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Research Article

Green Solvent Assisted UV–Spectrophotometric Method for Estimation of Efonadipine Hydrochloride Ethanolate in Bulk and Pharmaceutical Dosage Form

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ABSTRACT

A green solvent-assisted UV-spectrophotometric method has been developed and validated for the estimation of Efonadipine HCl Ethanolate in bulk and pharmaceutical dosage forms using Isopropyl alcohol as the solvent. Isopropyl alcohol, classified as a Class 3 solvent according to ICH Q3C guidelines, offers a safer and environmentally friendly alternative with minimal toxicity concerns. The method involves the measurement of absorbance at 251 nm the maximum wavelength (λ_{max}) of Efonadipine HCl Ethanolate using a UV-visible spectrophotometer. Validation of the method, as per ICH Q2(R1) guidelines, confirmed its accuracy, precision, linearity, and robustness. The linearity of the method was satisfactory over the range of 5 – 25 $\mu\text{g/mL}$ (Correlation coefficient: 0.9976). The %RSD for repeatability for sample measurement and sample application was found to be 0.693 and 0.636 respectively. The %RSD for Intra-day and Inter-day precision was found to be 0.200-0.987% and 0.213-1.192% respectively. The LOD and LOQ for EFO were found to be 0.612 and 1.856 respectively. Recovery of Efonadipine HCl ethanolate ranged from 98.89-100.43%. The method was successfully applied to the marketed formulation for quantitative analysis of Efonadipine HCl ethanolate. The assay result was found to be 99.82% for Efonadipine HCl ethanolate. The proposed method is simple, cost-effective, and sustainable, making it suitable for routine quality control analysis while adhering to the principles of green chemistry.

INTRODUCTION

Hypertension is one of the most common worldwide disease affecting humans. Because of the associated morbidity and mortality and the cost

to society, hypertension is an important public health challenge. Over the past several decades, extensive research, widespread patient education, and a concerted effort on the part of health care professionals have led to decreased mortality and

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morbidity rates from the multiple organ damage arising from years of untreated hypertension. Hypertension is defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. Hypertension is divided into two stages: Stage 1: includes patients with systolic blood pressure 140 – 159 mmHg or diastolic blood pressure 90 – 99 mmHg. Stage 2: includes patients with systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 100 mmHg. (1-3)

In August 2017, CDSCO has approved a Efonidipine HCl Ethanolate for the treatment of hypertension. Efonidipine hydrochloride ethanolate is chemically 2-(N-benzyl anilino) ethyl 5-(5, 5-dimethyl-2-oxo-1, 3,2λ5-dioxaphosphinan-2-yl)-2, 6-dimethyl 1-4-(3-nitrophenyl) -1, 4-dihydropyridine-3-carboxylate, hydrochloride. (Figure 1) Efonidipine is a dihydropyridine, calcium channel blocker with

anti-hypertensive activity. Efonidipine HCl Ethanolate works as a Calcium channel Blocker, Specifically Inhibiting both L-type & T-type calcium channels, leading to Vasodilation & decrease in heart rate by primarily acting on the (SA node) Sinoatrial node, thereby lowering blood pressure. (Figure 2) (4-10)

A review of the literature indicates that several UV spectrophotometric methods have been reported for the estimation of Efonidipine HCl Ethanolate in bulk and pharmaceutical dosage forms.(11) However, no UV-based method has been developed using a Class 3 solvent, as classified by the ICH Q3C guideline. Therefore, this study aims to develop a UV-spectrophotometric method for the estimation of Efonidipine HCl Ethanolate in bulk and pharmaceutical dosage forms using a Class 3 solvent, ensuring compliance with Q3C guidelines and principles of green chemistry.

