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Original article

Stability-indicating stress degradation studies of lafutidine using UV spectrophotometric method

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ABSTRACT

Introduction: Lafutidine is a H_2 receptor antagonist and is indicated for inhibition of acid secretion. UV spectrophotometry can be used for stress degradation studies of lafutidine.
Method: Lafutidine was subjected to different stress conditions as per International Conference on Harmonization (ICH) guidelines. A stability-indicating UV spectroscopic method was developed for analysis of the drug in the presence of the degradation products. It involved a 5-h study; in which methanol and distilled water were used as solvents. The amount of degraded drug was calculated by taking absorbance at 279 nm.
Results: Degradation of lafutidine was found to occur in alkaline, neutral and photolytic conditions whereas it was found to be stable in acidic condition
Conclusion: The method was found to be simple and cost effective. Hence this method can be successfully used to study stress degradation behavior of lafutidine in small industry where high end instruments are not available.

1. Introduction

Chemically, lafutidine is 2-[(2-furylmethyl)sulfinyl]-*N*-(2*Z*-4-{[4-(piperridin-1yl methyl) pyridin-2-yl]oxy}but-2-en-1-yl)acetamide[1] [Fig. 1]. It is a H_2 receptor antagonist and is reported to show potent and long-lasting antagonisms of histamine H_2 receptor-mediated effect.[2] It is effective against the esophageal lesions induced by acid reflux through inhibition of acid secretion.[3]

Analysis is an important component in the formulation development of any drug molecule. It becomes essential to develop a simple, sensitive, accurate, precise and reproducible method for the estimation of drug samples.

The UV spectrophotometric method was developed and validated in our previous studies as per International Conference on Harmonization (ICH) guidelines.[4] Spectrophotometry is generally preferred, especially by small-scale industries as the cost of the equipment is less and the maintenance problems are minimal. The method of analysis is based on measuring the absorption of a monochromatic light by colorless compounds in the near-ultraviolet path of spectrum (200–380 nm).[5] UV spectrophotometry can be used for stress degradation studies of lafutidine and its degraded products. The active pharmaceutical ingredient is subjected to a number of forced degradation conditions, including acidic, basic, and oxidative conditions, as per ICH guidelines.[6] Forced degradation should be one of the activities performed early in the development process to ensure that the method is discriminating before a lot of time, effort, and money have been expended. It is important to determine which conditions are responsible to degrade the drug.

Earlier publications have described high-performance liquid chromatography (HPLC),[7] liquid chromatography–mass spectrometry (LC–MS),[8] and liquid chromatography–electrospray ionization–mass spectrometry (LC–ESI–MS)[9] methods for quantification of lafutidine in human plasma, and its pharmaceutical dosage form. However, these methods involve arduous sample preparation and long chromatographic run times for biological samples. In addition to this, determination of stress degraded behavior of lafutidine is even more difficult and a time-consuming process. Hence, the major objective of this research is to study the stability behavior of lafutidine by simple UV spectrophotometric methods.

2. Materials and methods

2.1. Instrument and materials

The instruments used were Shimadzu 1800 double-beam UV/Visible spectrophotometer and Shimadzu 1600 analytical balance.

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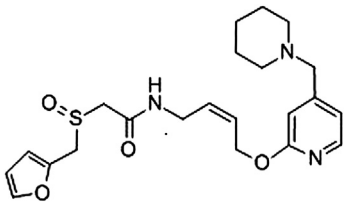

Fig. 1. Structure of lafutidine.

Lafutidine pure drug was obtained from Ajanta Pharmaceuticals Ltd., Mumbai, India as a gift sample with 99.9% (w/w) assay value and was used without further purification. All chemicals and reagents used were of analytical grade.

2.2. Methods

2.2.1. UV Spectrophotometric method of lafutidine

In our previous studies[4], we have developed and validated the UV spectrophotometric method of lafutidine. This method was used to study the stress degraded behavior of lafutidine.

2.2.2. Preparation of standard stock solution

Standard drug solution of lafutidine was prepared by dissolving 10 mg lafutidine in 5 ml methanol. This solution was transferred to 10 ml volumetric flask and its volume made up to mark with distilled water to obtain stock solution of 1 mg/ml concentration.

2.2.3. Preparation of calibration curve

Aliquots of 1–5 ml portion of stock solutions were transferred to series of 100 ml volumetric flasks, and the volume made up to mark with distilled water. Solutions were scanned in the range of 200–400 nm against blank. The absorption maxima values were found at 279 nm against blank. The calibration curve was plotted.

