Bulk and *in-house* Tablets

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Abstract

The main objective of the proposed methods is to disclose simple, accurate, precise, reproducible and sensitive UV-spectrophotometry methods for the estimation of Felodipine in Bulk and in-house formulation tablets. Further, this study is designed to validate the developed methods as per ICH guidelines. Felodipine is a long acting calcium channel blocker anti-hypertensive agent. Four simple UV-Spectrophotometric methods were established by using Double beam UV-Spectrophotometer (UV-2450, Shimadzu), Felodipine showed maximum absorbance at 237.60 nm (λ max). The calibration curves were plotted in the concentration range of 03-18 µg/mL. The % recovery was found to be in the range of 99-101%. The precision of the proposed method was calculated in terms of %RSD <2, methods are rugged and precise. Proposed methods can be used for routine analysis of Felodipine in bulk and in-house formulations.

Keywords: ***Curve spectrophotometric Methods; Felodipine.***

Introduction

Felodipine (FDP), (Molecular formula- $C_{18}H_{19}Cl_2NO_4$ M. W. - 384.3 gm.), chemically is 4-(2, 3-Dichlorophenyl)-1, 4-dihydro-2, 6-dimethyl-3, 5 pyridinedicarboxylic acid ethyl methyl ester (FIG. 1) [1,2].

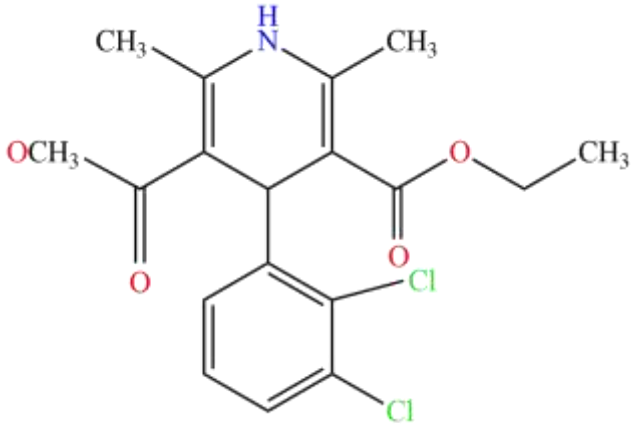

FIG. 1. **Chemical structure of Felodipine**.

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Felodipine is a long-acting calcium channel blocker (dihydropyridines class) used as an anti-hypertensive and in the treatment of angina [3]. The literature review shows the various methods for the determination of Felodipine by High Performance Liquid Chromatography (HPLC) [4], LC-MS Method for estimation of Felodipine in Human Plasma [5], Estimation of Felodipine in Rabbit Plasma by HPLC, regioisomeric impurity by UV Spectrophotometric method [6].
The objective of this work is to establish zero and first derivative UV Spectroscopy and its AUC technique. The current works emphasize simple, precise, sensitive and effective UV Spectroscopy method for estimation of Felodipine in bulk and *in-house* tablets. The method was validated as per ICH guidelines.

Experimental Works

Materials and method

Felodipine (Pure) were obtained as a gift sample from Glenmark Pharmaceutical Ltd, Mumbai. As the tablet formulation was not available in Indian market, tablet containing 10 mg Felodipine were prepared *in-house* using Dry Granulation technique. Prepared tablets were used as pharmaceutical formulation for further analysis.

Instrument

A double beam UV-VIS spectrophotometer (UV-2450, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe 2.21 with 1 cm quartz cells was used. An electronic balance (Model Shimadzu AUX 120) was used for weighing purpose.

Preparation of standard stock solution and determination of λ max

The standard stock solution of Felodipine was prepared by dissolving 10 mg of drug into a 100 mL volumetric flask and diluted up to the mark with methanol to make the concentration of 100 µg/mL. From the standard stock solution, 1 mL of solution was transferred into 10 mL of volumetric flask and diluted up to the mark obtaining 10 µg/mL and scanned in UV-visible range 400-200 nm, Felodipine shows a maximum absorbance at 237.40 nm (λ max).

Method Ⅰ (Zero Order Spectrometry) and method Ⅱ (AUC-Zero Order Spectrometry)

From the standard stock solution (100 µg/mL of Felodipine), different dilutions were prepared in the range of 3-18 µg/mL. In Method Ⅰ, the maximum absorbance was obtained at 237.40 nm, Shown in FIG. 2.

