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A new method for the spectrophotometric determination of fexofenadine hydrochloride

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A novel, sensitive and selective reaction has been proposed for the assay of fexofenadine hydrochloride (FFH) in bulk and dosage forms using chloramine-T (CAT) and two dyes malachite green (MAG) and xylene cyanol FF (XFF). Spectrophotometric method entail the addition of a known excess of chloramine-T to fexofenadine hydrochloride in hydrochloric acid medium followed by the determination of residual oxidant by reacting it with a fixed amount of malachite green, measuring the absorbance at 615 nm (method A), or xylene cyanol FF, measuring the absorbance at 612 nm (method B). The apparent molar absorptivities are calculated to be 4.09×10^4 L mol^{-1} cm^{-1}, 3.07×10^4 L mol^{-1} cm^{-1} for method A and B respectively. Both methods are of comparable accuracy and precision. There is no interference from common additives and excipients. The method has been applied to the determination of fexofenadine hydrochloride in pharmaceutical samples and the results are statistically compared with those of literature UV-spectrophotometric method by applying student's *t*-test and *F*-test.

Keywords: Fexofenadine hydrochloride, Spectrophotometry, Chloramine-T, Malachite green, Xylene cyanol FF.

Fexofenadine hydrochloride, the active ingredient of Allegra and Telfast, is a second-generation histamine H1-receptor antagonist with the chemical name α,α-dimethyl-4-[1-hydroxy-4-[4-(hydroxydiphenyl-methyl)-1-piperidinyl]butyl]-benzene acetic acid. It is a nonsedating antihistamine. Fexofenadine hydrochloride is used as the hydrochloride salt in the symptomatic relief of allergic conditions including seasonal allergic rhinitis and urticaria[1,2]. Besides, fexofenadine may prove a safer alternative in the treatment of asthma[3] and atopic dermatitis[4] and is rapidly absorbed with a long duration of action, making it suitable for once daily administration.

Several methods have been reported for the determination of fexofenadine hydrochloride. Fexofenadine has been determined in biological fluids by HPLC with mass spectrometry detection[5] ion spray tandem mass spectrometry detection[6,7] and fluorescence detection[8]. The quantitation of fexofenadine in pharmaceutical dosage forms was realized using HPLC methods with ultraviolet detection[9,10] potentiometric titration using membrane electrode[11] and spectrophotometric methods[12,15]. In the literature few spectrophotometric methods have been reported; these are based on extractable ion-pair complex formation with bromothymol blue and bromocresol purple. These methods, however, suffer from disadvantages such as lack of selectivity, and complexity.

The aim of the present investigation was to develop a sensitive, accurate and precise method for the determination of FFH in pure and dosage forms. The present method is based on the oxidation of FFH by chloramine-T and residual oxidant is determined by treating with malachite green and xylene cyanol FF.

Experimental Procedure

Apparatus

A SHIMADZU UV-2550 UV-VIS Spectrophotometer with 1 cm matched quartz cells was used for the absorbance measurements.

Reagents and solutions

All reagents used were of analytical reagent grade and distilled water was used for the preparation of all solutions. A 1000 µg mL^{-1} standard drug solution of fexofenadine hydrochloride was prepared in 50% ethanol and made up to the mark with distilled water. The stock solution was diluted appropriately to get the working concentration. Hydrochloric acid (5 M), chloramine-T (CAT) (0.02 M), xylene cyanol FF (0.05%) and malachite green (0.05%) was used.

Procedures

Method A

Different aliquots (0.2-4.0 µg mL^{-1}) of FFH were transferred in to a series of 10 mL calibrated flasks. Then, 2 mL of 5 M HCl was added followed by 1 mL of CAT solution. The contents were shaken well and were set aside for 15 min with occasional shaking. Then, 0.5 mL of malachite green was added to each flask, and the volume was adjusted up to the mark with distilled water and mixed well. The absorbance of each solution was measured at 615 nm against the corresponding reagent blank.