2.2.4. Forced degradation studies

A stock solution containing 10 mg lafutidine (LAF) in 10 ml methanol was prepared. This solution was used for forced degradation to provide an indication of the stability-indicating property and specificity of the proposed method. In all degradation studies, the absorbance of the drug was measured and the amount of degraded drug was calculated.

2.2.4.1. Acid and base induced degradation. Acid decomposition studies were performed by using 0.1 N, 0.2 N, and 0.5 N HCl, and basic decomposition studies were performed by using 0.1 N and 0.2 N NaOH. The concentration of LAF was 10 μg/ml for both acid and base degradation studies.

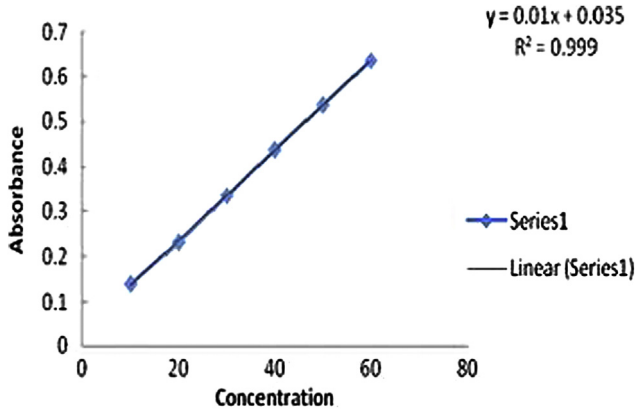

Fig. 2. Calibration curve of lafutidine (10–50 μg/ml).

Table 1
Calibration curve parameter.

Concentration (μg/ml)	Absorbance (average)
10	0.139
20	0.231
30	0.335
40	0.438
50	0.537
60	0.636

2.2.4.2. Hydrogen peroxide-induced degradation. To study hydrogen peroxide-induced degradation, initial studies were performed in 3% hydrogen peroxide at room temperature for 4 h. Subsequently, the drug was exposed to 30% hydrogen peroxide at room temperature for a period of 4 h. For the spectroscopic studies, the resultant solutions were scanned between 400 and 200 nm and the absorbance was taken.

2.2.4.3. Neutral hydrolysis. To study the degradation behavior of drug under neutral conditions, it was dissolved in methanol and the solution was kept for 4 h.

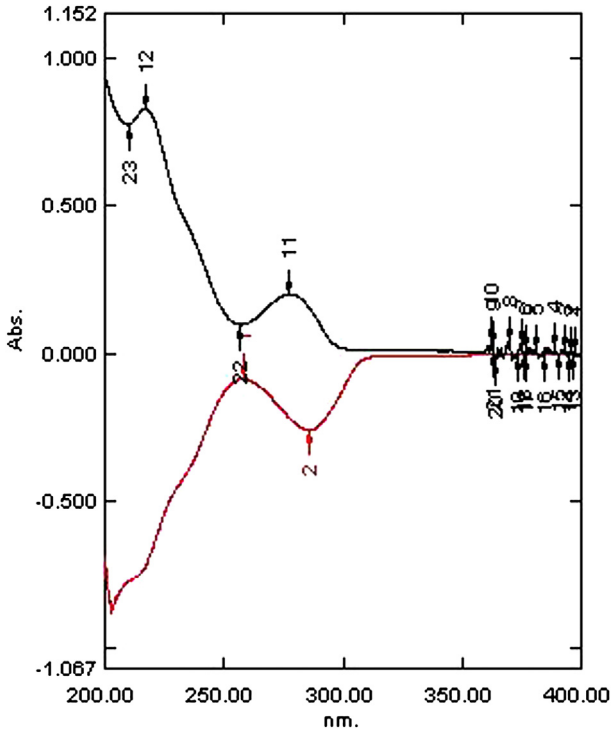

Fig. 3. Overlay graph of LAF and acid-degraded (0.1 N HCl) lafutidine.

Table 2
Acid degradation (0.5 N HCl) of lafutidine.