And in the Method Ⅱ, Area under Curve was chosen between the range of 233.00-240.20 nm, Shown in FIG. 3. The calibration curves were plotted as concentration *versus* absorbance for Zero Order and concentration *versus* AUC for Zero Order AUC in Method Ⅰ and Method Ⅱ, respectively Shown in FIG. 4 and 5**.**

Method Ⅲ (1st Order derivative spectrometry) and method Ⅳ (AUC-1st Order Derivative Spectrometry)

In Method Ⅲ and Method Ⅳ, For Method Ⅲ, Spectra of the above dilutions were derivative into a 1st order derivative by using UV-Probe 2.21 software, in this the delta lambda and scaling factor were selected 4 and 10, respectively. In this method the amplitude was recorded at 245.00 nm shown in **FIG. 6**. While Method Ⅳ, the AUC range for 1st derivative 242.20-248.80 nm selected, shown in **FIG. 7**. The calibration curves were plotted as concentration *versus* amplitude and concentration *versus* AUC for Method Ⅲ and Method Ⅳ, respectively shown in FIG. 7 and 8**.**

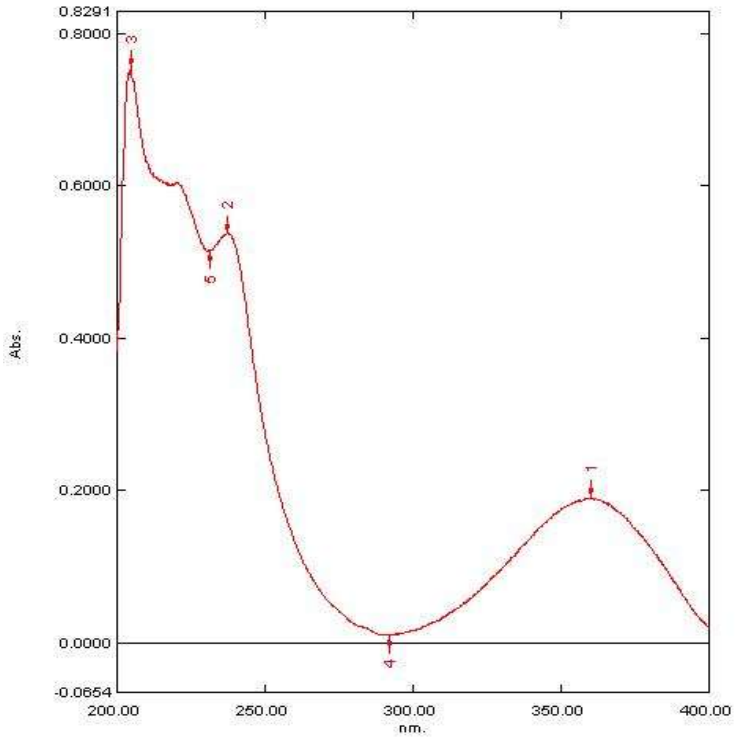

FIG. 2. **Zero order spectra of Felodipine**.