Method B

Different aliquots (0.6-4.0 µg mL^{-1}) of FFH were transferred in to a series of 10 mL calibrated flasks. Then, 2 mL of 5 M HCl was added followed by 1 mL of CAT solution. The contents were shaken well and were set aside for 15 min with occasional shaking. Then, 0.5 mL of xylene cyanol FF was added to each flask, and the volume was adjusted up to the mark with distilled water and mixed well. The absorbance of each solution was measured at 612 nm against the corresponding reagent blank.

Analysis of dosage forms

Fexofenadine hydrochloride tablet (Aventis Pharma Limited, Ankleshwar, 120 mg/tablet) was taken, and the sample stock solution was prepared by grinding the tablet using a mortar and pestle and transferring to a 100 mL volumetric flask by washing with ethanol. The solution was shaken for 30 min and filtered through Whatman no.1 filter paper and the clear solution was made up to 100 mL. Pipetted out 0.4 mL for FFH-MAG system and 0.6 mL for FFH-XFF system and analyzed for FFH content following the above procedure without any modification.

Absorption spectra

The method is based on the reaction of surplus CAT with the corresponding dye solution in acidic medium, which bleaches the coloured dye solution to colourless leucoform, the decolouration being caused by the oxidative destruction of the dye, which was measured at 615 and 612 nm for malachite green and xylene cyanol FF respectively. The absorption spectra for FFH-MAG system and FFH-XFF system are shown in Figs 1 and 2.

Results and Discussion

In the present method, two dyes malachite green and xylene cyanol FF have been used for the determination of FFH. The determinations of FFH are indirect and are based on the determination of surplus CAT after the oxidation reaction of FFH by CAT. The drug undergoes oxidation to the corresponding ketone according to the reaction scheme given in scheme 1, since the reaction stoichiometry is found to be 1:1. The oxidation is found to be complete and quantitative in 20-25 min. Formation of corresponding ketone is confirmed by performing Borsche's reagent test[16].