Name	Absorbance	Concentration in mg	% Degradation
Analyte at 0 h	0.136	10	0
Analyte at 1 h	0.126	9.2	8
Analyte at 2 h	−0.237	0	100
Analyte at 3 h	−0.237	Degraded	Degraded
Analyte at 4 h	−0.238	Degraded	Degraded

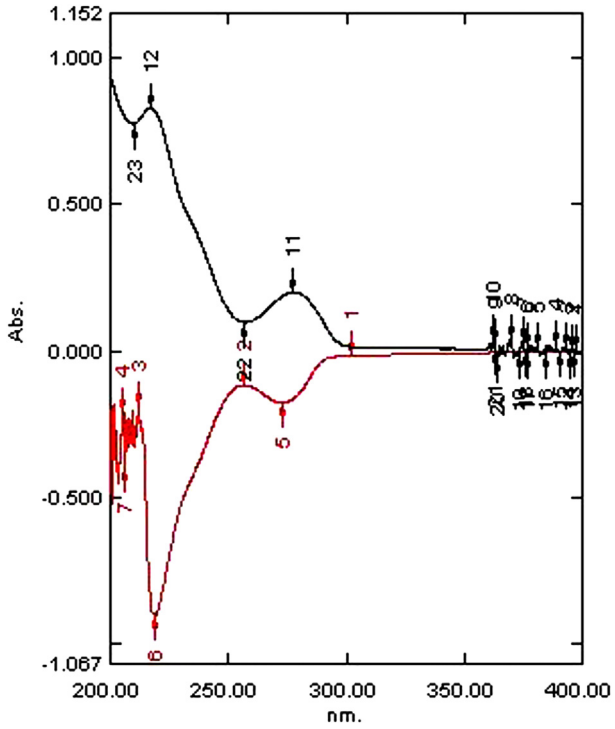

Fig. 4. Overlay graph of lafutidine and alkali-degraded (0.1 N NaOH) lafutidine.

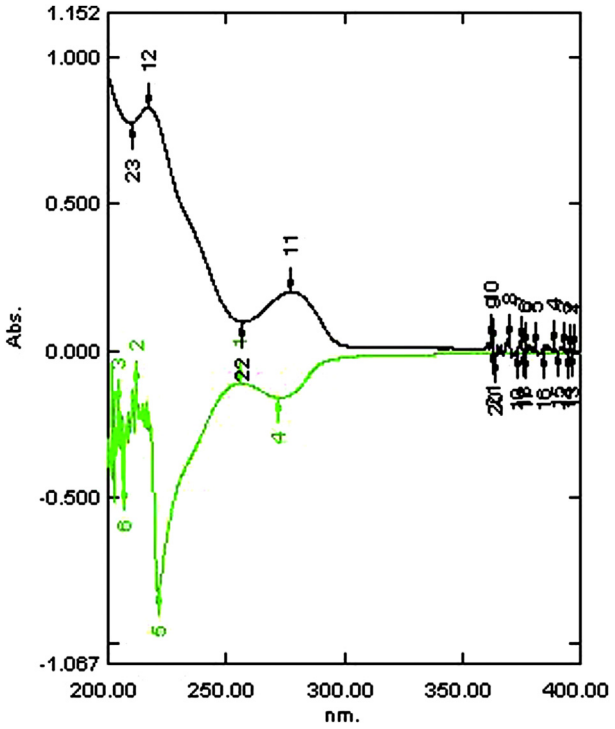

Fig. 6. Overlay graph of lafutidine and alkali-degraded (0.5 N NaOH) lafutidine.

2.2.4.4. Photolytic degradation. Photodegradation studies were performed by directly exposing lafutidine to sunlight during daytime (60,000–70,000 lux) for 2 days. Then, 10 μg/ml of the solution was scanned in UV.

Table 3
Alkali degradation (0.5 N NaOH) of lafutidine.

Name	Absorbance	Concentration in mg	% Degradation
Analyte at 0 h	0.137	10	0
Analyte at 1 h	0.134	9.8	2
Analyte at 2 h	−0.136	0	100
Analyte at 3 h	−0.135	Degraded	Degraded
Analyte at 4 h	−0.142	Degraded	Degraded

