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STABILITY INDICATING METHOD DEVELOPMENT AND VALIDATION OF FEXOFENADINE HYDROCHLORIDE IN BULK AND ITS PHARMACEUTICAL DOSAGE FORM BY USING RP-HPLC

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Abstract:

A simple, rapid and accurate method was developed for the determination of Fexofenadine Hydrochloride in bulk and pharmaceutical dosage form by RP-HPLC method using C_{18} column [4.6×250mm,5µm] in binary gradient mode. The mobile phase consisted of methanol and water in the ratio of 80:20 v/v. The flow rate was maintained at 1.2 mL/min and wavelength was maintained at 220 nm. The column oven temperature was maintained at 40°c. The retention time of Fexofenadine Hydrochloride was attained at 2.96 min. The method was linear over the concentration range from 7.5-40µg/mL and R^2 was found to be 0.999. The intraday and interday precision %RSD values were obtained <2.0. The LOD and LOQ were attained at 0.603 and 1.829µg/mL respectively. The accuracy results of the method was obtained 98.37-99.84% at different levels of concentrations. The method was proved as robust after deliberately changed parameters of flow rate, mobile phase composition, temperature and wavelength. The method was shown ability to words different stress conditions of acid, base, peroxide and UV-Light. The method was used for routine analysis of Fexofenadine hydrochloride in pharmaceutical dosage form.

Key Words: *Fexofenadine hydrochloride, RP-HPLC, Methanol, Stability studies.*

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INTRODUCTION:

Fexofenadine hydrochloride is chemically 4-[1-hydro xy-4-[4-(hydroxyl diphenylmethyl)]-α, α-Dimethyl-hydrochloride (Figure 1)[1&2]. It is second generation long lasting H_1 receptor antagonist which has a selective and peripheral H_1 antagonistic action. It is an active metabolite of terfenadine and like terfenadine it completes with histamine for H_1 receptor sites on effectors cells in gastro intestinal tract, blood vessels and respiratory tract, it appears that fexofenadine hydrochloride does not cross the blood brain barrier to any appreciable degree resulting in a reduced potential for sedation[3-5]. It is usually taken orally in the form of tablet or suspension form, after oral administration it reaches maximum plasma concentrations within few hours. In literature, various analytical methods such as spectroscopic, HPLC, HPTLC, LCMS, were reported for quantification of Fexofenadine hydrochloride either in individual or in combined dosage forms both in formulations and biological matrices[5-10]. The developed method was more sensitive and selective compared with other reported methods and it was validated according to the ICH guidelines[11].

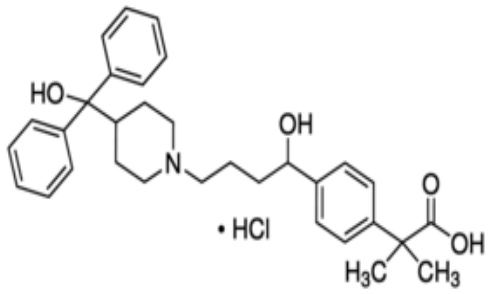

Fig: 1 Structure of Fexofenadine Hydrochloride

MATERIALS AND METHODS:

Fexofenadine hydrochloride API was obtained from Aurobindo Pharma Ltd and tablets were purchased from local market. The chemicals methanol (HPLC grade) was procured from Merck chemical (Tirupati, AP, India) and Water (HPLC grade) from local market. The HPL C was Shimadzu LC-20AD model in binary gradient mode. The column was used intersil and specifications were C18 [4.5×250mm; 5µ].

Preparation of Mobile Phase

The mobile phase was prepared by mixing of water and methanol in the ration of (80:20 v/v) and degassed with ultrasonic water bath for 5min and finally filtered with 4.5µ membrane filter and it was used as diluent and mobile phase for separation of drug.

Preparation of Standard Solution

Accurately weighed and transferred 10mg of Fexofenadine hydrochloride pure form into 10ml volumetric flask and add few quantities of diluent, dissolved it. The volume was made up to the mark with diluent. From the above stock solution pipetted out 0.3mL and transferred into 10mL volumetric flask and made the mark with diluent. The final concentration of solution was obtained 30µg/mL.

Preparation of Sample Solution

Accurately weighed 10 tablets of Fexofenadine hydrochloride and calculated average weight. The tablets were crushed into powder and weighed equivalent to 21.21 mg and transferred into 10mL volumetric flask. Add few quantities of diluent and sonicated to dissolve for 5min. The volume was made up to the mark with diluent and filtered the solution through 4.5µ membrane filter. From the above solution pipetted out 0.3mL of solution and transferred into 10mL volumetric flask and made up to the mark with diluent. The final concentration of the solution was obtained 30µg/mL.

Detection of Wavelength

The solution was scanned over the range of 200-400 nm and the spectrum was obtained. From the spectra considerable absorbance was observed at 220 nm. It was selected for the analysis of Fexofenadine hydrochloride.