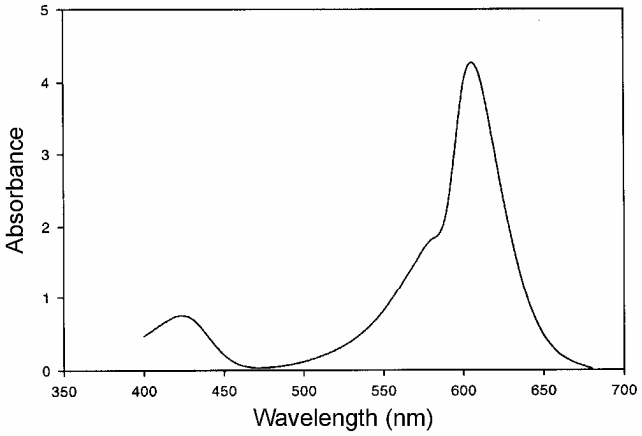


Fig. 1—Absorption spectrum for fexofenadine hydrochloride malachite green system

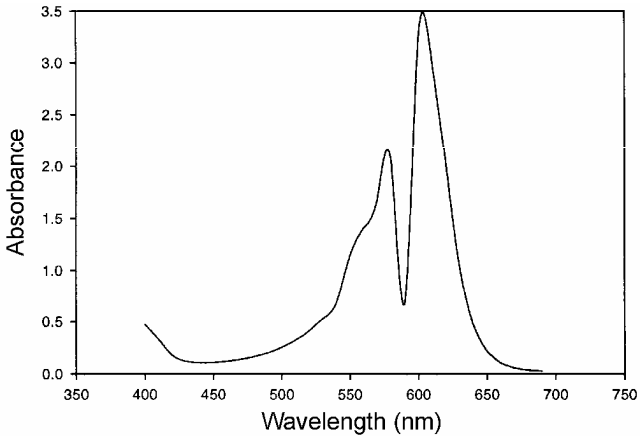
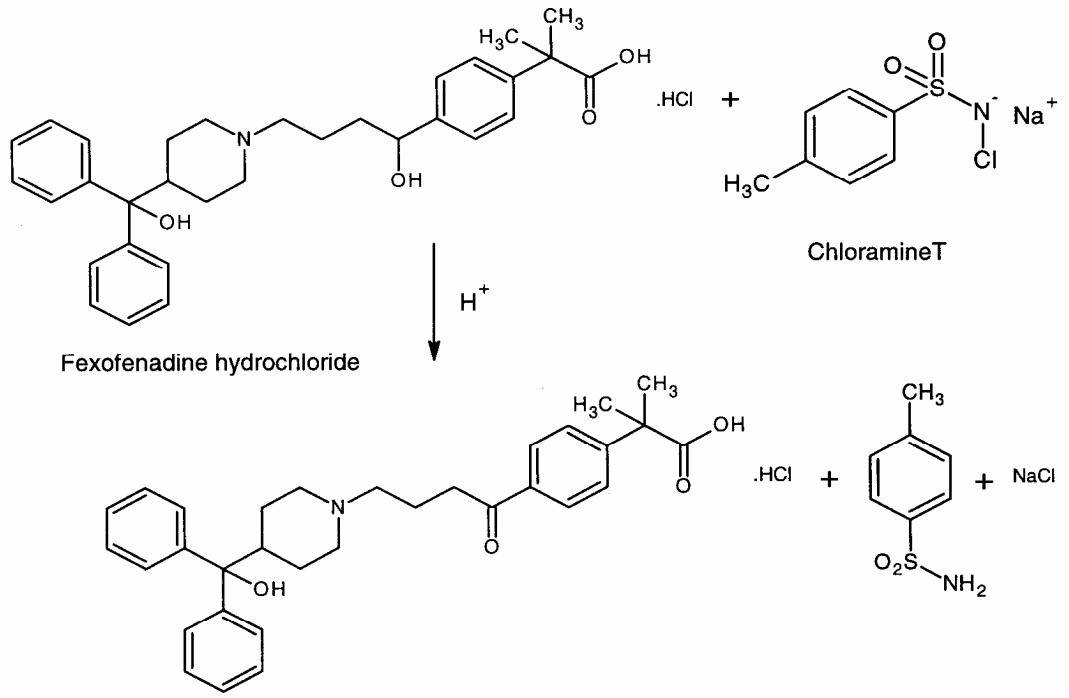


Fig. 2—Absorption spectrum for fexofenadine hydrochloride-xylene cyanol FF system

FFH when added in increasing concentration to a fixed concentration of CAT, will get oxidized and there will be a concomitant decrease in CAT concentration. A concomitant increase in the concentration of dye resulted when a fixed concentration of the dye is added to decreasing concentration of CAT. Preliminary experiments were performed to fix the concentration of the dye and are found to be 0.05% (0.5 mL) and 0.05% (1 mL) for



(*RS*)- 2-[4-[1-oxo- 4-[4-(hydroxy- diphenyl- methyl)-4-Methylbenzenesulfonamide 1-piperidyl]butyl]phenyl]- 2-methyl- propanoic acid hydrochloride

Reaction Scheme 1

malachite green and xylene cyanol FF respectively. The use of excess of reagent produced no further increase in absorbance.

Preliminary investigation showed that hydrochloric acid was better than sulphuric, phosphoric or acetic acid. One mL of 5 M hydrochloric acid was ideal for the oxidation step in both methods and the same quantity of acid was employed for the estimation of the dye. It was found that the maximum colour was developed within 20 min and remained almost stable for about 2 h.