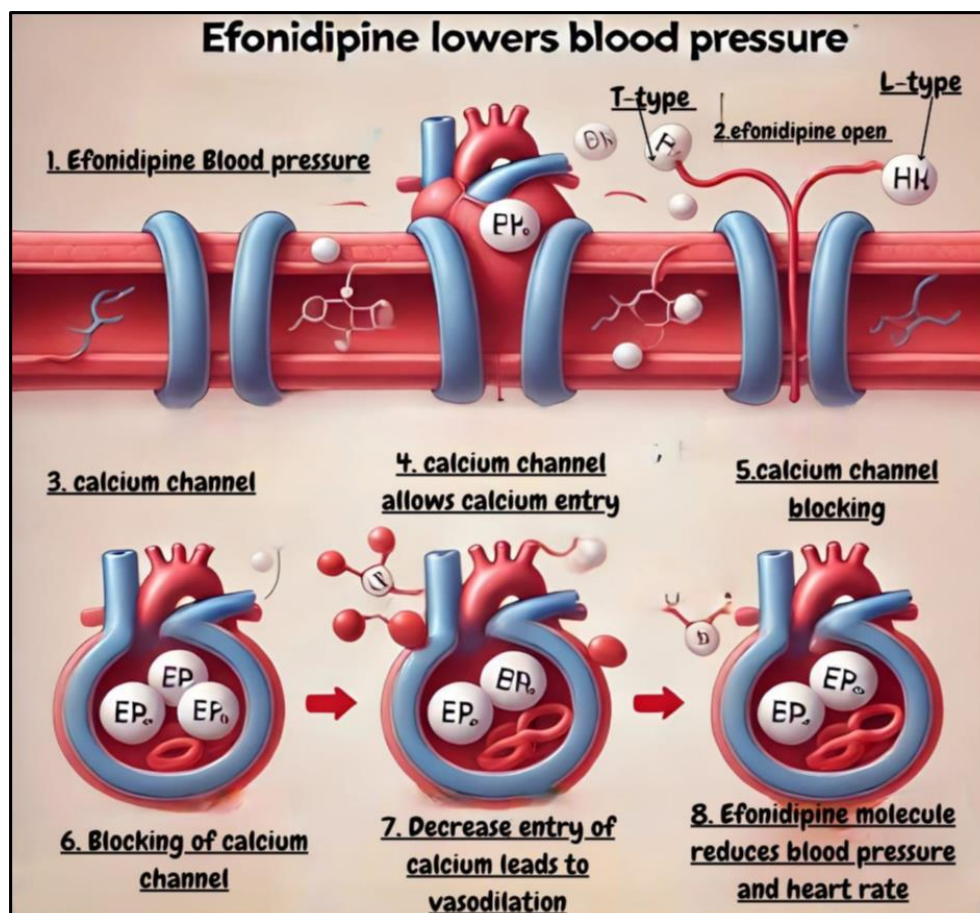


Figure 1: Mechanism of action of efonidipine HCl ethanoate

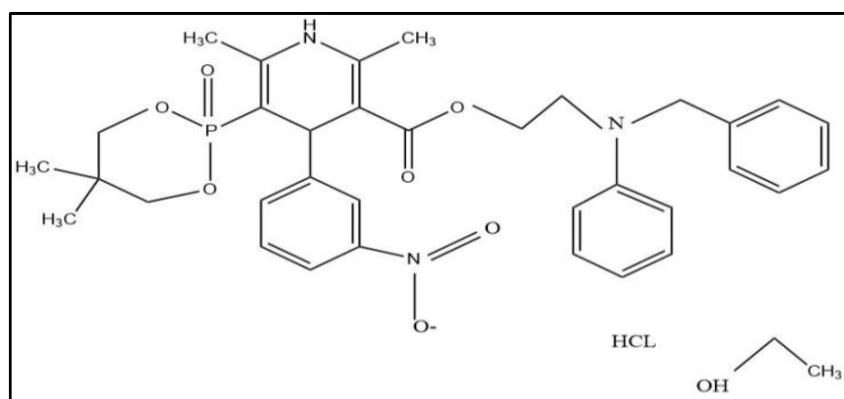


Figure 2: Structure of efonidipine HCl ethanoate

1. MATERIALS AND METHODS

1.1 Instruments And Software

The study was performed using UV-Spectrophotometer (SHIMADZU UV 1900i; Software: Lab solution UV-Vis), which features a double beam with a 1 cm matched cell. The Electronic analytical balance (Scaletac; Model: MH-0095) was used for the weighing.

