Journal of Pharmaceutical and Biomedical Analysis
28 (2002) 1041–1053

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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Stability indicating methods for the determination of loratadine in the presence of its degradation product

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Received 12 June 2001; received in revised form 25 September 2001; accepted 1 October 2001

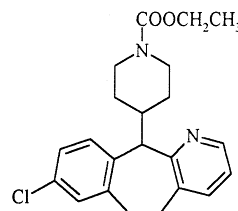
Abstract

Four stability-indicating procedures have been suggested for determination of the non sedating antihistaminic agent loratadine. Loratadine being an ester undergoes alkaline hydrolysis and the corresponding acid derivative is produced as a degradation product. Its identity was confirmed using IR and MS. The first procedure is based on determination of loratadine by HPLC with detection at wavelength, 250 nm. Mobile phase is acetonitrile:orthophosphoric acid (35:65) using benzophenone as an internal standard. Sensitivity range is 5.00–50.00 μg/ml. Second determination is a densitometric procedure based on determination of loratadine in the presence of its degradate at λ 246 nm using the mobile phase; methanol:ammonia (10:0.15). Sensitivity range is 1.25–7.50 μg per spot. The third procedure is a spectrophotometric one where a mixture of loratadine and its degradate are resolved by first derivative ratio spectra. Sensitivity range is found to be 3.00–22.00 μg/ml, upon carrying out the measurements at wavelengths 236, 262.4 and 293.2 nm. The fourth procedure is based on second derivative spectrophotometry, where D_2 measurements are carried out at λ 266 nm. The sensitivity range is 3.00–22.00 μg/ml. The validity of the described procedures was assessed by applying the standard addition technique. Statistical analysis of the results have been carried out revealing high accuracy and good precision. The suggested procedures could be used for determination of loratadine both in pure and dosage forms, as well as in the presence of its degradate. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Antihistaminic drugs; Loratadine; HPLC; Densitomerty; Derivative ratio; Second derivative spectrophotometry

1. Introduction

Loratadine, clantin; claritine, clarityne, lisino, is a non sedating-histamine H 1-receptor antagonist [1]. It is 4-(8-chloro-5, 6 dihydro-11 H-benzo-[5,6]cyclohepta[1,2-b]pyridin-11-ylidene). 1-piperidine carboxylic acid ethyl ester. Loratadine occurs as white crystals, m.p. 136 °C, soluble in alcohol and ether. It has the following structural formula [2].



Loratadine
$C_{22}H_{23}ClN_2O_2$
Mol.wt 382.89

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PII: S0731-7085(01)00664-1

Various analytical procedures have been reported for quantitative determination of loratadine both in dosage forms and in biological fluids. They include spectrophotometry [3–6], atomic absorption spectrometry [7], colorimetry [7], densitometry [8], polarography [9], HPLC [10], GLC [11] and GC-MS [12,13].

This manuscript deals with the determination of loratadine; the intact molecule, in the presence of its degradate, the corresponding acid derivative. Degradation was enhanced by refluxing loratadine with 0.5 M alcoholic potassium hydroxide for 4 h, acidifying with 1 M hydrochloric acid and extraction with ether. During hydrolysis, the ester linkage of loratadine suffers cleavage, leading to formation of the corresponding acid and ethyl alcohol. Elucidation of the structure of the degradation product was carried out using mass spectroscopy and IR.

The main goal of the present work is to introduce stability indicating methods for determination of loratadine in the presence of its degradate.

Four procedures have been introduced; HPLC, densitometry, derivative ratio spectrophotometery and second derivative spectrophotometery.

The suggested procedures were applied for determination of loratadine in pure form, in dosage forms and in the presence of its degradate.

2. Experimental

2.1. Instruments

μ Bondapak™ C18 125°A 10 μm 4.6 × 250 mm HPLC cartridge column, SPD-10 A UV- Vis Detector, LC- 10 Ad Liquid Chromatograph Shimadzu. Shimadzu Cs, 9000 flying spot densitometer. Precoated TLC Plates Sil GF_{254} (20 × 10 cm) from Merck. UV-1601 PC UV- VISIBLE Spectrophotometer Shimadzu.

2.2. Samples and pharmaceutical dosage forms

Loratadine, authentic sample; kindely supplied by Schering Plough Corporation USA. Its purity was checked by determination of its m.p.[2], and was analyzed to contain $99.63 \pm 0.73\%$ using the HPLC manufacturer procedure [14]. Claritine Tablets: labeled to contain 10 mg of loratadine/tablet, are produced by Medical Union Pharmaceuticals Co, Abu Sultan, Egypt, under Authority of Schering–Plough Corporation/USA Batch number 000741. Claritine Syrup: labeled to contain 10 mg of loratadine per 10 ml, are produced by Medical Union Pharmaceuticals Co, Abu Sultan Egypt, under Authority of Schering–Plough Corporation/USA Batch number 00251.

2.3. Standard drug solutions and reagents

Loratadine standard solution 10 mg/100 ml methanol (HPLC procedure). Loratadine standard solution 50 mg/100 ml methanol (Densitometric procedure). Loratadine standard solution 10 mg/100 ml ethanol (derivative ratio and second derivative spectrophotometry procedures). Benzophenone standard solution 10 mg/100 ml methanol. Acetonitrile:orthophosphoric acid mobile phase, (35:65). Alcoholic KOH (0.5 M). 1 M HCl, E. Merck, W. Germany; ether from E. Merck, Germany.

All solvents used were HPLC and spectroscopic grade. Methanol, ether, ethanol and hydrochloric acid were obtained from E. Merck, Germany.