RESULTS & DISCUSSION:

Validation of analytical method

The validation of developed method was performed with different parameters like linearity, precision, accuracy, limit of detection (LOD), limit of quantification (LOQ), and Robustness and stress indicated studies[11].

System suitability

Different parameters were studied for system suitability like retention time (Rt), peak area A, tailing factor (N). All the performed parameters of the method met the guidelines and peak area >2000, %RSD of tailing factor < 2% and retention time (Rt) >2 was good for HPLC method. The developed method was suitable for the analysis of Fexofenadine hydrochloride in marketed dosage form. The standard and sample chromatograms were shown in figure 2 & 3.

Specificity

The specificity of the method was studied by injected the mobile phase (Blank), the optimised standard and sample solutions were prepared and injected into chromatographic system and no interference was

observed between Fexofenadine hydrochloride and other ingredients, hence method proved as specific (Figure 2&3).

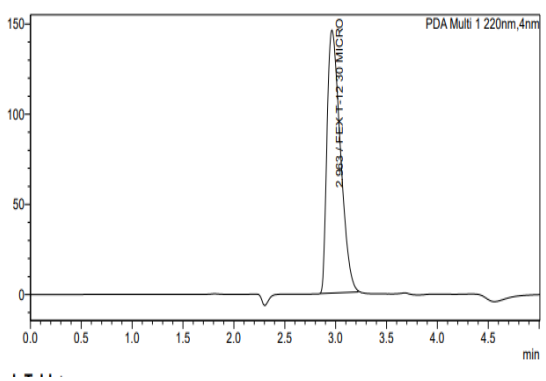

Fig: 2 Standard chromatogram of FXD

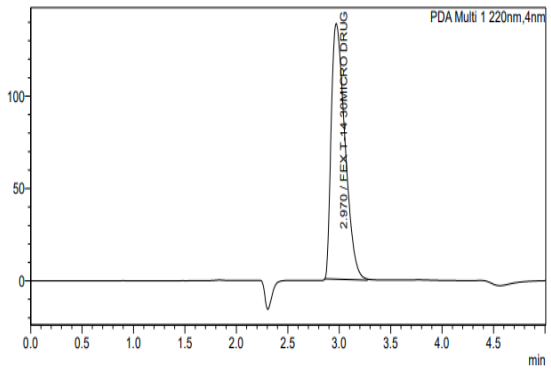

Fig: 3 Sample chromatogram of FXD

Linearity

The linearity of the method was studied by prepared 7.5, 15, 22.5, 30, 37.5, and 40 µg/mL of standard solutions and injected into the chromatographic system and peak area was measured. The linearity graph was plotted between (Figure 4) peak area on Y-axis verses concentration on X-axis and regression equation of (y- 443254x and R^2= 0.9996) and results were shown in table 1.

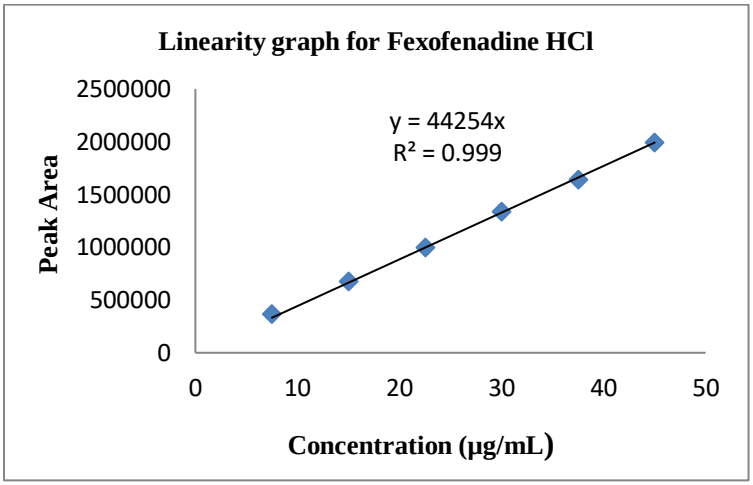

Fig:4 Linearity of the Fexofenadine Hydrochloride

Table : 1 Results of Linearity

Linearity level (%)	Concentration (µg/mL)	Peak area
25	7.5	366173
50	15	673721
75	22.5	997117
100	30	1336623
125	37.5	1638900
150	45	1992918
	Slope =44254x	
Regression coefficient values R^2=0.999		

Precision

The precision of the method was assessed by intraday and inter-day variation. The optimized concentration of sample solution was injected six replicates into chromatographic system at different time intervals. The interday precision of the method was studied at different days with six replicated injections at each day. The %RSD was calculated for both intraday and interday precision and intraday values were found to be 0.90, 0.93 and 0.80 at different time intervals and interday values were found to be 1.05, 0.49 and 1.43 for day-1, for day-2, for day-3.