1.2 Materials And Reagents

Efonidipine HCl ethanoate was gifted sample from reputed company, India. Iso-propyl alcohol AR was purchased from Chemdyes Corporation Rasayan Ghar, Rajkot. The marketed formulation EFNOCAR -40 (Zuventus Healthcare Limited, India) tablet was purchased from local pharmacy.

1.3 Preparation Of Solution

Accurately weighted quantity of Efonidipine HCl Ethanoate 10 mg was transferred to 10 mL volumetric flask, dissolved and diluted to the mark with Isopropyl Alcohol (1000 µg/mL). Aliquot 1 ml was withdrawn from standard stock solution of Efonidipine HCl Ethanoate and was transferred to 10 mL volumetric flask and was diluted to the mark with IPA resulting 100 µg/mL concentration of solution. (Working standard solution A) Aliquot 1 ml was withdrawn from working standard

solution A of Efonidipine HCl Ethanoate and was transferred to 10 mL volumetric flask and was diluted to the mark with IPA resulting 10 µg/mL concentration of solution. (Working standard solution B)

2.4 Determination Of Wavelength For Measurement

The working standard solution of Efonidipine HCl Ethanoate (10 µg/mL) was scanned in the range of 200 – 400 nm keeping IPA as blank. Each solution was scanned between 200 – 400 nm. Wavelength was selected from the spectra of Efonidipine HCl Ethanoate.

2.5 Preparation Of Calibration Curve

From working standard solution A of Efonidipine HCl Ethanoate (100 µg/mL) aliquot of 0.5 mL, 1 mL, 1.5 mL, 2 mL, 2.5 mL were taken and transferred into 10 mL volumetric flasks and diluted up to mark with IPA which resulted in the concentration range of 5 – 25 µg/mL respectively. The absorbance of solutions was measured at 251 nm. Graph of absorbance vs concentration was plotted at wavelengths and regression line equation was found.

2.6 Validation

2.6.1 Linearity

Linearity was determined by analysing 5 independent levels of calibration curves in range of 5 - 25 µg/mL for Efonidipine HCl Ethanolate 5 times. Plot the curve of absorbance vs respective concentration and regression coefficient & regression line equation was determined.

2.6.2 Repeatability

2.6.2.1 Repeatability Of Sample Application

Repeatability of the sample application was determined by preparing solution of 15 µg/mL of Efonidipine HCl Ethanolate respectively for seven times and measure the absorbance at selected wavelengths. The results of repeatability sample preparation were reported in terms of %RSD.

2.6.2.2 Repeatability Of Sample Measurement

Repeatability of the sample measurement was determined by measuring the absorbance of 15 µg/mL Efonidipine HCl Ethanolate solution respectively for seven times at selected wavelengths. The results of repeatability sample measurement were calculated in terms of %RSD

2.6.3 Intermediate Precision

2.6.3.1 Intraday Precision

Intraday precision was determined by measuring the corresponding response for 3 times on same day for each level of calibration curve in a range of 5- 25 µg/mL for of Efonidipine HCl. The results of intraday precision were calculated in terms of %RSD.

2.6.3.2 Interday Precision

Interday precision was determined by measuring the corresponding response for on 3 different days for each level of calibration curve in a range of 5 - 25 µg/mL for of Efonidipine HCl. The results of

Interday precision were calculated in terms of %RSD.

2.6.4 LOD AND LOQ

The limit of detection and limit of quantitation were calculated from the standard deviations of the intercepts and mean slope of the calibration curves of Efonidipine HCl Ethanolate using the equation given below

$$LOD=3.3\sigma/s \text{ and } LOQ=10\sigma/s$$

Where σ = the standard deviation of the Y-intercept of the five calibration curves; S = mean slope of the five calibration curves

2.6.5 ACCURACY

The accuracy in terms of the extraction efficiency of the method was determined by the standard addition method. The known amount of Efonidipine HCl ethanolate was added to the pre-analysed sample at three levels (i.e. 80%, 100%, 120%) and analysed.

