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UV Spectrophotometric Estimation of Fexofenadine hydrochloride by First Order Derivative and Area under Curve Methods in Bulk and Pharmaceutical Dosage Form

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ABSTRACT

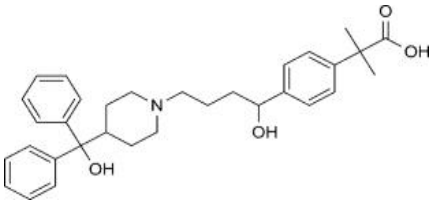
Simple and precise UV spectrophotometric methods by first order derivative and area under curve [AUC] - have been developed and validated for the estimation of fexofenadine hydrochloride in bulk and its tablet formulation. The standard and sample solutions of fexofenadine hydrochloride were prepared in 0.1 N Hydrochloric acid. Fexofenadine hydrochloride was estimated at 225 nm for the first order derivative UV-spectrophotometric method (A), while in area under curve (AUC) method (B) the zero order spectrum of fexofenadine hydrochloride was measured in between 215 nm to 225 nm. Beer's law was obeyed in the concentration range of 1 to 14 µg / ml with coefficient of correlation value 0.9998 for first order derivative method. Similarly in AUC method, Beer's law was obeyed in the concentration range of 1 to 14 µg / ml with coefficient of correlation value 0.9941. These methods were tested and validated for various parameters according to ICH guidelines. The precision expressed as relative standard deviation were of 0.5873 % and 0.1394 % for the above two methods respectively. The proposed methods were successfully applied for the determination of fexofenadine hydrochloride in pharmaceutical formulation. Results of the analysis were validated statistically and were found to be satisfactory. The proposed methods are simple, easy to apply, low-cost and require relatively inexpensive instruments.

Keywords: Fexofenadine hydrochloride, UV spectroscopy, Derivative spectroscopy, Area under curve method.

INTRODUCTION

Fexofenadine is described as second or third generation antihistamine. Its chemical name is RS -2 [4-(hydroxydiphenyl- methyl)-1 piperidyl]butyl] phenyl]- 2methyl-propanoic acid. ($C_{32}H_{39}NO_4$). It is indicated for relief from physical symptoms associated with seasonal allergic rhinitis and for the treatment of chronic urticaria. It prevents the aggravation of rhinitis and urticaria and reduces the severity of the symptoms associated with those conditions, providing relief from the repeated sneezing, runny nose, itchy eyes and generated body fatigue. This drug is official in USP [1], IP [2] pharmacopoeia. In literature survey EE capillary electrophoresis [3], HPLC [4-7] and spectrophotometric [8-11], non aqueous titration [12] methods have been reported for assay of fexofenadine.

Structure of fexofenadine hydrochloride



MATERIAL AND METHODS

Shimadzu UV-1800 was used with 10 mm matched quartz cell to measure absorbance of solution.

A Shimadzu analytical balance with 0.01 mg was used.

CHEMICAL AND REAGENTS

Reference standard of fexofenadine hydrochloride was obtained from reputed firm with certificate analysis. All spectral absorbance measurements were made on Shimadzu UV-1800 with 10 mm matched cell.

PREPARATION OF STANDARD SOLUTION

About 10 mg of standard fexofenadine hydrochloride was weighed accurately and transferred in 100 ml of volumetric flask. About 30 ml of 0.1 N Hydrochloric acid was added and sonicated for 15 minutes. The volume was adjusted up to the mark with 0.1 N Hydrochloric acid to give concentration as 100 µg /ml.