2.4. Procedures

2.4.1. Method of preparation of the degradation product

Heat 1 g of loratadine by refluxing with 100 ml 0.5 M alcoholic KOH for about 4 h. Acidify with 1 M HCl and then extract the degradation product three times each with 10 ml ether. Evaporate under vacuum and dry in a desiccator. The degradate identity was checked and confirmed by carrying out mass spectroscopy and IR. Its m.p. was also determined.

2.4.2. Determination of loratadine in the presence of its degradate using HPLC procedure

For construction of the calibration graph, take aliquot portions of loratadine standard solution 10 mg/100 ml in methanol: (0.5–5 ml) into a series of 10 ml measuring flasks. Add 1 ml ben-

zophenone as an internal standard (10 mg% in methanol) and complete to volume with methanol. Inject 20 μl of the solution from each flask and record the chromatograms maintaining the flow rate at 2.0 ml/min. Monitor the effluent at λ 250 nm using acetonitrile:orthophosporic acid (35:65) as a mobile phase. Measure the peak area corresponding to concentration of each and divide by the peak area of internal standard. Construct a calibration graph representing the relation between the concentration and ratio of peak area. Concentration of unknown samples could be derived from the calibration graph or calculated from the following regression equation:

$$Y = 0.0187\ X + 0.0007 \qquad r = 1$$

where

$$Y = \frac{\text{Peak area of sample}}{\text{Peak area of internal standard}}$$

X is the concentration of loratadine in μg/ml and r is the correlation coefficient.

Laboratory mixtures were prepared containing loratadine and its degradate in the ratios from 10–80% of the degrade. They were treated similarly to determine loratadine content.

2.4.2.1. Determination of loratadine in claritine tablets using HPLC procedure. Accurately weigh 20 tablets and pulverize in a small mortar. Transfer a weighed quantity of powder equivalent to 10 mg loratadine into a beaker and extract with 80 ml methanol using a magnetic stirrer. Filter into a 100 ml measuring flask and complete to volume with methanol. Determine loratadine concentration by taking (0.5–5 ml) into 10 ml measuring flasks, add 1 ml benzophenone as internal standard (10 mg% in methanol). Complete to volume with methanol and proceed as previously described under Section 2.4.2 starting from "inject 20 μl of the solution ...".

2.4.2.2. Determination of loratadine in claritine syrup using HPLC procedure. Into a 50 ml separating funnel, accurately measure 10 ml of claritine syrup and extract three times each with 10 ml of chloroform. Evaporate to dryness and dissolve in 100 ml methanol. Determine loratadine concentration by taking (0.5–5 ml) into 10 ml measuring flasks, add 1 ml benzophenone as internal standard (10 mg% in methanol). Complete to volume with methanol and proceed as previously described under Section 2.4.2 starting from "inject 20 μl of the solution ...".

2.4.3. Determination of loratadine in the presence of its degradate using densitometric procedure

For the construction of calibration graph, apply 2.5, 5, 7.5, 10, 12.5 and 15 μl from stock solution 50 mg/100 ml of loratadine in methanol on a TLC plate. Place in a chromatographic tank previously saturated for 1 h with the developing mobile phase, methanol:ammonia (10:0.15). Develop the plate by ascending chromatography for a distance of 16 cm then remove and dry in air. Detect the spots under UV lamp and scan the plate at 246 nm. Construct the calibration curve, representing the relation between concentration and integrated peak area from which the concentration of unknown samples can be deduced or the following regression equation is used:

$$Y = 2.4236\ X + 1.641 \qquad r = 0.9999$$

where Y is the area under the peak, X is the concentration of loratadine in μg/spot and r is the correlation coefficient.

Laboratory mixtures were prepared containing loratadine and its degradate in the ratio of 10–80% of the degradate. They were treated similarly, to determine loratadine content.

2.4.3.1. Determination of loratadine in claritine tablets using densitometric procedure. Accurately weigh 20 tablets and pulverize in a small mortar. Transfer a weighed quantity of powder equivalent to 5 mg and extract with 8 ml methanol, filter in 10 ml measuring flask and complete to volume with methanol. Determine loratadine concentration by applying 2.5–15 μl of this solution on a TLC plate and proceed as described previously under Section 2.4.3 starting from "place in chromatographic tank ...".

2.4.3.2. Determination of loratadine in claritine syrup using densitometric procedure. Into a 50 ml separating funnel, accurately measure 5 ml of

claritine syrup claimed to contain 5 mg of loratadine and extract three times each with 10 ml of chloroform. Evaporate to dryness and dissolve in 10 ml methanol. Determine loratadine concentration by applying 2.5–15μl of this solution on a TLC plate and proceed as previously described under Section 2.4.3 starting from "place in chromatographic tank ...".

2.4.4. Spectrophotometric determination of loratadine in the presence of its degradate using derivative ratio spectrophotometric procedure

For construction of calibration graph, take aliquot portions of loratadine standard solution 10 mg/100 ml ethanol (3–22 ml) into a series of 100 ml measuring flasks. Dilute to volume with ethanol. Each absorption spectrum of loratadine standard solution was divided by the spectrum of degraded loratadine (20 μg/ml) as a divisor. The first derivative of ratio spectra were recorded and the values of the derivatives were measured at λ 236, 262.4 and 293.2 nm. Construct a calibration graph representing the relation between concentration and peak amplitude from which the concentration of unknown samples can be calculated. The following regression equations can be also used:

At λ 236 nm

$$Y = 0.0153\ X - 0.0026 \qquad r = 0.9997$$

At λ 262.4 nm

$$Y = -0.0216\ X - 0.0004 \qquad r = 0.9997$$

At λ 293.2 nm

$$Y = 0.039\ X + 0.0007 \qquad r = 1$$

where Y is the peak amplitude, X is the concentration of claritine in μg/ml and r is the correlation coefficient.

