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International Journal of Pharmaceutical Chemistry and Analysis

Journal homepage: www.ipinnovative.com

Original Research Article

Forced degradation study of different brands of levocetirizine dihydrochloride by UV-spectroscopy

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ARTICLE INFO

Article history:
Received 17-06-2020
Accepted 30-07-2020
Available online 12-08-2020

Keywords:
Levocetirizine dihydrochloride
Degradation studies
Different brands
UV-spectrophotometer

ABSTRACT

The goal of this study is to carry out degradation studies of Levocetirizine market-available tablet brands. Forced degradation is the process which involves degradation of the drug products which can be studied to determine the molecule's stability. Various brands of levocetirizine dihydrochloride (Okacet-L, LECOPE, Levocet, 1-AL) were used. It is an H_1 receptor antagonist and is used in the treatment of persistent or seasonal allergic rhinitis and chronic idiopathic urticaria. As per ICH recommendations, this drug has been subject to various stress conditions during the study. In the presence of degradation products, an ultraviolet spectroscopic (UV) method for drug analysis has been developed. The pH 7.0 phosphate buffer was used as solvent. The amount of degraded drug was determined by taking the 230 nm absorbance. All products have been degraded under conditions of acidic, oxidation, photolytic and thermal degradation, and less degraded in alkaline conditions. In all conditions of degradation the tablet of brands Levocet and LECOPE showed less degradation than the brand name tablets Okacet-L and 1-AL.

1. Introduction

Levocetirizine dihydrochloride (LCT), (-)-cetirizine dihydrochloride; 2-[2-[4-[(*R*)-(4-chlorophenyl)-phenyl-methyl]piperazin-1-yl]ethoxy]acetic acid dihydrochloride, (Figure 1) is a third generation non sedative antihistamine, H_1-receptar antagonist and is the active enantiomer of cetirizinedihydrochloride.[1–4] It is used to treat seasonal or perennial allergic rhinitis and chronic idiopathic urticarial.[5–7]

Analysis is an essential component in the formation of any drug molecule in formulation. Development of a simple, sensitive, accurate, precise and reproducible method for estimating the drug sample becomes important.[8]

In previous studies, the UV spectrophotometric method was developed and validated in accordance with the guidelines of the International Conference on Harmonization (ICH).[4] Generally speaking, spectrophotometry is preferred, particularly by small industries as the equipment cost is less and the maintenance is minimal. The analytical approach is based on measuring the absorption of a monochromatic light by colourless compound in spectral near-ultraviolet region (200-380 nm).[9] UV spectrophotometry may be used to test LCT and its degraded products for

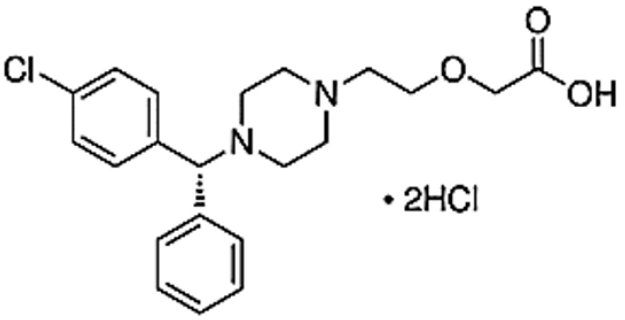

Fig. 1: Chemical structure of Levocetirizine dihydrochloride

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https://doi.org/

stress degradation. According to ICH guidelines, the active pharmaceutical ingredient is subject to a range of forced degradation conditions, including acidic, basic, hot liquid, photolytic and oxidative conditions.[10]

Force degradation should be one of the early development activities to ensure that the method is discriminatory before a lot of time, effort, and money has been increased. Defining the conditions responsible for degrading the drug is essential.[8]

Earlier publications had described stability indicating liquid chromatography tandem mass spectrometric (LC-MS/MS).[11] liquid chromatography (LC),[12] reverse phase high performance liquid chromatography (RP-HPLC),[7] methods for quantification of LCT in human plasma and pharmaceutical dosage form. However, these methods involve difficult sample preparation and long chromatographic run time with an organic phase and different buffer proportions. In addition, it is even more difficult and time-consuming to determine the stress-degraded behaviour of LCT. Hence, the main aim of this work is to study LCT's stability behaviour using simple UV-spectrophotometric method.

2. Materials and Methods

2.1. Chemicals and reagents

API of LCT pure drug was obtained from Emcure Pharmaceuticals Ltd., Pune, India, as a gift sample with 99.38% (w/w) assay value. Levocetirizine dihydrochloride brands used were Okacet-L 5 mg tablets of Cipla Ltd., LECOPE 5 mg tablets of Mankind Pharma Ltd., Levocet 5 mg tablets of Hetero Healthcare Limited, 1-AL 5 mg tablets of FDC Limited. All chemicals and reagents used were of analytical grade.

2.2. Instrumentation

The instruments uses was Double-beam UV/Visible spectrophotometer (Shimadzu 1800) consisting quartz cell with 1 cm path length loaded with UV-Probe software (Ver. 2.50), Analytical balance (Radwag AS 220/X), UV Cabinet (Lablink Instruments), Ultra-sonicator (Labman), Hot Air Oven (Aadarsh Technologies), Water Bath (Labline).

2.3. UV-Spectrophotometric method of LCT dihydrochloride.

As with previous research,[4] the UV spectrophotometric method of levocetirizine dihydrochloride developed and validated. This method was used to study the LCT dihydrochloride stress degraded behaviour.