Estimation from tablets

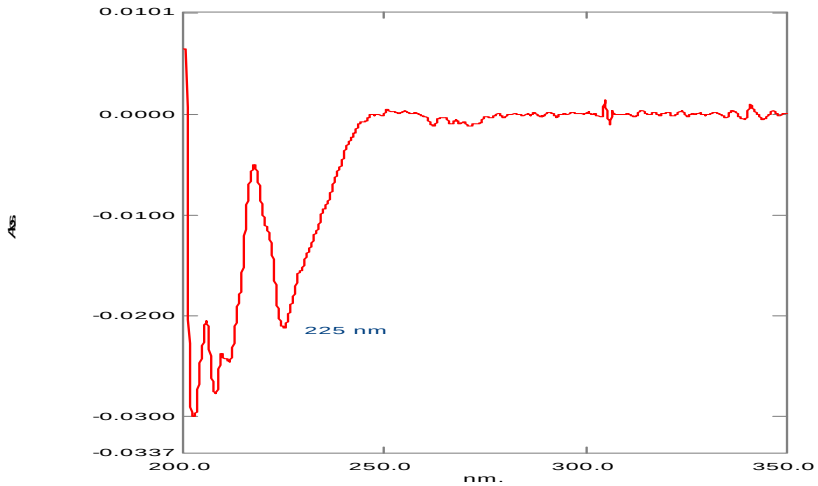
Twenty tablets were weighed accurately and average weight of each tablet was determined. Powder equivalent to 10 mg of fexofenadine hydrochloride was weighed and transferred in 100 ml of volumetric flask. A 30 ml of 0.1 N Hydrochloric acid was added and sonicated for 15 minutes and filtered. The filtrate and washing were diluted up to the mark with 0.1 N Hydrochloric acid to give concentration as 100 µg /ml. Such solution was used for analysis.

Experimental

Method A: First order derivative method

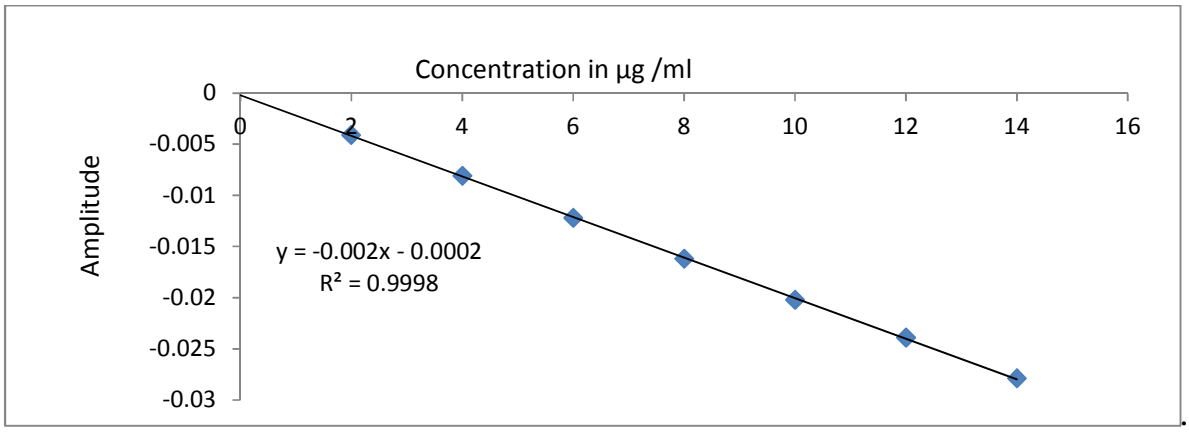
For the selection of analytical wavelength, 10 µg /ml solution of fexofenadine hydrochloride was scanned in the spectrum mode from 300 nm to 200 nm by using 0.1 N Hydrochloric acid as blank. The first order derivative spectrum was obtained by using derivative mode by UV probe 2.42 software. From the spectrum, the amplitude of the derivative spectrum was measured between 225 nm (Fig. 2).

Fig. 2. First order derivative spectrum of fexofenadine hydrochloride (10 µg/ml) showing absorbance at 225 nm



Into series of 10 ml graduated flask, varying amount of standard solutions of fexofenadine hydrochloride was pipette out and volume was adjusted with 0.1 N Hydrochloric acid as solvent. Solutions were scanned between 300 nm to 200 nm in spectrum mode. The first order derivative spectra were obtained by using derivative mode. Amplitudes of the resulting solutions were measured at 225 nm by using 0.1 N Hydrochloric acid as blank. The calibration curve was prepared in the concentration range of 1 to 14 µg/ml. (Fig. 3)