Laboratory mixtures were prepared containing loratadine and its degradate in the ratios 10–80% of the degradate. They were treated similarly to determine loratadine content.

2.4.4.1. Spectrophotometric determination of loratadine in claritine tablets using derivative ratio spectra procedure. Accurately weigh 20 tablets and pulverize in a small mortar. Transfer a weighed quantity of powder equivalent to 10 mg loratadine into a small beaker and extract with 80 ml ethanol using a magnetic stirrer. Filter into a 100 ml measuring flask and complete to volume with ethanol. Determine loratadine concentration by measuring different volumes of this solution (3–22 ml) into 100 ml measuring flasks. Complete to volume with ethanol and proceed as previously described under Section 2.4.4 starting from "each absorption spectrum ...".

2.4.4.2. Determination of loratadine in claritine syrup using derivative ratio spectra procedure. Into a 50 ml separating funnel accurately transfer 10 ml of claritine syrup claimed to contain 10 mg of loratadine. Extract three times each with 10 ml chloroform, evaporate to dryness and dissolve in 100 ml ethanol. Determine loratadine concentration by measuring different volumes of this solution (3–22 ml) into 100 ml measuring flasks. Complete to volume with ethanol and proceed as previously described under Section 2.4.4 starting from "each absorption spectrum ...".

2.4.5. Spectrophotometric determination of loratadine in the presence of its degradate using second derivative procedure

Transfer accurately aliquot portions (3–22 ml) of loratadine from its stock solution (10 mg/100 ml ethanol) into a series of 100-ml measuring flasks and complete to the mark with ethanol. Record the second derivative curves of each solution against ethanol as a blank. Measure D_2 at λ 266 nm and plot the calibration curve representing the relationship between the measured D_2 values and the corresponding concentration. The concentration of unknown samples can be deduced by using such calibration curve or by using the following regression equations:

$$D_2 = 0.0064\ X + 0.0001 \qquad r = 1$$

where (D_2) is second derivative value and X is the concentration in μg/ml and r is the correlation coefficient.

Laboratory mixtures were prepared containing loratadine and its degradate in the ratios 10–80% of the degradate. They were treated similarly to determine loratadine content.

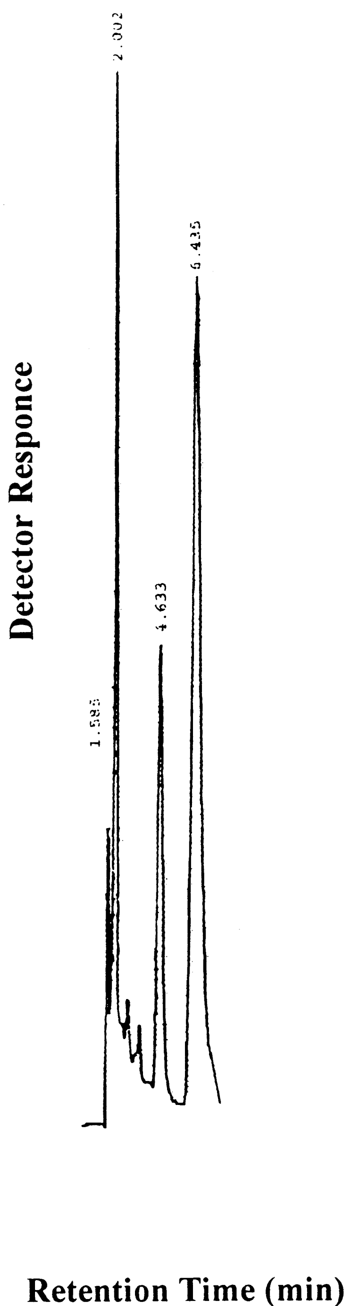


Fig. 1. HPLC spectra of loratadine (at 4.633 min) in presence of 60% degraded loratadine (at 2.002 min) using benzophenone as an internal standard (at 6.435 min).

2.4.5.1. Spectrophotometric determination of loratadine in claritine tablets using second derivative procedure. Accurately weigh twenty tablets and pulverize in a small mortar. Transfer a weighed quantity of powder equivalent to 10 mg loratadine, into a small beaker and extract with 80 ml ethanol using a magnetic stirrer. Filter into a 100 ml measuring flask and complete to volume with ethanol. Determine loratadine concentration by measuring different volumes of this solution (3–22 ml) into 100 ml measuring flasks. Complete to volume with ethanol and proceed as previously described under Section 2.4.5 starting from "record the second derivative curves ....".

2.4.5.2. Spectrophotometric determination of loratadine in claritine syrup using second derivative procedure. Into a 50 ml separating funnel accurately transfer 10 ml of claritine syrup claimed to contain 10 mg of loratadine and extract three times each with 10 ml chloroform. Evaporate to dryness and dissolve in 100 ml ethanol. Determine loratadine concentration by measuring different volumes of this solution (3–22 ml) into 100 ml measuring flasks. Complete to volume with ethanol and proceed as previously described under Section 2.4.5 starting from "record the second derivative curves ....".