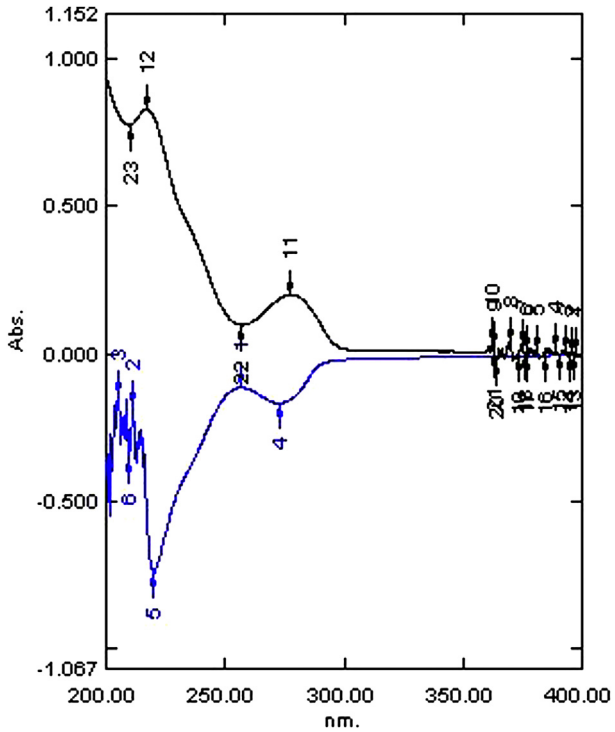

Fig. 5. Overlay graph of lafutidine and alkali-degraded (0.2 N NaOH) lafutidine.

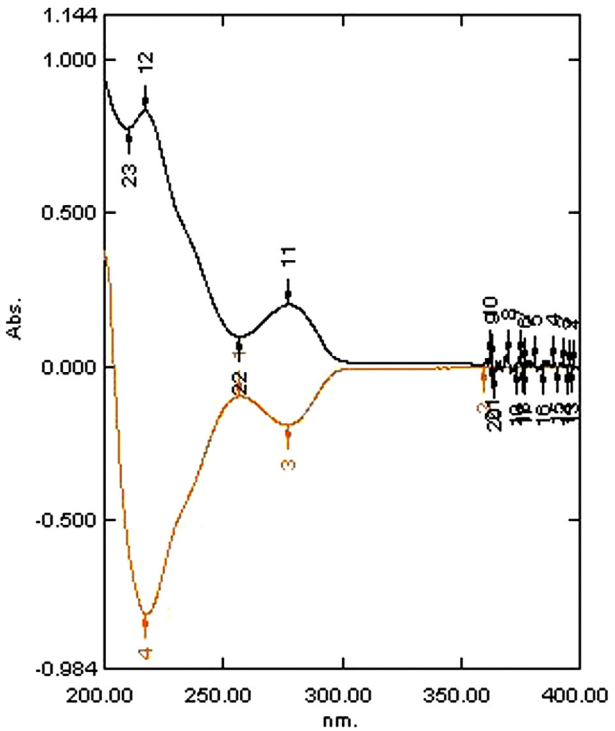

Fig. 7. Overlay graph of LAF and neutral-degraded lafutidine.

Table 4
Neutral degradation of lafutidine.

Name	Absorbance	Concentration in mg	% Degradation
Analyte at 0 h	0.139	10.22	0
Analyte at 1 h	0.134	9.85	2
Analyte at 2 h	−0.175	0	100
Analyte at 3 h	−0.176	Degraded	Degraded
Analyte at 4 h	−0.189	Degraded	Degraded

3. Results and discussion

3.1. Linearity and Calibration Curve

The linearity range was found to be 10–50 μg/ml. The calibration curve is shown in Fig. 2 and Table 1. From the calibration curve, concentration of drug in percentage was calculated.

3.2. Forced degradation studies

3.2.1. Acid degradation

The acid degradation was performed using 0.1 N HCl. The overlay graph of LAF and acid-degraded lafutidine is shown in Fig. 3. The percentage of degraded drug was calculated. It was found that lafutidine is degraded within 2 h. The results are shown in Table 2.

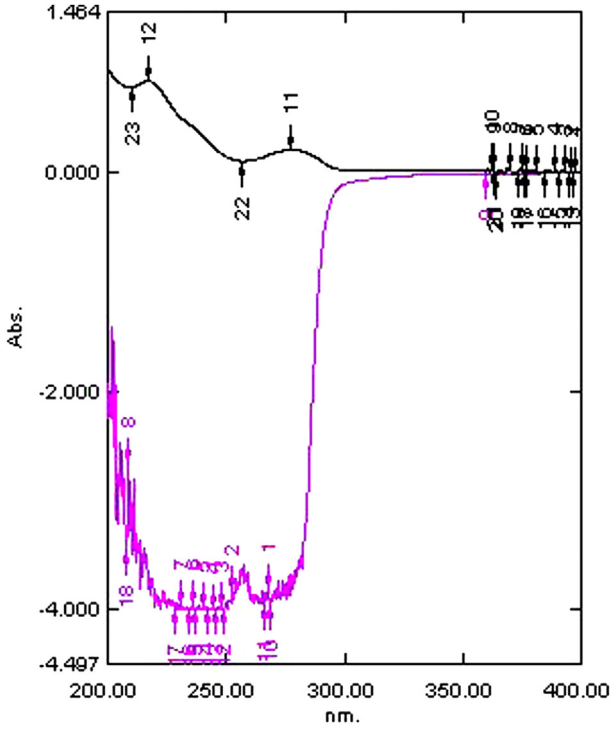

Fig. 8. Overlay graph of lafutidine and photolytic-degraded lafutidine.