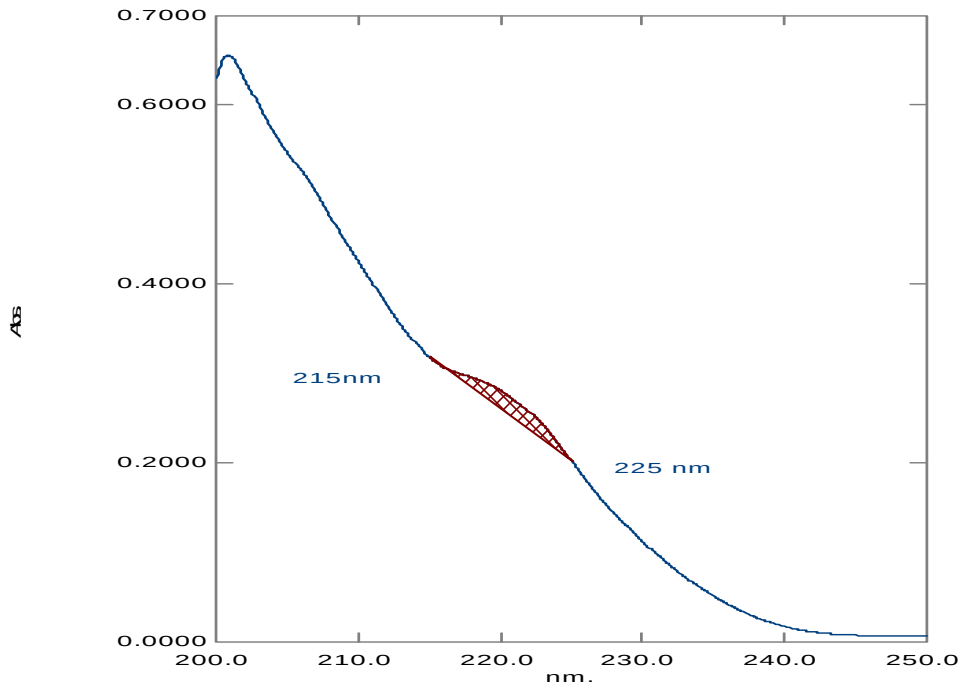
Fig. 3. Calibration curve for fexofenadine hydrochloride at 214 nm by first order derivative Spectroscopy



Method B: Area under curve (AUC) method

Area under curve method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelengths such as λ_1 and λ_2. The area under curve between λ_1 and λ_2 were calculated by UV probe 2.42 software. In this method, 10 µg/ml solution of fexofenadine hydrochloride was scanned in the spectrum mode from 300 nm to 200 nm. From zero order spectrum the AUC calculation was done. The AUC spectrum was measured between 215 nm to 225 nm (Fig. 4).

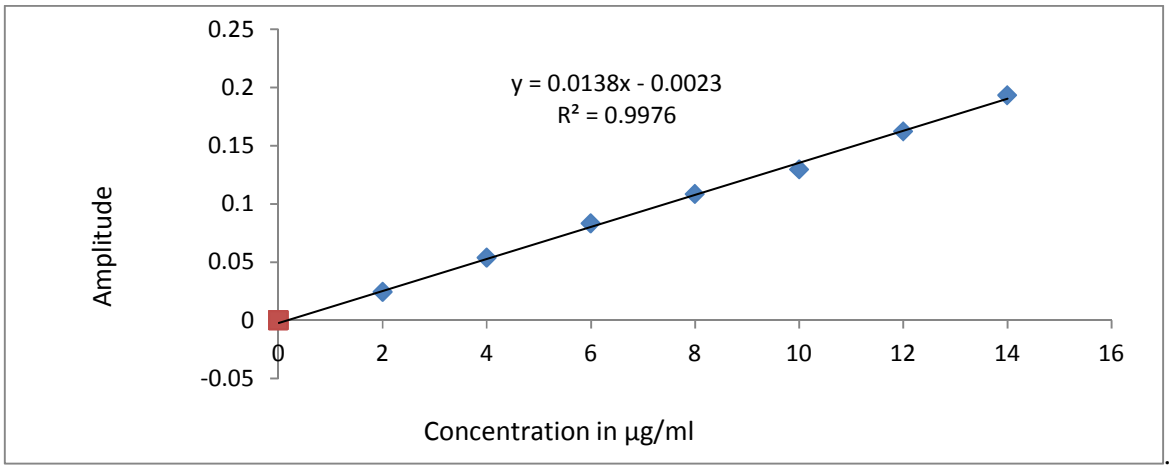
Fig. 4. Area under curve spectrum of fexofenadine hydrochloride (10 µg/ml) showing area from 215 nm to 245 nm