3. Results and discussion

3.1. HPLC method

Various solvent systems were tried to find out the best mobile phase for separation of loratadine and its degradation product. Acetonitrile and orthophosphoric acid (35:65) gave better resolution as shown in Fig. 1. Under the experimentally described conditions, the analyte peak was well defined, resolved and free from tailing. The retention time was ($t_r = 4.633$ min) at a flow rate of 2.0 ml/min. The optimum wavelength for detection was 250 nm at which good detector response was obtained for loratadine. Linearity to concentration was obtained in the concentration range 5.00–50.00 μg/ml as shown in Fig. 2. The calibration curve could be represented by the regression equation and correlation coefficient as mentioned before under procedure Section 2.4.2.

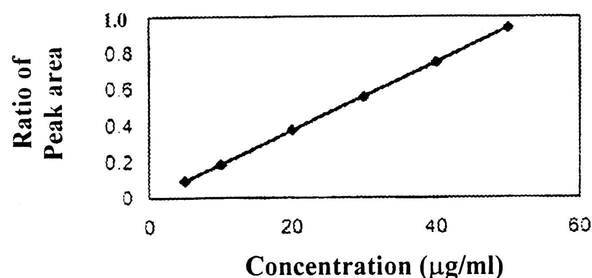


Fig. 2. Linearity of concentration of loratadine to peak area of loratadine/peak area of internal reference standard (ratio of peak area) using HPLC procedure.

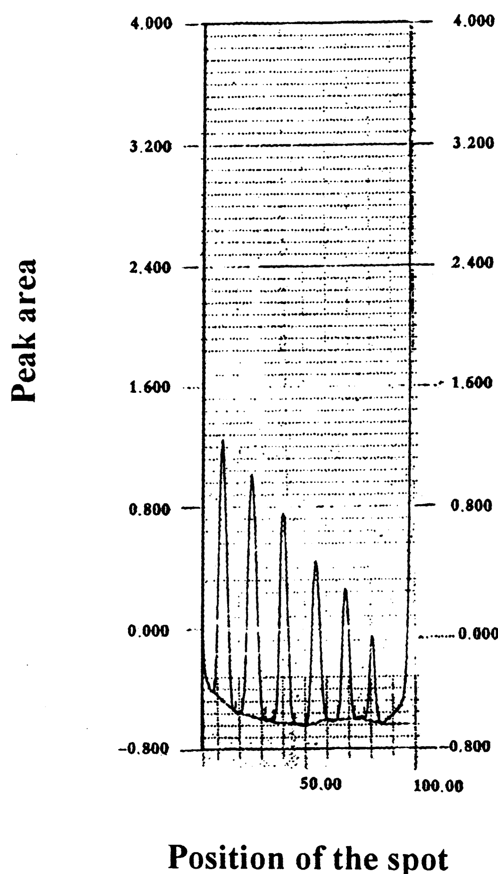


Fig. 3. Scanning profile of loratadine (1.25–7.50 μg/spot) at λ 246 nm.

In literature D. Zhong, H. Blume [10] had suggested a HPLC procedure for determination of loratadine and its metabolite decarboxyethoxy loratadine in human plasma. The mobile phase was acetone, water, ammonium dihydrogen phosphate and ortho-phosphoric acid with fluorescence detection. They did not mention about stability or degradate.

3.2. Densitometric method

This method is concerned with application of the densitometric technique for determination of loratadine. The best separation of the studied drug from its degradate was obtained using methanol:ammonia (10:0.15) as the developing mobile phase. The R_f value was found to be 0.72 for loratadine and 0.25 for its degradate. Quantitatively the chromatogram was scanned at 246 nm as shown in Fig. 3. By applying this technique a linear correlation was obtained between the concentrations 1.25–7.50 μg/spot of loratadine and the spot area as shown in Fig. 4. The linear regression equation was calculated as mentioned before under procedure Section 2.4.3.

In literature G. Indrayanto, et al. [8] had described a method for determination of loratadine in dosage forms. They used different experimental conditions and did not mention about stability. The developing system was chloroform, ethylacetate and acetone. They did not mention about degradate.

3.3. Derivative ratio spectrophotometric method

The present work is concerned with the application of a derivative ratio technique for determination of loratadine in the presence of its degradation product. In practice, measurements were carried out at three wavelengths, 236, 262.4 and 293.2 nm as shown in Fig. 5. Linear correlation was obtained between the concentration 3.00–22.00 μg/ml of loratadine and the peak amplitude as shown in Figs. 6–8. The corresponding linear regression equations were calculated as mentioned before under procedure Section 2.4.4.

In literature F. Onur, et al. [6], had determined loratadine and pseudoephedrine mixture in pharmaceutical preparation using ratio spectra derivative spectrophotometry. They did not mention about stability or the degradate. Measurement of

loratadine in the presence of pseudoephedrine sulfate were carried out at 286.1, 298.2, 305.7 and 331.7 nm using 0.1 N hydrochloric acid. Wavelength, 305.7 nm was selected for determination of loratadine in the pharmaceutical preparation containing their mixture.