Accuracy

The accuracy data of method was studied in terms of percentage recoveries of Fexofenadine hydrochloride. The accuracy was conducted at three levels of 50%, 100% and 150%. The % mean recovery of the method was calculated (Table 2) by injected sample solution at three replicates of 100% and six replicated injections for 50% and 150% solutions. The % mean recoveries values reported in table 2.

%Recovery = µg/mL Added×100

Table 2. Results of Accuracy

Paramters	Peak area	Amount added (mg)	Amount found (mg)	% Recovery	% Mean recovery
50%**	661031	14.9777	15.0928	100.76%	100.76%
100%*	1315016	29.9553	30.0248	100.23%	100.23%
150%**	1996258	44.9330	45.5791	101.43%	101.43%

****Six replicated injections** ***Three replicated injections**

Robustness

The robustness of the method was calculated by varying the instrumental conditions such as flow rate (± 0.2mL/min), Mobile phase composition (± 5mL of organic phase), Temperature (± 5ºC) and change in wavelength (±2nm). The optimal concentration of sample solution was injected into chromatographic system for chromatograms. The % assay values were found in between 100.39% -100.89% for flow rate change, for mobile phase composition change, 98.03%-100.02% for change of temperature and 100.02%-100.99% for wavelength change.

LOD and LOQ

The LOD and LOQ studies were calculated through the slope of the calibration curve and standard deviation of the response of the curve. The LOD was studied by formula 3.3×σ/S and LOQ was calculated by 10 × σ /S. The LOD and LOQ Values were found to be 0.603µg/mL and 1.829µg/ mL.

Forced Degradation studies

The forced degradation studies were conducted for drug with different stress conditions of acid, base, peroxide and UV-Light (Figure 5). The acidic conditions (0.1N HCl heated for 20min at 50°C), alkaline (0.1N NaOH heated for 20min at 50°C), Peroxide (3% H_2O_2 stored at room temperature for 24hrs) and UV-Light (≤200 nm for 3 days). The results were discussed in table 3.

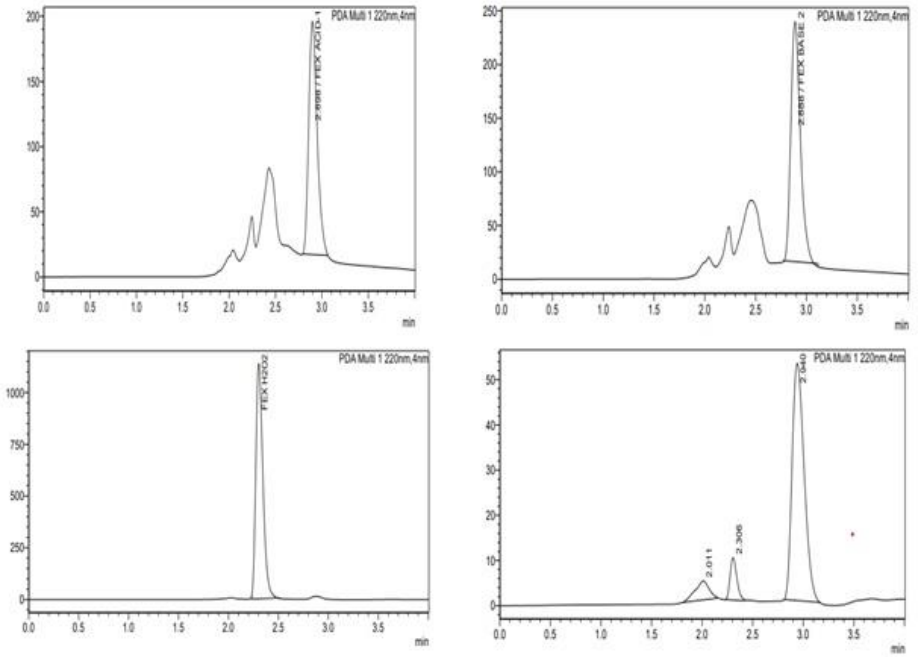

Figure: 5 Stability indicating chromatograms of Acid, Alkaline, Peroxide and UV-Light

Table 3. Forced degradation results of Fexofenadine hydrochloride

Condition	Peak area	%Assay	% Degradation
Acid (50°C for 20 min)	1235251	94.030	5.970
Base (50°C for 20 min)	1196761	91.100	8.900
H_2O_2 (Kept at room temperature)	1205102	91.735	8.265
UV (≤200 nm for 3 days)	1209604	92.078	7.922

CONCLUSION:

An economical, simple, accurate and précised RP-HPLC method has been developed and validated for the estimation of Fexofenadine hydrochloride in bulk and pharmaceutical dosage form. The method was validated according to the ICH guidelines and results were obtained within the range as per guidelines. All the validation parameters were shown good values when compared with some reported method. The method was applied for routine analysis of Fexofenadine hydrochloride by academicians and pharmaceutical industries.

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