Table 5
Photolytic degradation of lafutidine.

Name	Absorbance	Concentration in mg	% Degradation
Analyte at 0 h	0.145	10.24	0
Analyte at 1 h	0.111	8.16	19.4
Analyte at 2 h	−0.255	0	100
Analyte at 3 h	−3.476	Degraded	Degraded
Analyte at 4 h	−3.614	Degraded	Degraded

Table 6
Oxidative degradation (30% hydrogen peroxide) of lafutidine.

Name	Absorbance	Concentration in mg	% Degradation
Analyte at 0 h	0.105	7.72	3
Analyte at 1 h	0.085	6.25	4.75
Analyte at 2 h	−0.254	0	100
Analyte at 3 h	−0.256	Degraded	Degraded
Analyte at 4 h	−1.009	Degraded	Degraded

3.2.2. Alkali degradation

The alkali degradation was performed using 0.1 N NaOH, 0.2 N NaOH, and 0.5 N NaOH. The overlay graph of LAF and alkali-degraded lafutidine is shown in Figs. 4–6, respectively. The percentage of degraded drug was calculated It was found that lafutidine is degraded within 2 h. The results are shown in Table 3.

3.2.3. Neutral degradation

The neutral degradation was performed. The overlay graph of LAF and neutral-degraded lafutidine is shown in Fig. 7. The percentage of degraded drug was calculated. It was found that lafutidine is degraded within 2 h. The results are shown in Table 4.

3.2.4. Photolytic degradation

The photolytic degradation was performed using sunlight. The overlay graph of LAF and photolytic-degraded lafutidine is shown in Fig. 8. The percentage of degraded drug was calculated. It was found that lafutidine is degraded within 2 h. The results are shown in Table 5.

3.2.5. Oxidative degradation

Oxidative degradation was performed by using 30% hydrogen peroxide. The percentage of degraded drug was calculated. It was found that lafutidine is degraded within 2 h. The results are shown in Table 6 [Fig. 9].

Overall, we can say that this method is useful in studying the stability of the drug in bulk and pharmaceutical formulation (tablets) at different storage conditions.

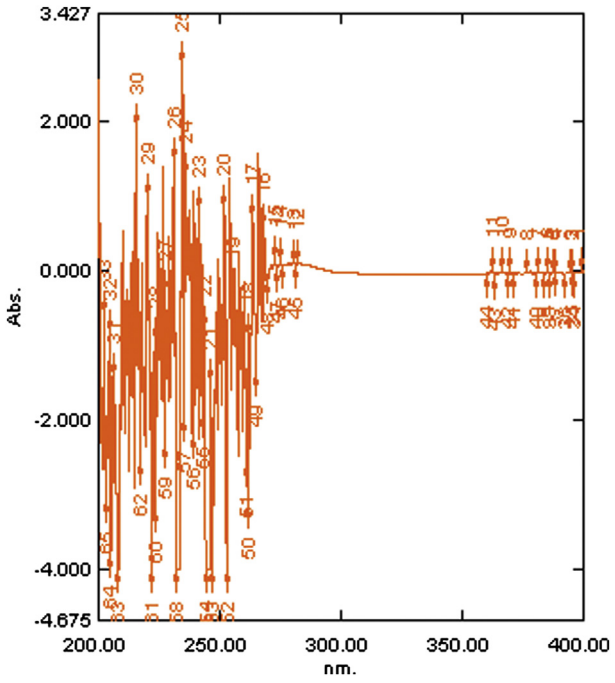

Fig. 9. Overlay graph of lafutidine and oxidatively degraded lafutidine.

4. Conclusion

Stress degradation study of lafutidine was done using UV spectrophotometric method. The method was found to be simple and cost effective. It was found that lafutidine was degraded in alkali and photolytic conditions. This method also provides quantification of lafutidine in presence of degraded products. Hence it can be successfully used to study stress degradation behavior of lafutidine in small scale industries where high end instruments are not available.

Conflicts of interest

All authors have none to declare.

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