3.4. Second derivative spectrophotometric method

Second derivative spectrophotometric method is used for the determination of loratadine in the presence of its degradation product. The zero order and first order absorption spectra of lo-

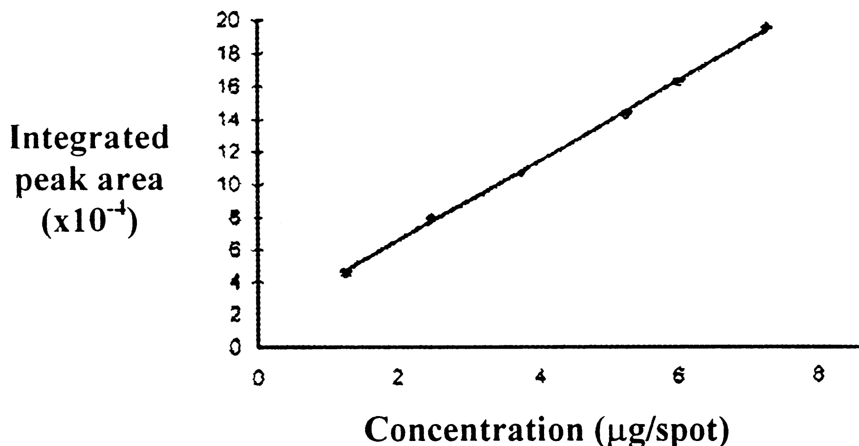


Fig. 4. Linearity of spot area to concentration of loratadine via TLC scanning procedure.

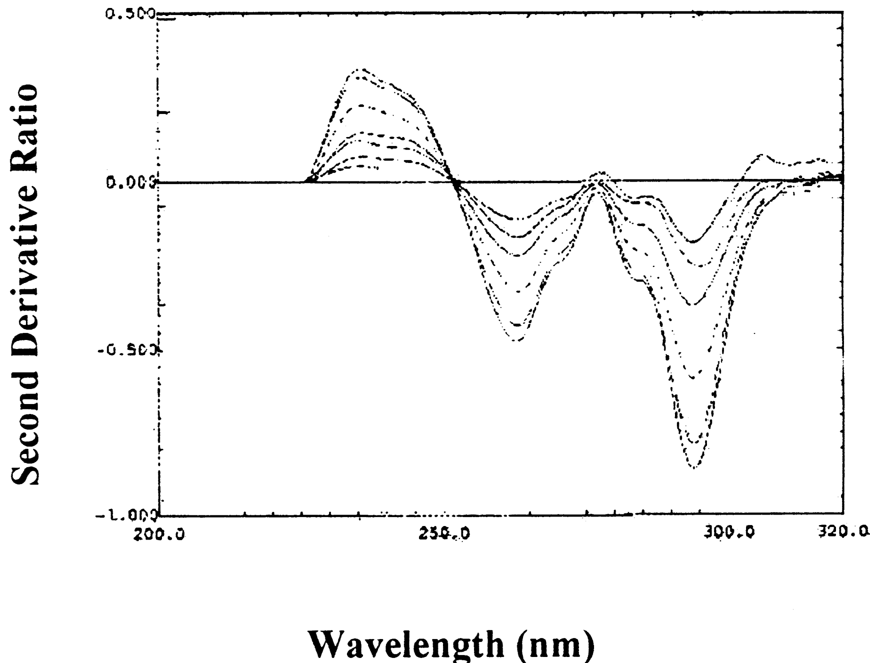


Fig. 5. Derivative ratio spectra of loratadine in the presence of its degradate (using 3.00–22.00 µg/ml loratadine in ethanol and 20.00 µg/ml of its degradate.

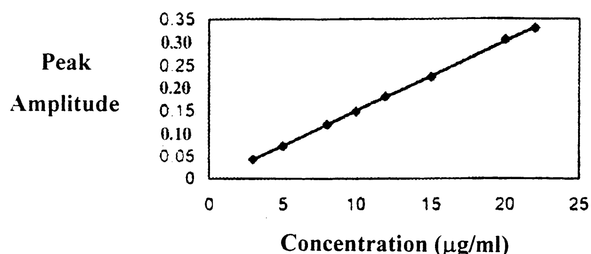


Fig. 6. Linearity of peak amplitude to concentration of loratadine via derivative ratio spectra at λ 236 nm.

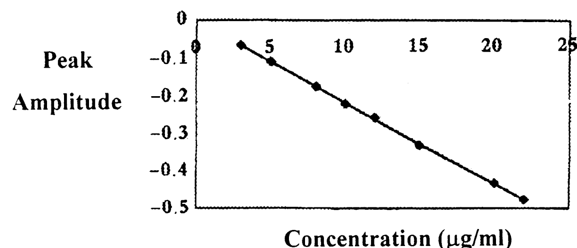


Fig. 7. Linearity of peak amplitude to concentration of loratadine via derivative ratio spectra at λ 262.4 nm.

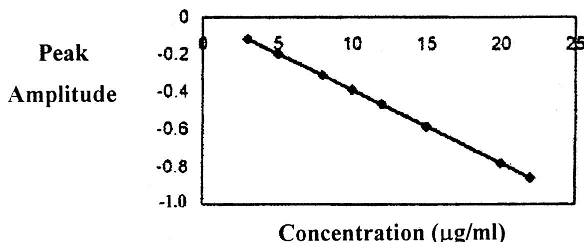


Fig. 8. Linearity of peak amplitude to concentration of loratadine via derivative ratio spectra at λ 293.2 nm.

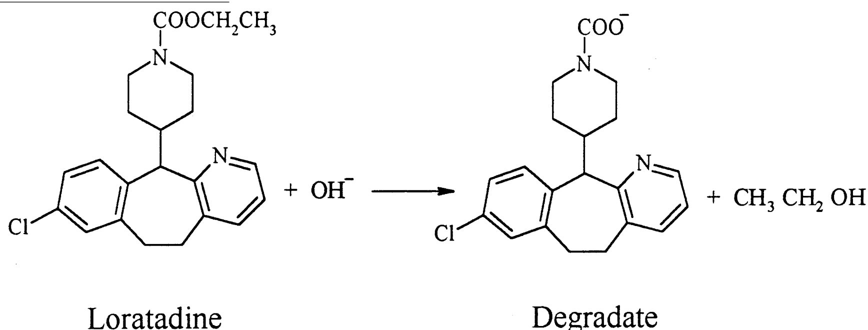
ratadine and its degradation product in ethanol suffer an overlapping which interferes with the direct determination of pure loratadine. The present work is devoted to the application of second derivative spectrophotometry to resolve such spectral overlapping for determination of intact loratadine in the presence of its degradation product at λ 266 nm as shown in Fig. 9.