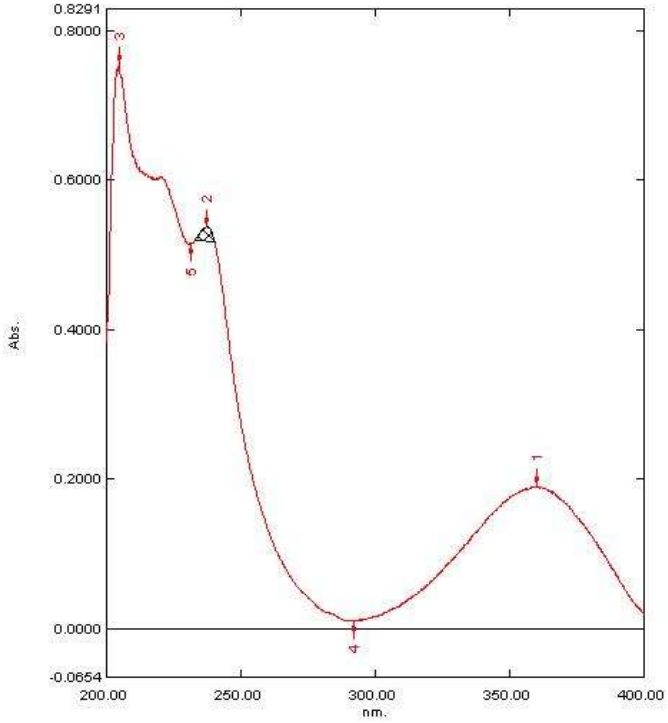

FIG. 3. **Zero order AUC spectra of Felodipine.**

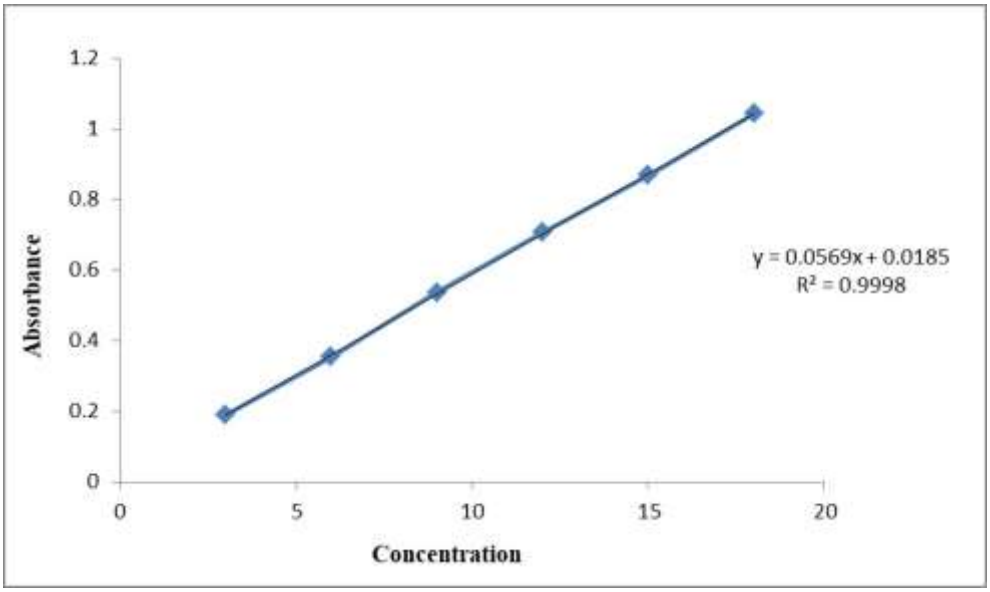

FIG. 4. **Linearity curve of Felodipine by zero order Spectrometry.**

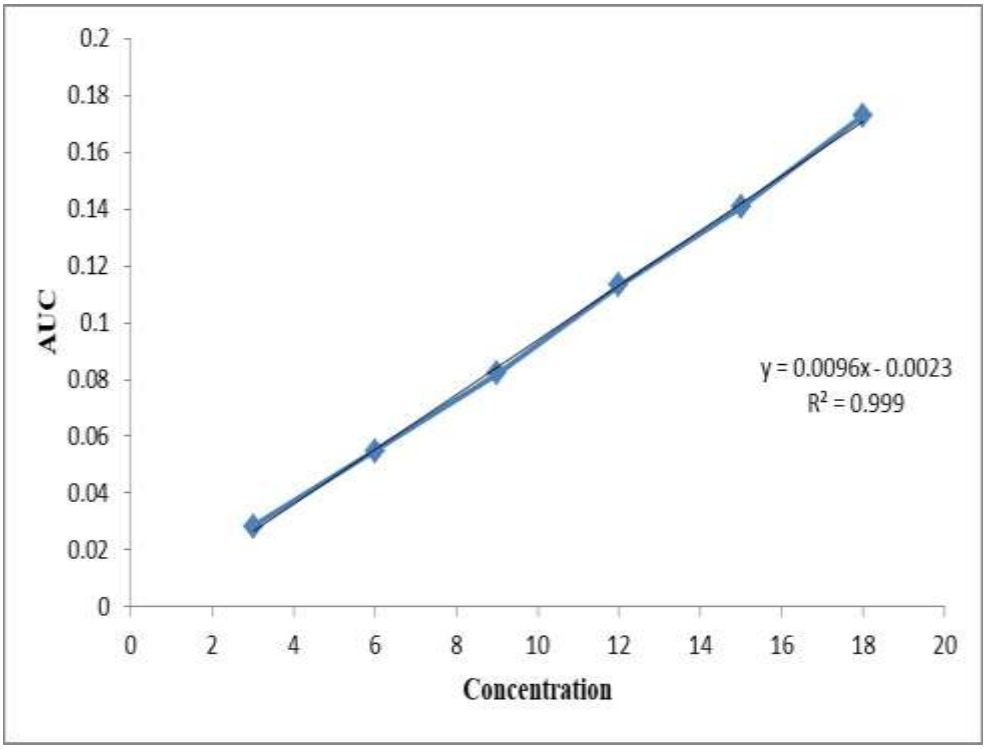

FIG. 5. **Linearity curve of Felodipine by zero order AUC spectrometry.**

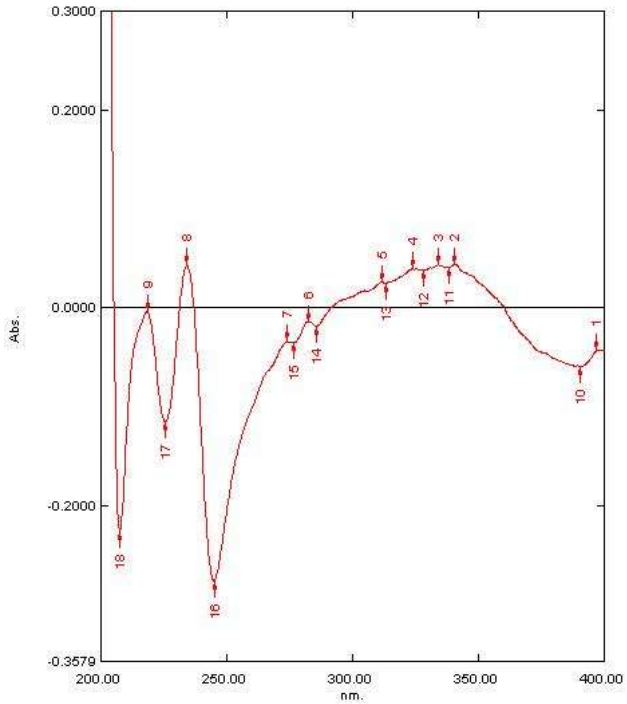

FIG. 6. **1st Order spectra of Felodipine.**

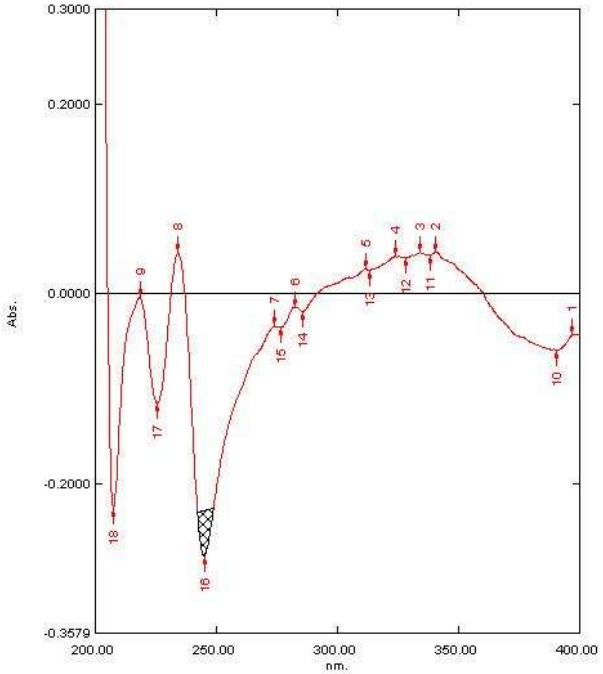

FIG. 7. **1st Order AUC spectra of Felodipine.**

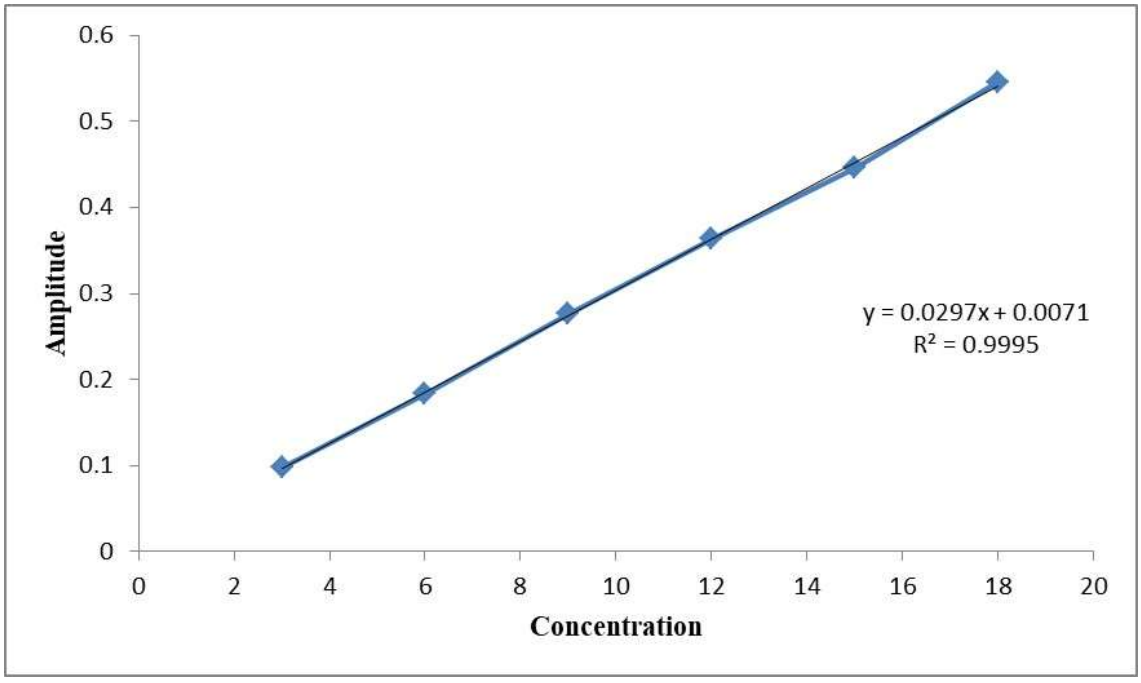

FIG. 8. **Linearity curve of Felodipine by 1st order spectrometry.**

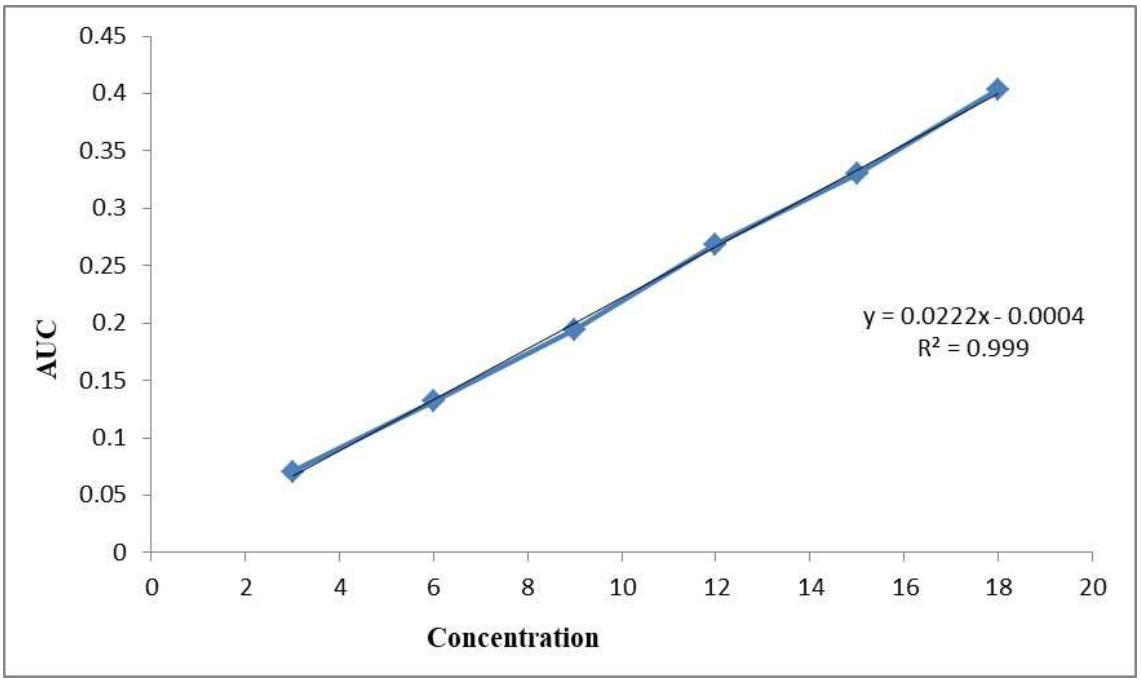

FIG. 9. **Linearity curve of Felodipine by 1st order AUC spectrometry.**

Validation of the Method

Study of linearity curves

From the standard stock solution, aliquots portion in the range of 0.3, 0.6, 0.9, 1.2, 1.5 and 1.8 mL were transferred into a 10mL volumetric flask and diluted up to the mark using methanol to prepare 3, 6, 9, 12, 15 and 18 µg/mL. The dilutions were scanned on a spectrophotometer in the range of 400-200 nm. The graph was plotted between concentration *versus* absorbance, amplitude and AUC.

