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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF FEXOFENADINE IN BULK AND PHARMACEUTICAL DOSAGE FORM BY UV SPECTROSCOPY

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ABSTRACT

A new simple, accurate, rapid, precise, reproducible and cost-effective spectrophotometric method for the quantitative estimation of Fexofenadine. The developed UV spectrophotometric method for the quantitative estimation of Fexofenadine is based on measurement of absorption at maximum wavelength 248.5 nm using, Methanol & Ammonium acetate buffer as a solvent. The stock solution of Fexofenadine was prepared and subsequent suitable dilution was prepared in distilled water to obtained standard curve. The standard solution of Fexofenadine shows absorption maxima at 248.5 nm. The drug obeyed beer lambert's law in the concentration range of 5 - 25 µg/ml with regression 1 at 248.5 nm. The overall % recovery was found to be 99.17% which reflects that the method was free from the interference of the impurities and other excipients used in the marketed dosage form. The low value of % RSD was indicative of accuracy and reproducibility of the method. The % RSD for inter-day and intra-day precision was found to be 0.943888 & 0.649186 respectively which is <2% hence proved that method is precise. The results of analysis have been validated as per International Conference on Harmonization (ICH) guidelines. The developed method can be adopted in routine analysis of Fexofenadine in bulk and tablet dosage form.

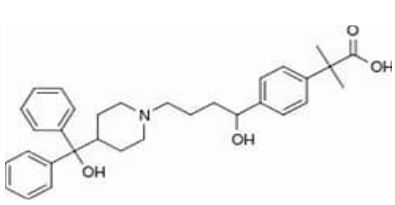
KEYWORDS: Fexofenadine, UV Visible Spectrophotometry, Method development, Validation, ICH guidelines, Accuracy & Precision.

INTRODUCTION

DRUG PROFILE

Name: Fexofenadine.

Description: Fexofenadine belongs to a group of medicines called antihistamines. It is used to treat various allergic conditions such as hay fever, conjunctivitis and some skin reactions such as eczema, hives, and reactions to bites and stings. It relieves watery eyes, runny nose, sneezing, and itching.



IUPAC Name: (±)-4-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-dimethyl benzene acetic acid.

Chemical formula: $C_{32}H_{39}NO_4$.

Molecular mass: 501.667 g·mol−¹.

Category: Therapeutically, fexofenadine is a selective peripheral H 1 blocker. It is classified as a second-generation antihistamine because it is less able to pass the blood–brain barrier and cause sedation, compared to first-generation antihistamines.

Mechanism of action: Fexofenadine is an antihistamine that works by selectively blocking peripheral H1 receptors. This blockage prevents the activation of the H1 receptors by histamine, which in turn prevents the symptoms associated with allergies from occurring.

Pharmacodynamics: Fexofenadine is an antihistamine drug that blocks the H 1 -receptor sites on effector cells. It is rapidly absorbed from the GI tract after oral administration, reaching peak plasma levels in about 2 hours. It has a long-lasting effect of up to 12 hours on reducing histamine-induced skin wheal and flare. It does not cross the blood-brain barrier significantly, resulting in a low potential for sedation.

Absorption: rapidly absorbed from the gastrointestinal tract after oral administration.

Volume of distribution: approximately 5.4-5.8 L/kg.

Protein binding: 60% to 70%.

Metabolism: Fexofenadine undergoes very minimal metabolism, with only 5% of an ingested dose being metabolized by the liver. The identified metabolites include a methyl ester of fexofenadine (constituting 3.6% of the total dose) and MDL 4829 (making up 1.5% of the total dose). The specific enzymes responsible for this metabolism have not been fully elucidated.

Route of elimination: Most of the substance is excreted unchanged via the feces (approximately 80%) and urine (around 11–12%).

Half-life: 14.4 hours.

Clearance: The oral clearance of fexofenadine is approximately 50.6 L/h, and the renal clearance is approximately 4.32 L/h.