A linear correlation was obtained between the concentration of loratadine and the D_2 values in the range of 3.00–22.00 μg/ml at λ 266 nm. Results are shown in Fig. 10. The regression equation was calculated as mentioned before under procedure Section 2.4.5.

F. Onur, et al. [6], had also determined loratadine and pseudoephedrine mixture in pharmaceutical preparations using first derivative spectrophotometry. They did not mention about stability or degradate. A linear correlation was obtained between the D_1 values and the concentration in the range of 5.00–40.00 μg/ml at 306.6 nm for loratadine in 0.1 N hydrochloric acid. However, the range in the present work is 3.00–22.00 μg/ml and peak amplitude is measured at 266 nm using ethanol as a solvent.

3.5. Separation and identification of the degradation product

Degradation of loratadine was influenced by reaction with 0.5 M alcoholic potassium hydroxide and reflux for 4 h. It was followed by acidification with 1 M HCl and extraction with ether. Etherial extract was evaporated under vacuum and kept in a desiccator. Its m.p. was determined and found to be 142 °C. Being an ester, the degradate was expected to be the corresponding acid of loratadine as shown in the following equation:



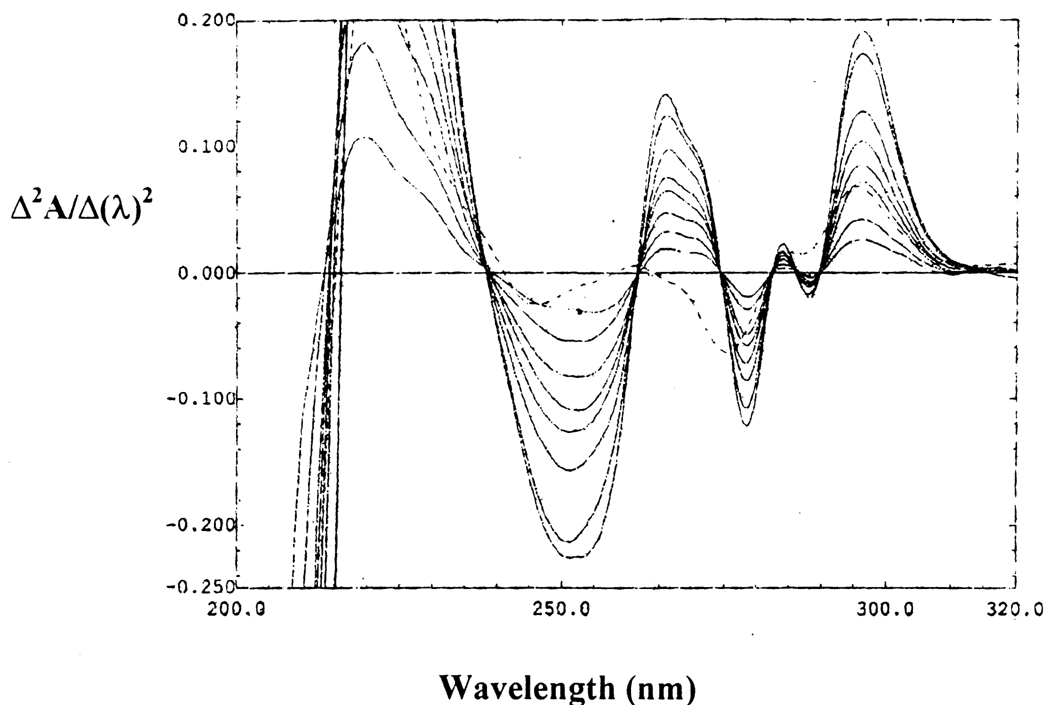


Fig. 9. Second derivative spectra of loratadine in the presence of its degradate (using 3.00–22.00 μg/ml^{-1} of loratadine) in ethanol at λ 266 nm (zero-crossing point of degraded loratadine).

This was confirmed by mass spectroscopy as shown in Fig. 11. It shows that the parent peak of the degraded loratadine at m/z 352 while the whole molecular weight of loratadine is 382.89. This indicates that the ester group suffers cleavage by 0.5 M alcoholic potassium hydroxide leading to formation of the corresponding acid m/z 352 as shown in Fig. 11 and ethylalcohol. It was further confirmed by IR spectroscopy as shown in Figs. 12 and 13. IR spectroscopy of the degraded loratadine (Fig. 12) shows the new broad band at wavenumber 4000–3200 cm^{-1} related to the corresponding aliphatic hydroxyl group of the carboxylic acid [15]. This band is not found in the pure loratadine as shown in Fig. 13, since loratadine is an ester it has no band in the region of 4000–3200 cm^{-1} [15].

The proposed methods were successfully applied for the analysis of loratadine in pure or dosage forms, tablets and syrup as shown in Sections 2.4.1 and 2.4.2 and Section 2.4.3, respectively. L.O.D. and L.O.Q. are shown in Table 1.

The validity of the procedures was further assessed by applying the standard addition technique. Results obtained are presented in Tables 2 and 3 proving no interference from additives or excipients.