Accuracy/Recovery studies

The accuracy of the method was determined by calculating recoveries of Felodipine by the standard addition method. The study was carried out by adding known amount of standard drug to the developed *in-house* tablet formulation at three 80, 100 and 120% level. The solutions were reanalyzed by proposed method. The accuracy of the method noted.

Precision

Precision of the method was performed as intra-day and inter-day. Intra-day precision was determined by examining the 6, 9 and 12 µg/mL of Felodipine for three times in the same day. Inter-day precision was determined by analyzing the 6, 9 and 12 µg/mL of Felodipine for three days.

Sensitivity (LOD and LOQ)

The Sensitivity measurements of Felodipine by proposed method were determined in terms of Limit of Detection (LOD) and Limit of Quantification (LOQ) by using the equation designed by International Conference on Harmonization (ICH) guidelines.

$$LOD=3.3\times\sigma/S$$

$$LOQ=10\times\sigma/S$$

Where **σ=** Standard Deviation

s= slope

Repeatability

Repeatability of the proposed method was determined for 9 µg/mL concentration of Felodipine by analyzing for six times for all the methods.

Ruggedness

Ruggedness of the proposed method was determined for 9 µg/mL concentration of Felodipine by analyzing of aliquots from a homogenous slot by two analysts using same environmental and operational conditions. The results are in acceptable range that is %RSD values <2 for all the methods.

Results and Discussion

Method validation

The proposed method was validated as per ICH guidelines. The solutions of the drug were prepared as per the earlier adopted procedure given in the experiment.

Linearity studies

Felodipine showed a good linear relationship for all the methods are shown in TABLE 1**.** The given concentration ranges 03-18 µg/mL.

Parameters	Method Ⅰ	Method Ⅱ	Method Ⅲ	Method Ⅳ