Into series of 10 ml graduated flask, varying amount of standard solutions of fexofenadine hydrochloride were pipette out and volume was adjusted with 0.1 N Hydrochloric acid. Solutions were scanned between 300 nm to 200

nm in spectrum mode. The AUC calculations were done and the calibration curve for fexofenadine hydrochloride was plotted in the concentration range of 1 to 14 µg/ml (Fig. 5).

Fig. 5. Calibration curve for fexofenadine hydrochloride by area under curve spectroscopy



Results of analysis are given in table 1.

Table 1: Values of results of optical and regression of drug

Parameter	First order derivative method	Area under curve (AUC) method
Detection Wavelength (nm)	225	215-225
Beer Law Limits (µg/ml)	1-14	1-14
Correlation coefficient(r^2)	0.9998	0.9976
Regression equation (y=b+ac)		
Slope (a)	-0.002	0.0138
Intercept (b)	-0.0002	-0.0023

Validation

Accuracy

Accuracy of the proposed methods was carried as on the basis of recovery studies. It is performed by the standard addition method. Recovery studies were performed by adding standard drug at different levels to the pre-analyzed tablets powder solution and the proposed method was followed. From the amount of the drug estimated, the percentage recovery was calculated. The results of the analysis are shown in table (2, 3).

Table 2: Results of recovery of fexofenadine hydrochloride for first order derivative method

Amount of Sample Added in (µg/ml)	Amount of Standard Added in (µg/ml)	Total amount recovered	Percentage recovery (%)	Standard deviation	Percentage of relative standard deviation (C.O.V.)
2	0	1.9721	98.606	0.0355	1.801
2	2	3.9372	98.432	0.0429	1.091
2	4	5.8954	98.257	0.0482	0.8189
2	6	7.8536	98.170	0.0521	0.6640
				Mean =0.0447	Mean =1.0939

Table 3: Results of recovery of fexofenadine hydrochloride for area under curve (AUC) method

Amount of Sample Added in (µg/ml)	Amount of Standard Added in (µg/ml)	Total amount recovered	Percentage recovery (%)	Standard deviation	Percentage of relative standard deviation (C.O.V.)
2	0	1.9989	99.947	0.00989	0.4948
2	2	3.9684	99.212	0.0110	0.2771
2	4	5.9737	99.5623	0.01263	0.2114
2	6	7.9768	99.7111	0.01232	0.1545
				Mean =0..0114	Mean =0.2845

Precision

The method precision was established by carrying out the analysis of homogenous powder blend of tablets. The assay was carried out of drug by using proposed analytical method in six replicates. The values of relative standard deviation lie well within the limits indicated the sample repeatability of the method. The results obtained are tabulated in table 4.

Table 4: Precision- method precision

Experiment no.	Weight of fexofenadine hydrochloride taken in mg	Content in mg. of fexofenadine hydrochloride	
		First order derivative method	Area under curve method
1	10	9.853	10.044
2	10	9.804	10.014
3	10	9.853	10.037
4	10	9.707	10.029
5	10	9.804	10.0367
6	10	9.756	10.0514
	Standard deviation	0.0574	0.0139
	%RSD	0.5873	0.1394

Inter-day and intra-day precision

An accurately weighed quantity of tablets powder equivalent to 10 mg of fexofenadine hydrochloride was transferred to 100 ml of volumetric flask. A 30 ml of 0.1 N Hydrochloric acid was added and sonicated for 15 minutes and filtered. The filtrate and washing were diluted up to the mark with 0.1 N Hydrochloric acid to give concentration as 100 µg /ml. Such solution was used for analysis.