For the purpose of comparison, the results of the suggested procedures were statistically analyzed upon carrying out the reference method for analysis of loratadine. The results are represented in Table 4 which shows comparable accuracy (t-test) and precision (F-ratio) since the calculated

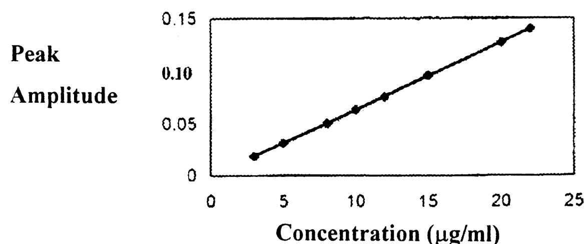


Fig. 10. Linearity of peak amplitude to concentration of loratadine at λ 266 nm via second derivative technique.

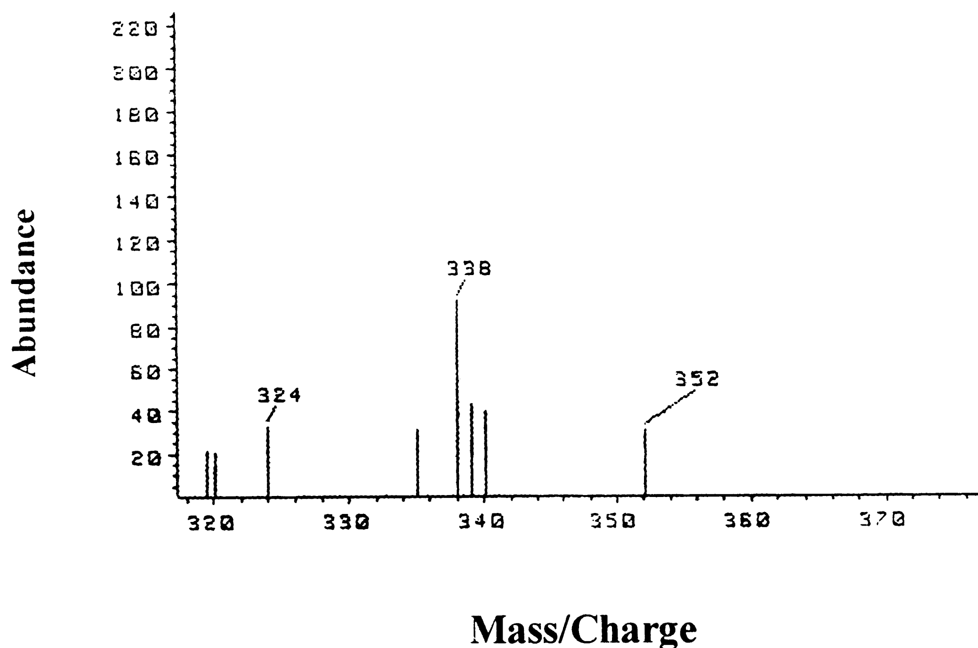


Fig. 11. Mass spectroscopy of the degradation product of loratadine.

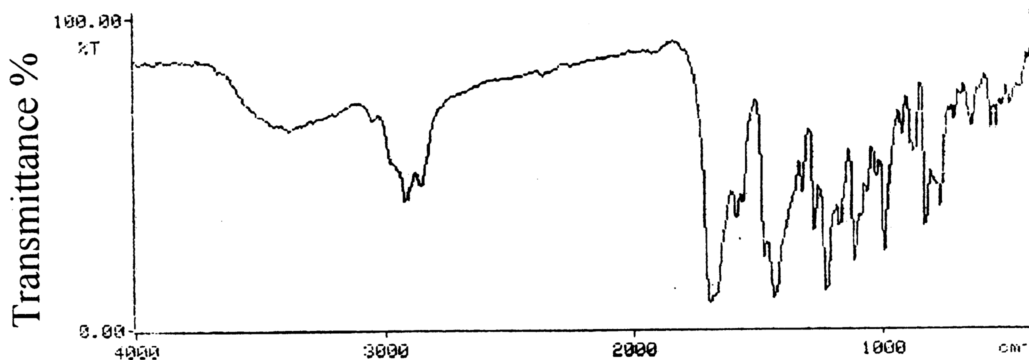


Fig. 12. IR spectroscopy of the degradation product of loratadine.

values of (t) and F are less than the theoretical values [16].

To assess the stability-indicating efficiency of the proposed methods, the degradation product of loratadine was mixed with its intact sample in different ratios (10–80%) and mixtures were analyzed by the proposed methods. The results obtained are shown in Table 5. It is clear that the accuracy of the proposed methods are not affected up to 80% of the degradation product.

Thus, it could be concluded that the suggested procedures are simple, sensitive and stability indicating. They can be recommended for routine analysis of loratadine both in pure and dosage forms without interference of the degraded loratadine as shown in Table 4.