Analytical data

The adherence to Beer's law is studied by measuring the absorbance values of solution containing varying drug concentration. A straight line graph is obtained by plotting absorbance against concentration of fexofenadine hydrochloride. The calibration graphs are described by the equation: Y = a + b X (where Y = absorbance, a = intercept, b = slope and X = concentration in μgml^{-1}) obtained by the method of least squares. The calibration graph was linear in the range of 0.2-4.0 $\mu g\ mL^{-1}$ of FFH for FFH-MAG system, 0.6-4.0 µg/mL of FFH for FFH-XFF system. The molar absorptivity, Sandell's sensitivity for FFH-MAG and FFH-XFF were found to be 4.09×10^4 L mol^{-1} cm^{-1}, 0.012 µg cm^{-2}, 3.07×10^4 L mol^{-1} cm^{-1}, 0.016 µg cm^{-2} respectively. Slope, intercept and correlation coefficient for FFH-MAG system is found to be 0.006, 0.045, 0.9986, while that for FFH-XFF system is found to be 0.057, 0.006, 0.9986 respectively. A comparison table of performance characteristics of reported methods and proposed method is given in Table 1. The parameters showing the sensitivity of the method such as molar absorptivity, Sandell's sensitivity were found to be higher compared with the existing method in the literature[15]. To evaluate the accuracy and precision of the methods, pure drug within the working limits are analyzed, each determination being repeated five times (Table 2). In order to check the validity of the proposed methods, fexofenadine hydrochloride was determined in commercial formulation. From the results (Table 3), it is clear that there is close agreement between the results obtained by the proposed methods and the label claim. The results were also compared statistically by a student's *t*-test for accuracy and variance ratio *F*-test for precision with those of the literature method[14] at 95% confidence level. The low values of the relative standard deviation in percentages and the error indicated the high accuracy of the two methods.

Table 1—Comparison table for proposed and reported methods

Reagent	Range	λ_{max} (nm)	Molar absorptivity	Method	Ref.
Bromothymol blue	10.0-50.0	412	2.30×10^4	Spectrophotometry	[14]
Potassium iodide	20.0-70.0	363	1.15×10^4	Colorimetric	[15]
Proposed method					
Using MAG	0.2-4.0	615	4.09×10^4	Spectrophotometry	
Using CV	0.6-4.0	612	3.07×10^4	Spectrophotometry	

Table 2—Evaluation of accuracy and precision

Amount taken (µg mL^{-1})	Amount found[a] (µg mL^{-1})	RE (%)	SD (µgmL^{-1})	RSD (%)
Using MAG as a Reagent				
0.20	0.201	0.50	0.001	0.49
0.40	0.404	1.00	0.003	0.74
0.60	0.606	1.00	0.010	1.65
0.80	0.807	0.88	0.008	0.99
1.00	0.982	-1.80	0.010	1.00
Using XFF as a reagent				
1.00	1.006	0.60	0.01	0.99
2.00	2.026	1.30	0.04	1.97
3.00	3.038	1.27	0.02	0.65
4.00	4.032	0.80	0.02	0.42

a-Average of five determinations, SD- Standard deviation, RE-Relative error

Table 3—Results of assay of formulations by the proposed method using MAG & XFF as reagents

Sample	FFH (mg) certified	Found±SD[a]	Recovery (%)	[a]*t*-test	[b]*F*-test
Using MAG					
FFH	120.00	120.04±0.04	100.03	2.18	4.00
Using XFF					
FFH	120.00	119.99±0.07	99.98	0.13	1.30

[a]Mean ±Standard deviation (n=5) [mg/tablet], [b]Tabulated t-value at 95% confidence level is 2.31, [c]Tabulated *F*-value at 95% confidence level is 6.39

Fexofenadine hydrochloride tablet- Aventis Pharma Limited, Ankleshwar

Interference study

Selectivity can be described as the capability of the method to accurately measure the response of the analysed compound with no interferences originating from sample matrix. High percentage recovery observed with assay samples of pharmaceutical dosage forms, including standard addition experiments, indicates that the proposed method was not affected by interferences from excipients used in formulations.

Applications

Compared to other existing methods, the developed method has the advantage of good sensitivity without the need for heating or extraction. The proposed method has been applied to the determination of fexofenadine hydrochloride in pure and dosage form. The results were compared statistically with those of the tabulated value at 95% confidence level. The calculated student's *t*-test (Table 3) did not exceed the tabulated value, indicating that there was no significant difference between the proposed method and the tabulated value in respect to accuracy and precision.

Conclusions

The present work employed simple, sensitive and selective method for the spectrophotometric determination of fexofenadine hydrochloride. The method offers linear ranges of applicability, stable coloured species and shorter contact times, and is free from either heating or extraction steps. There is no interference from common additives and excipients. Statistical analysis of the results indicates that the method yields exact values. Hence the proposed method has been successfully applied to the determination of fexofenadine hydrochloride in pharmaceutical samples.

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