Procedure:

Tablet powder equivalent to 40 mg of Efonidipine HCl ethanolate was accurately weighed and transferred to four individual 100 mL volumetric flasks. Standard Efonidipine HCl ethanolate 32 mg, 40 mg and 48 mg was spiked in the first, second and third volumetric flask respectively. Fourth flask was kept as control. The flasks were filled to about 80% with IPA, sonicated for 20 minutes and diluted up to mark with IPA. These solutions were filtered through Whatman filter paper (Paper no. 42) individually; the first few mL was discarded. From the resulting solutions 0.25 mL aliquot was withdrawn and diluted up to mark with 10 ml with IPA. (80% level: 18 µg/mL EFO; 100% level: 20 µg/mL EFO; 120% level: 22 µg/mL EFO) The absorbance was measured at 251 nm. From the calibration curve of Efonidipine HCl ethanolate, the amount of Efonidipine HCl



ethanolate was calculated and % recovery was determined.

HCl ethanolate in marketed formulation was determined.

2.7 ASSAY

Twenty tablets were accurately weighed and powdered. Tablet powder equivalent to 40 mg of Efonidipine HCl ethanolate was accurately weighed and transferred to four individual 100 mL volumetric flasks. The flasks were filled to about 80% with IPA, sonicated for 20 minutes and diluted up to mark with IPA. (400 µg/mL EFO) Make final solution 15 µg/mL from above solution. The measured absorbance of resulting solution at 251 nm. The amount of Efonidipine

3 RESULTS AND DISCUSSION

3.1 Determination Of Wavelength For Measurement

To determine wavelength for measurement, 15 µg/mL solution of Efonidipine HCl Ethanolate was scanned in range of 200 – 400 nm keeping IPA as blank. The absorbance maxima (λ max) of Efonidipine HCl Ethanolate were obtained 251 nm respectively. (Figure 3)

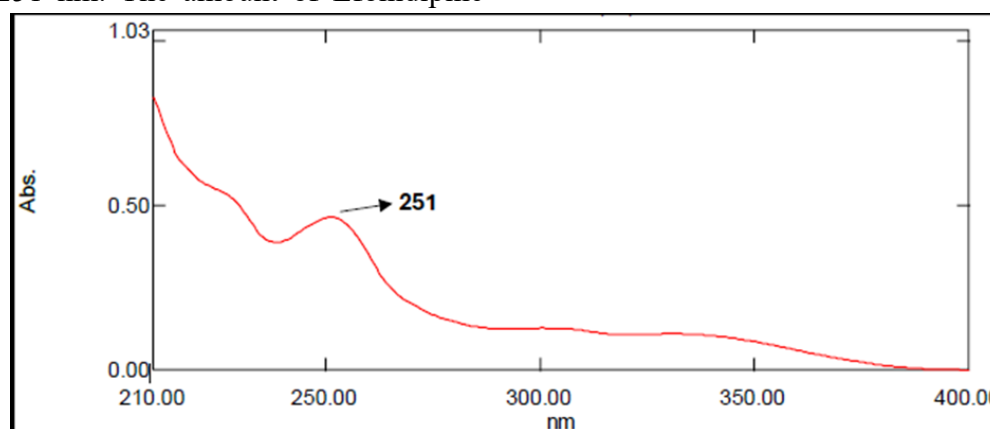


Figure 3: UV Spectrum of Efonidipine HCl ethanolate in IPA

3.2 VALIDATION

3.2.1 LINERITY

Representative calibration curve of Efonidipine HCl Ethanolate was obtained by plotting absorbance of Efonidipine HCl Ethanolate at 251 nm against concentration over the range of 5 – 25 µg/mL (n=5). It was found to be linear in the above-mentioned range with regression coefficient 0.9976 at 251 nm. The average linear regressed equation for the calibration curve was

$y=0.0268x+0.3213$ at 251 nm. Linearity data is depicted in figure 4 and 5.