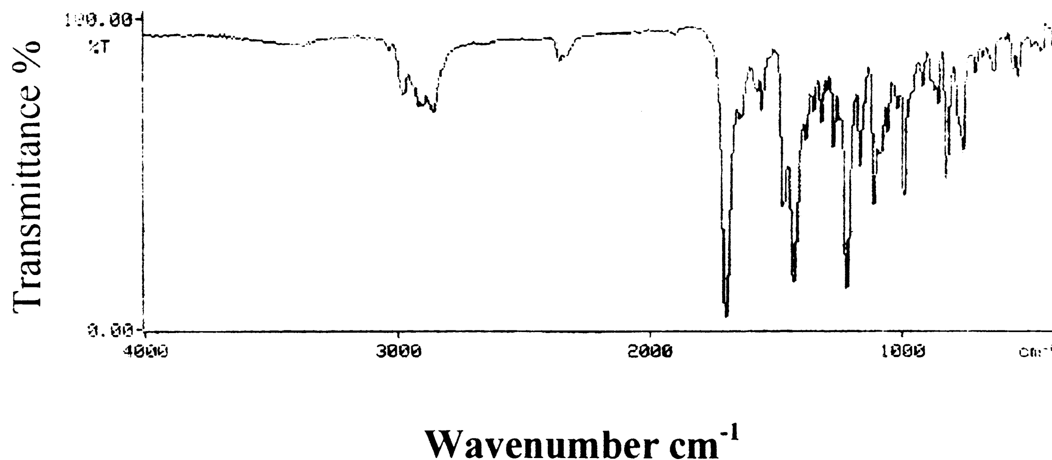


Fig. 13. IR spectroscopy of the pure loratadine.

Table 1
Determination of authentic loratadine via the suggested procedures*

Technique	Sensitivity range (μg/ml)	L.O.D. (μg/ml)	L.O.Q. (μg/ml)	Mean% recovery ± R.S.D.
HPLC	5.00–50.00	4.14	5.00	100.02 ± 0.349
Densitometry At λ 246 nm	1.25–7.50 μg/spot	1.11 μg/spot	1.25 μg/spot	100.26 ± 0.874
Derivative ratio				
At λ 236 nm	3.00–22.00	2.18	3.00	99.83 ± 1.101
At λ 262.4 nm	3.00–22.00	2.13	3.00	99.87 ± 0.901
At λ 293.2 nm	3.00–22.00	2.17	3.00	99.95 ± 0.115
2nd derivative				
At λ 266 nm	3.00–22.00	2.20	3.00	99.33+0.511

*, Average of at least three separate determinations.

Table 2
Determination of loratadine in claritine* tablets by applying the proposed procedures and results of standard addition

Technique	Claimed	Found	% Found	Mean% Recovey **	R.S.D.
HPLC	10 μg/ml	10.02	100.20	100.15	0.408
Densitometry	1.25 μg/spot	1.24	99.20	99.89	1.203
Derivative ratio					
At λ 236 nm	3 μg/ml	3.05	101.67	99.82	0.293
At λ 262.4 nm	3 μg/ml	3.04	101.33	101.53	0.465
At λ 293.2 nm	3 μg/ml	2.98	99.33	99.79	0.137
2nd derivative					
At λ 266 nm	3 μg/ml	2.95	98.33	99.50	1.239

*, Claritine tablets claimed to contain 10 mg of loratadine/tablet. **, These results are the average of three experiments.

Table 3
Determination of loratadine in claritine* syrup by applying the proposed procedures and results of standard addition

Technique	Claimed	Found	% Found	Mean% recovery**	R.S.D.
HPLC	10 μg/ml	9.96	99.60	99.96	0.647
Densitometry	1.25 μg/spot	1.25	100.00	99.72	0.263
Derivative ratio					
At λ 236 nm	3 μg/ml	2.98	99.33	100.59	1.248
At λ 262.4 nm	3 μg/ml	2.99	99.67	100.19	0.817
At λ 293.2 nm	3 μg/ml	3	100%	100.11	0.598
2nd derivative					
At λ 266 nm	3 μg/ml	2.95	98.33	99.25	0.937

*, Claritine syrup claimed to contain 10 mg of loratadine per 10 ml syrup. **, These results are the average of three experiments.

Table 4
Statistical comparison of the results obtained by adopting the proposed procedures as compared with the reference method* for the analysis of authentic loratadine

Technique	Mean ± R.S.D.	n	Variance	Student's t-test	F
Reference [14] Method	99.63 ± 0.733	7	0.533	–	–
HPLC	100.02 ± 0.349	6	0.122	0.940 (2.201)**	4.369 (4.95)**
Densitometry	100.26 ± 0.874	6	0.767	1.270 (2.201)**	1.439 (4.39)**
Derivative ratio at λ 236 nm	99.83 ± 1.101	8	1.208	0.401 (2.160)**	2.266 (4.21)**
At λ 262 nm	99.87 ± 0.901	8	0.810	0.512 (2.160)**	1.520 (4.21)**
At λ 293 nm	99.95 ± 0.115	6	0.165	0.354 (2.160)**	3.230 (3.87)**
2nd Derivative at λ 266 nm	99.33 ± 0.511	8	0.258	0.840 (2.160)**	2.066 (3.87)**

*, Reference method is HPLC Manufacture procedure. **, Figures in parentheses are the theoretical t and F values at $P = 0.05$.

Table 5
Recoveries of loratadine in the presence of its degradate*

Techniques		% Recovery					Mean ± R.S.D.
% of Degradation product		10%	20%	40%	60%	80%	
HPLC $n = 5$		100.22	100.05	99.53	100.10	101.20	100.22 ± 0.607
Densitometry $n = 5$		100.00	99.00	99.11	100.00	100.67	99.76 ± 0.699
Derivative ratio $n = 5$	At λ 236 nm	101.50	100.75	100.00	100.13	100.75	100.63 ± 0.594
	At λ 262.4 nm	99.17	99.69	100.17	100.50	99.00	99.71 ± 0.641
	At λ 293.2 nm	100.22	99.94	100.17	100.25	99.25	99.97 ± 0.418
2nd Derivative $n = 5$	At λ 266 nm	100.61	100.50	98.83	99.38	101.25	100.11 ± 0.983

*, These results are the average of three experiments.

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