For first order derivative method

Solution was scanned between 300 nm to 200 nm in spectrum mode. The first order derivative spectrum was obtained by using derivative mode. Amplitude of the resulting solution was measured at between 220 nm to 210 nm by using 0.1 N Hydrochloric acid as blank. The amplitude of final solution was read after 0 hr., 3 hrs. and 6 hrs. in 10 mm cell 225 nm for first order derivative (method A). Similarly the amplitude of the same solution was read on 1^{st}, 2^{nd} and 5^{th} day. The amount of fexofenadine hydrochloride was estimated by comparison with standard at 225 nm for first order derivative, table 5.

For area under curve method

Solution was scanned between 300 nm to 200 nm in spectrum mode. The area under curve of resulting solutions was measured at between 245 nm to 255 nm by using 0.1 N Hydrochloric acid as blank. The area under curve of final solutions was read after 0 hr., 3 hrs. and 6 hrs. in 10 mm cell at 215 nm to 225 nm (method B). Similarly area under curve of the same solution was read on 1^{st}, 2^{nd} and 5^{th} day. The amount of fexofenadine hydrochloride was estimated by comparison with standard at 215 nm to 225 nm, table 5.

Table 5: Summary of validation parameter for intra-day and inter-day

Sr. no.	Parameters	First order derivative method	Area under curve (AUC) method
(A)	Intra-day precision (n=3) Amount found ± % RSD	98.59 % 0.6035	98.97% 0.2475
(B)	Inter-day precision (n=3) Amount found ± % RSD	97.981% 0.1537	97.469% 0.3168
(c)	Ruggedness Analyst to analyst(n= 3) %RSD	0.5984	0.2765

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from back-ground levels. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations-

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

Where σ is the standard deviation of the signal to noise ratio of the sample and S is the slope of the related calibrations graphs.

The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision and variability .The values of LOD and LOQ are given in table 6.

Table 6: Values of results of LOD and LOQ

parameters	First order derivative method	Area under curve (AUC) method
Limit of Detection (µg/ml)	0.1298	0.03193
Limit of Quantification (µg/ml)	0.3933	0.09677

Ruggedness

The ruggedness of the method is defined as degree of reproducibility of results obtained by analysis of fexofenadine hydrochloride sample under variety of normal test conditions such as different laboratories, different analysts and different lots of reagents. Quantitative determination of fexofenadine hydrochloride was conducted spectrophotometrically on one laboratory. It was again tested in another laboratory using different instrument by different analyst. The assays obtained in two different laboratories were well in agreement. It proved ruggedness of the proposed methods.

RESULT AND DISCUSSION

The first order derivative and area under curve UV-spectroscopic methods are useful for routine analysis of fexofenadine hydrochloride in bulk drug and formulation. The derivative spectroscopy method applied has the advantage that it locates hidden peak in the normal spectrum. It eliminates the interference caused by the excipients and the degradation products present, if any, in the formulation. The method was validated according to International Conference on Harmonization guidelines for validation of analytical procedures. Fexofenadine hydrochloride has the absorbance maxima at 225 nm (method A) and in the AUC spectrum method areas were measured between 215 nm to 225 nm (method B). The polynomial regression data for the calibration plots showed good linear relationship in the concentration range of 1 to 30 µg/ml and given in table1. Recovery studies were carried out by adding the pure drug to the previously analyzed tablet powder sample and shown in table 2, 3. The percentage recovery value indicates non interference from excipients used in formulation. The reproducibility and accuracy of the method were found to be good, which was evidenced by low standard deviation.

CONCLUSION

The most striking features of two methods are its simplicity and rapidity, not requiring tedious sample solutions preparations which are needed for other instrumental methods. From the results obtained it can be concluded that the proposed methods are fully validated and found to be simple, sensitive, accurate, precise, reproducible, rugged

and robust and relatively inexpensive. So, the developed methods can be easily applied for the routine quality control analysis of fexofenadine hydrochloride in pharmaceutical formulation.

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