Toxicity

Safety Profile: Fexofenadine has a favourable safety profile. Even when taken at doses up to 10 times the recommended amount, no cardiovascular or sedative effects have been observed in humans. Research has shown no clinically significant adverse effects compared to a placebo.

Common Side Effects: The most common side effects include headache, drowsiness, nausea, dizziness, and menstrual cramps. However, these are generally mild.

Brand Names: telfast, allegra, fexalergic, fext, stedler, fexogail, fexowish, fexogearv, alfexo, histakem.

MATERIALS AND METHODS

Chemicals and Reagents: methanol, water, acetonitrile, ethanol, chloroform, ammonium acetate.

Instruments

SHIMADZU UV-1601 UV – Vis spectrophotometer, Electronic Balance **(CITIZEN BALANCE BL-220H),** Ultra Sonicator **(ANALYTICAL),** pH meter **(INFRA DIGI IR-501),** Pipettes and Burettes **(Borosil),** Beakers **(Borosil).**

Reagents and Solutions

Diluent preparation: In a 100ml volumetric flask take 30:70 v/v methanol and ammonium acetate buffer.

Preparation of standard Stock Solution of Fexofenadine: 100mg of Fexofenadine was weighed accurately and transferred into 100ml volumetric flask. About 10 ml of diluent was added and sonicated to dissolve. The volume was made up to the mark with same solvent. The final solution contained about 100µg/ml of Fexofenadine. Working standard solution of Fexofenadine containing 10µg/ml for method. Finally add those above solutions and prepare the final solution is about 10µg/ml.

Preparation of Sample Solutions

Take 20 Tablets average weight and crush in a mortar by using pestle and weight powder 100 mg equivalent weight of Fexofenadine sample into a 100ml clean dry volumetric flask, dissolve and make up to volume with diluent. Further dilution was done by transferring 0.1 ml of the above solution into a 10ml volumetric flask and make up to volume with diluent.

Determination of wavelength of maximum absorbance for Fexofenadine

The absorbance of the final solution scanned in the UV spectrum in the range of 200 to 400nm against solvent mixture as blank.

Optimization of selection of Solvent

It is well known that the solvents do exerts a profound effect on the quality and the shape of the peak. The choices of solvents for UV method development are: Methanol, Ethanol, Water, Chloroform, Acetonitrile, Ammonium acetate buffer. First optimize the different solvents. From that solvents methanol and ammonium acetate buffer satisfied the all the optimized conditions.

Wavelength Selection

The standard solutions are prepared by transferring the standard drug in a selected solvent and finally diluting with the same solvent or Diluent. That prepared solution is scanned in the UV visible wavelength range of 200-400nm.This has been performed to know the maxima of Fexofenadine. While scanning the Fexofenadine solution we observed the maxima at 248.5 nm. The visible spectrum has been recorded on SHIMADZU UV-1601. The scanned visible spectrum is attached in the following page. The λ_{max} of the Fexofenadine was found to be 248.5nm in diluents as solvent system.

METHOD VALIDATION

1. Accuracy

Recovery study: To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (75%, 100%, and 125%) of pure drug of Fexofenadine were taken and added to the pre-analysed formulation of concentration 10µg/ml. From that percentage recovery values were calculated. The results were shown in Table-1.

2. Precision

Repeatability

The precision of each method was ascertained separately from the peak areas & retention times obtained by actual determination of six replicates of a fixed amount of drug. Fexofenadine (API) the percent relative standard

deviations were calculated for Fexofenadine is presented in the Table-2.

Intermediate Precision

Intra-assay & inter-assay

The intra & inter day variation of the method was carried out & the high values of mean assay & low values of standard deviation & % RSD (% RSD < 2%) within a day & day to day variations for Fexofenadine revealed that the proposed method is precise.

The results were shown in Table-3.