Beer-Lambert's Range (µg/mL)	3-18	3-18	3-18	3-18
λ max (nm)	237.60	233.00-240.20	245.00	242.20-248.80
Slope	0.0569	0.0096	0.0297	0.0222
Intercept	0.0185	0.0023	0.0071	0.0004
Correlation coefficient	0.999	0.999	0.999	0.999
Limit of detection (µg)	0.1514	0.7080	0.1260	0.2764
Limit of quantitation (µg)	0.4590	2.1454	0.3819	0.8378

TABLE 1**. System suitability test results (n=5).**

Accuracy

The % recovery of Felodipine at three concentration level 80, 100 and 120% were calculated for all the methods and the results shown in TABLE 2.

% Value	Initial amount (µg/mL)	Amount added (µg/mL)	% Recovery			
			Method Ⅰ	Method Ⅱ	Method Ⅲ	Method Ⅳ
80	6	4.2	100.0659	100.0434	99.9228	99.9906
100	6	6	99.9853	100.0868	99.9719	99.7372
120	6	7.2	100.0049	99.9710	100.0047	99.4119

TABLE 2**. System suitability test results (n=5).**

Precision

The precision of the developed method was expressed in terms of intra-day and inter-day. The % relative standard deviation's (RSD) values for all the methods were found to be less than 2 and results shown in TABLE 3.