Table 1: Linearity data

SR.NO.	CONC. (µg/mL)	Absorbance at 251 nm
1	5	0.466
2	10	0.585
3	15	0.709
4	20	0.855
5	25	1.005

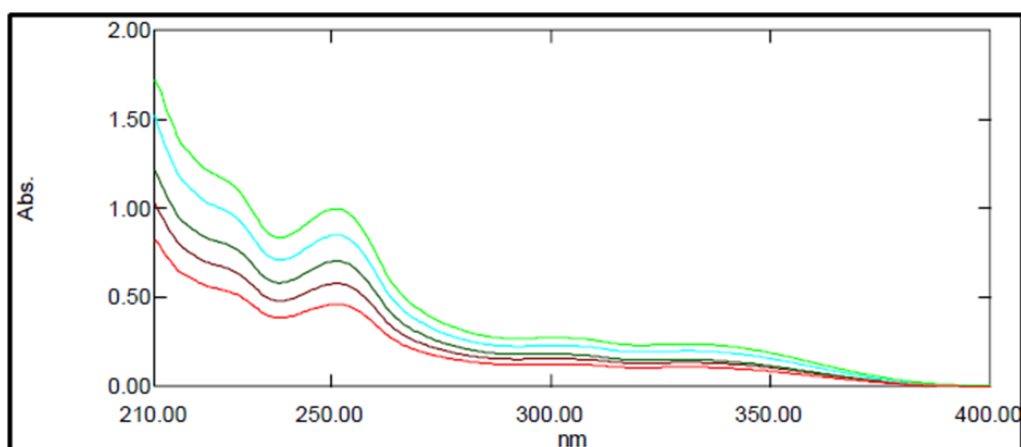


Figure 4: Calibration curve of Efonidipine HCl Ethanolate

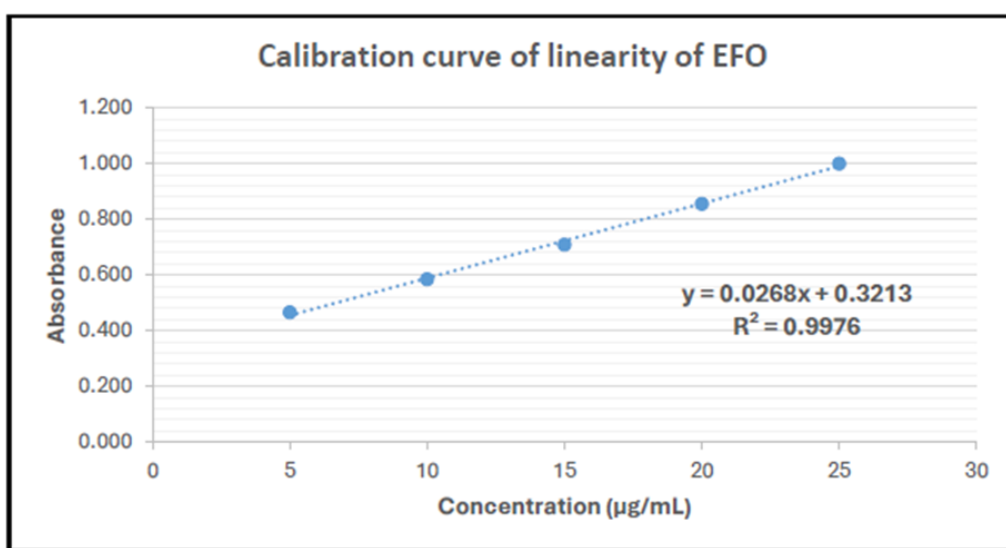


Figure 5: Calibration curve of linearity of Efonidipine HCl ethanolate

3.2.2 Repeatability

3.2.2.1 Repeatability Of Sample Measurement

The %RSD for measurement of absorbance for of Efonidipine HCl Ethanolate was found to be 0.693%. The data for repeatability of measurement is depicted in table 2.

3.2.2.2 Repeatability Of Sample Application

The %RSD for repeatability of sample application for absorbance of Efonidipine HCl Ethanolate was found to be 0.636%. The data for repeatability of application is depicted in table 2.