3. Linearity & Range

The calibration curve showed good linearity in the range of 5-25µg/ml, for Fexofenadine (API) with correlation coefficient (r^2) of 1 (Fig-2). A typical calibration curve has the regression equation of y = 0.0319x + 0.0031 and R^2=1 for Fexofenadine.

Standard solutions of Fexofenadine in the concentration range of 5 µg/ml to 25 µg/ml were obtained by transferring (5,10,15 and 20,25 ml) of Fexofenadine stock solution (100ppm) to the series of clean & dry 10 ml volumetric flasks. The volumes in each volumetric flask were made up with the solvent system and mixed.

The absorbances of the solutions were measured at 248.5 nm against the solvent system as blank and calibration curve is plotted. The Lambert-Beer's Law is linear in concentration range of 5 to 25 µg/ml at 248.5 nm for Fexofenadine. The results were shown in Table-4.

4. Method Robustness

Robustness of the method was determined by carrying out the analysis under different Wavelength i.e. at 246.5 nm, 248.5 nm and 250.5 nm. The respective absorbances of 10µg/ml were noted SD < 2%) the developed UV-Spectroscopic method for the analysis of Fexofenadine (API). The results were shown in Table-5.

5. LOD & LOQ

The LOD and LOQ were calculated using the equations LOD = 3.3 × σ / S and LOQ = 10 × σ / S where σ is the standard deviation of intercept of Calibration plot and S is the average of the slope of the corresponding Calibration plot.

The Minimum concentration level at which the analyte can be reliable detected (LOD) & quantified (LOQ) were found to be 0.28556497 & 0.653484 µg/ml respectively.

6. ASSAY OF FEXOFENADINE IN DOSAGE FORM

FEXOFENADINE 20mg.

Assay of marketed tablet formulation Brands

Fexofenadine was procured from the local market as tablets of strength having 120mg, marketed with brand names of Allegra. When referring to the generic drug name Fexofenadine. These marketed formulations were manufactured by the **Sanofi India Ltd**, respectively.

Weighed accurately about twenty tablets and calculate the weights of individual tablets and finally calculate the average weight. They were triturated to fine powder by using a mortar and pestle. The powdered tablet equivalent to 5mg of Fexofenadine was dissolved in 15ml of diluent with the help of sonication process and the final volume was made up to the mark with the diluent in 25 ml volumetric flask. The resulted solution was filtered using Whatman filter paper (0.45µm). This final solution was further diluted to obtain 10µg/ml concentration of the solution by using diluents used as a solvent and observed by UV analysis. This procedure was repeated in triplicate.

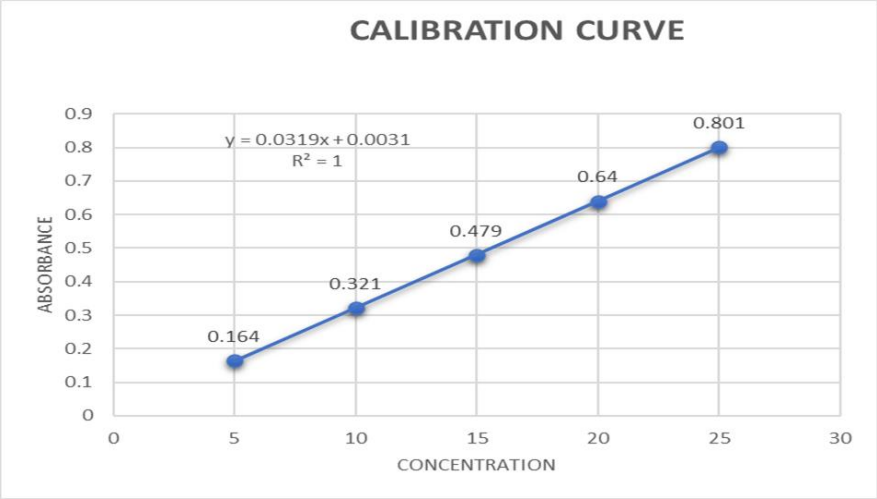
Amount Present.