Sensitivity

The LOD and LOQ for all the proposed methods were shown in TABLE 1.

Repeatability

Repeatability for Felodipine was determined for all the methods by analyzing 9 µg/mL concentration for six times and the % amount found was determined with %RSD <2. The results of repeatability are summarized in TABLE 4.

Conc. (µg/mL)	Intra-day[a] %RSD				Inter-day[a] % RSD			
	Method Ⅰ	Method Ⅱ	Method Ⅲ	Method Ⅳ	Method Ⅰ	Method Ⅱ	Method Ⅲ	Method Ⅳ
6	0.0610	0.5016	0.182781	0.504148	0.5440	0.1002	0.064877	0.380348
9	0.5431	0.0442	0.173815	0.15015	02953	0.4938	0.037418	0.195403
12	0.3407	0.4108	0.14044	0.357009	0.2631	0.1892	0.049225	0.434371
[a]Average of three estimates								

TABLE 3**. Precision.**

Method	Amount taken (µg/mL) (n=6)	Amount found[a] (%)	% RSD
Method Ⅰ	9	99.9934	0.0806
Method Ⅱ	9	99.9807	0.1703
Method Ⅲ	9	99.9688	0.1305
Method Ⅳ	9	99.9499	0.1952
[a]Average of six estimations			

TABLE 4**. Precision.**

Ruggedness

The method was performed by changing analyst and the method was found to rugged with % Relative standard deviation (RSD) <2 **TABLE 5.**

Method	Amount taken (µg/mL) (n=3)	Amount found (%)[a]	
		Analyst I	Analyst II
Method Ⅰ	9	99.9824	99.9479
Method Ⅱ	9	99.9228	100
Method Ⅲ	9	99.9812	100.0062
Method Ⅳ	9	99.9916	100.0083
[a]Average of six estimations			

TABLE 5**. Ruggedness.**

Determination of Felodipine in in-house tablet

The % amounts reveal from in-house tablet, that there is no interruption from excipients present in it. The % amount for all the method was determined results shown in TABLE 6.

Conclusion

Method (Ⅰ, Ⅱ, Ⅲ, Ⅳ) has been developed for quantitative analysis of Felodipine in Bulk and i-house formulation. The results show that the developed UV Spectrophotometric methods are simple, accurate, precise, reproducible and sensitive.

Consequently, these methods can be used routine analysis and quality control for estimation of Felodipine in Bulk and Pharmaceutical formulations.

The authors are thankful to the Principal, R.C. Patel Institute of Pharmaceutical Education and Research, Shirpur - 425405 (MS), India, for providing the laboratory facility.

Method	Concentration (µg/mL) (n=6)	Amount found (µg/mL)(n=6)	Amount found[a] (%)	% RSD
Method Ⅰ	9	8.9988	99.9869	0.0834
Method Ⅱ	9	8.9930	99.9228	0.2028
Method Ⅲ	9	8.9960	99.9563	0.1595
Method Ⅳ	9	8.9992	99.9916	0.2085
[a]Average of six estimations				

TAB.6**. Analysis of *in-house* Tablet.**

REFERENCES

1. The Merck Index. An Encyclopedia of Chemicals, Drugs and Biologicals, Merck Research Laboratories, USA Merck and Co Inc, 2006.
2. Indian Pharmacopeia. Ministry of Health and Family Welfare, The Indian Pharmacopoeial Commission, Ghaziabad, Government of India, India.
3. Nimje HM, Oswal RJ, Kshirsagar SS, et al. Spectrophotometric Analysis for Estimation of Felodipine in Tablet Dosage Form by Calibration Curve Method. Res J Pharm Technol. 2016; 4: 1805-06.
4. Basavaiah K, Chandrashekar U, Prameela HC. Determination of felodipine in bulk drug and in tablets by high performance liquid chromatography, IJCT. 2003.
5. Sreedevi V, Kumar PR, Thatavarti R. LC-MS method development and validation for the estimation of felodipine in human plasma and stability studies of freeze thaw analyte. Int J Pharm Biomed Res. 2011; 2:65-73.
6. Akash A, Pawar S, Pande VV, et al. Development and Validation of UV spectrophotometric method for estimation of regioisomeric impurity in Felodipine bulk and formulation. In J Pharmaceu Chem. 2015; 05:128-133.