Table 2: Repeatability data

Sr. No	Parameters	Conc. (µg/mL)	Absorbance (mean ± SD) (n = 7)	%RSD
1	Repeatability of sample measurement	15	0.711 ± 0.009	0.693
2	Repeatability of sample application	15	0.709 ± 0.005	0.636

3.2.3 Intermediate Precision

The %RSD for Intra-day and inter-day precision of Efonidipine HCl Ethanolate were found to be

0.200-0.987% and 0.213-1.192% respectively, as shown in table 3. The result indicate that method is precise for measurement of drugs.

Table 3: Intra day and Inter day precision data

Sr. No.	Conc. (µg/mL)	Intraday precision		Interday precision	
		Absorbance (Mean ± SD)	% RSD	Absorbance (Mean ± SD)	% RSD
1	5	0.464 ± 0.004	0.987	0.469 ± 0.001	0.213
2	10	0.584 ± 0.005	0.906	0.587 ± 0.007	1.192
3	15	0.708 ± 0.002	0.373	0.710 ± 0.006	0.845
4	20	0.855 ± 0.003	0.410	0.856 ± 0.005	0.683
5	25	1.002 ± 0.002	0.200	1.001 ± 0.005	0.512

LOQ	1.856
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3.2.4 LOD AND LOQ

The LOD and LOQ for Efonidipine HCl Ethanolate were found to be 0.612 µg/mL and 1.856 µg/mL respectively. The data for Efonidipine HCl Ethanolate are depicted in table 4.

Table 4: LOD and LOQ data

Parameters	Efonidipine HCl ethanolate
LOD	0.612

3.2.5 ACCURACY

Accuracy was determined in terms of recovery study and the recoveries were done at three levels i.e., 80 %, 100 % and 120%. The recovery of Efonidipine HCl ethanolate was found to be 98.89-100.43%. The data for accuracy of method for Efonidipine HCl ethanolate was depicted in table 5.

Table 5: Recovery data

Level	Amount of tablet powder equivalent to drug amount (mg)	Amount of drug spiked (mg)	Final conc. Of solution (µg/mL)	Absorbance	Amount of drug recovered (mg)	% Recovery
0 %	40	-	10	0.582	-	-
80 %	40	32	18	0.794	31.64	98.89
100 %	40	40	20	0.849	39.84	99.62
120 %	40	42	22	0.905	48.21	100.43

3.3 ASSAY

Applicability of the proposed method was tested by analysis pharmaceutical dosage form of Efonidipine HCl ethanolate. The amount of

Efonidipine HCl ethanolate was found to be 99.82 %. The result is within the range of acceptance limit.

3.4 Summary Of Validation Parameters

Table 6: Summary of validation parameters

Sr. No.	Parameters	Efonidipine HCl ethanolate
1	Linearity range (µg/mL)	5 – 25
2	Regression equation	Y = 0.0268x + 0.3213



3	Corelation coefficient	0.9976
Precision (% RSD)		
4	Repeatability of sample measurement	0.693
	Repeatability of sample application	0.636
	Intra-day precision	0.200 – 0.987 %
	Inter-day precision	0.213 – 1.192 %
5	% Recovery	98.89 – 100.43 %
6	LOD ($\mu\text{g/mL}$)	0.612
7	LOQ ($\mu\text{g/mL}$)	1.856

4 CONCLUSION

In UV-visible spectrophotometry, the method involved measurement at wavelength 251 nm. The method was validated as per ICH Q2(R1) guidelines. The linearity of the method was satisfactory over the range of 5 – 25 $\mu\text{g/mL}$ (Correlation coefficient – 0.9976). The %RSD for repeatability for sample measurement and sample application was found to be 0.693 and 0.636 respectively. The %RSD for Intra-day and Inter-day precision was found to be 0.200-0.987% and 0.213-1.192% respectively. The LOD and LOQ for EFO were found to be 0.612 and 1.856 respectively. Recovery of Efonidipine HCl ethanolate ranged from 98.89-100.43%. The method was successfully applied to the marketed formulation for quantitative analysis of Efonidipine HCl ethanolate. The assay result was found to be 99.82% for Efonidipine HCl ethanolate.

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