RESULTS AND DISCUSSION

The standard solutions of Fexofenadine in methanol and Water (10µg/ml) subjected to scan individually at the series of wavelengths of 200 nm to 400 nm. Absorption maximum of Fexofenadine was found to be at 248.5nm. Therefore, 248.5 nm was selected as λ_{max} of Fexofenadine for the present study. The calibration curve of Fexofenadine was found to be linear in the range of 5-25 µg/ml at 248.5 nm. Therefore, it was clear that Fexofenadine can be determined without interference of any irrelevant substance in single component pharmaceutical products. The used technique was initially attempted on bulk drugs in their synthetic sample and concentrations were estimated.

The % recovery was carried out at 3 levels, 75%, 100% and 125% of Fexofenadine standard concentration. Three samples were prepared for each recovery level. The solutions were then analyzed, and the percentage recoveries were found to be satisfactory within the acceptable limits as per the content of the label claim for marketed tablet dosage form. The newly developed method was validated according to the ICH guidelines and the method validation parameters.

The developed method was subjected to do the various method validation parameters such as, accuracy, precision, linearity and range, limit of detection and limit of quantification, robustness, and ruggedness etc.



Calibration curve of Fexofenadine (API).

1. Accuracy

Table 1: Results of accuracy.

Level of Recovery	Sample Conc. (µg/ml)	Absorbance	% Recovery	Mean % Recovery
75%	7.5	0.245	99.46	99.46
75%	7.5	0.243	98.86	
75%	7.5	0.240	99.06	
100%	10	0.319	99.1	99.06
100%	10	0.322	98.4	
100%	10	0.320	98.7	
125%	12.5	0.408	99.48	99.013
125%	12.5	0.402	99.44	
125%	12.5	0.405	99.12	

Acceptance criteria: correlation coefficient should not be less than 0.999.

2. Precision

Table 2: Results of Repeatability.

S.No.	Conc. (µg/ml)	Wavelength (nm)	Absorbance
1	10	248.5	0.325
2	10	248.5	0.317
3	10	248.5	0.322
4	10	248.5	0.322
5	10	248.5	0.321
6	10	248.5	0.319
Mean ± S.D.			0.321
Standard Deviation			0.002757
% RSD			0.896382

Table 3: Results of intra-Day & inter-Day.

Conc. taken (µg/mL)	Observed Conc. Of Fexofenadine (µg/ml) by the proposed method			
	Intra-Day		Inter-Day	
	Absorbance	Statistical Analysis	Con. found (µg/mL)	Statistical Analysis
10	0.323	Mean = 0.3206	0.327	Mean = 0.3236
10	0.319	SD = 0.002082	0.321	SD = 0.003055
10	0.320	%RSD = 0.649168	0.323	%RSD = 0.943888

Table 4: Results of Linear Curve.

Concentration (µg/ml)	Absorbance
5	0.164
10	0.321
15	0.479
20	0.640
25	0.801

Acceptance criteria: correlation coefficient should not be less than 0.999.

Table 5: Result of Method Robustness Test.
Change in Wavelength

Concentration(µg/ml)	Wavelength	Absorbance	Statistical Analysis
10	246.5	0.324	Mean =0.3255 SD =0.02258 % RSD = 0.6938
10		0.326	
10		0.329	
10	250.5	0.327	
10		0.324	
10		0.323	

CONCLUSION

From the experimental studies it can be concluded that best UV-Spectroscopic method is developed for Fexofenadine in bulk and marketed pharmaceutical dosage form. The developed method for the drug (Fexofenadine) was found to be accurate and precise.

The great features of spectrophotometric methods are their simplicity, economical and rapidity. The results of method validation showing that the developed analytical procedure is suitable for its intended purpose and meets the Guidelines given by the ICH.

The developed method was successfully applied for the routine analysis of Fexofenadine in bulk and pharmaceutical dosage form in the future.

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