2.4. Preparing asolution

2.4.1. Phosphate buffer pH 7.0

Mix. of 0.50 gm of di-sodium hydrogen phosphate anhydrous and 0.301 gm of Potassium dihydrogen orthophosphate in 1000 ml water.

2.4.2. Diluent

The pH 7.0 phosphate buffer is used as the diluent.

2.4.3. Preparing a standard stock solution

Weight exactly 10 mg of LCT dihydrochloride in a 100 ml volumetric flask. Place in 70 ml of diluent, dissolve and dilute to volume with diluent to obtain a stock solution of 100 μg / ml.

2.4.4. Preparing a calibration curve

Aliquots of 0.5-2.5 ml of the stock solution portion were transferred to a series of 10 ml volumetric flasks and the volume was added to the diluent mark. In the range of 200-400 nm, the solution was scanned against blank. The average absorption value was found to be 230.60 nm versus blank. The calibration curve is plotted in the Figures 2 and 3.

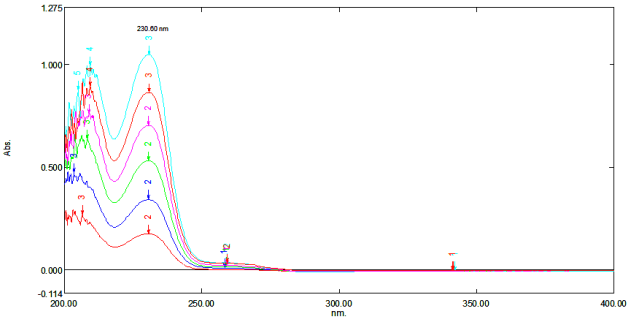

Fig. 2: Linearity UV scan of Levocetirizine dihydrochloride

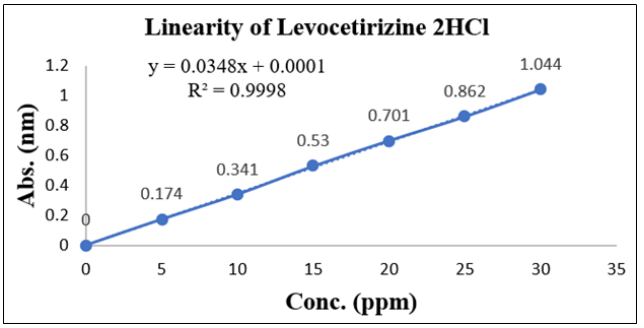

Fig. 3: Linearity graph of Levocetirizine dihydrochloride

2.5. Preparation of working solution

2.5.1. Preparing 0.1 M HCl Solution

Add Conc 2.1 ml. Hydrochloric acid in 250 ml volumetric flask, adjust the volume with distilled water to make 0.1 M HCl solution.

2.5.2. Preparing 0.1 M NaOH Solution

Weight and transfer 1.0 gm of NaOH in 250 ml of Volumetric flask, adjust the volume with distilled water to make 0.1 M NaOH solution.

2.5.3. Preparing 0.3% H_2O_2 Solution

Pipette out 2.5 ml of 30% H_2O_2 solution and added into 250 ml of volumetric flask, adjust the volume up to the mark with distilled water to make 0.3% H_2O_2 solution.

2.5.4. Preparing a Levocetirizine Dihydrochloride solution

The tablets of each of the brands have been weighed individually. Each brand of tablets was crushed in a mortar pestle. Powdered was administered equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) were carefully weighed in each 100 ml volumetric flask, all of which were transferred individually. Add 70 ml of diluent, sonicate to dissolved and dilute to volume with diluent to make up the volume up to 100 ml respectively for each sample. Filter the solution with the Whatman filter paper no. 41; pipette out 5 ml and transfer in 50 ml volumetric flask. By using spectrophotometer with a wavelength of 230.60 nm, all samples were determined.

2.6. Forced degradation studies

2.6.1. Acid degradation

The tablets of each of the brands have been weighed individually. Powdered was administered equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) was carefully weighed in each 100 ml volumetric flask, all of which were transferred individually. Add 10 ml of diluent and 10 ml of 0.1 M HCl solution. Place aside at room temperature for 3 hours, then add 10 ml of 0.1 M NaOH solution. Make a volume of 100 ml with a diluent. Filter this solution through the no. 41 Whatman filter paper and then pipette 5 ml in 50 ml volumetric flask. By using a spectrophotometer at 230.60 nm wavelength, all brand absorbance was determined.

2.6.2. Alkali degradation

The tablets of each of the brands have been weighed individually. Powdered was administered equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) were carefully weighed in each 100 ml volumetric flask, all of which were transferred individually. Add 10 ml of diluent and 10 ml of 0.1 M NaOH solution. Place aside at room temperature for 3 hours, then add 10 ml of 0.1 M HCl solution. Make a volume of 100 ml with a diluent. Filter this solution through the 41 Whatman filter paper and then pipette 5 ml in 50 ml volumetric flask. By using a spectrophotometer with a wavelength of 230.60 nm, all brand absorbance was determined.

2.6.3. Oxidation degradation

The tablets of each of the brands have been weighed individually. Powdered was administered equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) were carefully weighed in each 100 ml volumetric flask, all of which were transferred individually. Add 10 ml of diluent and 10 ml of 0.3 % H_2O_2 solution. Place aside at room temperature for 3 hours. Make a volume of 100 ml with a diluent. Filter this solution through the no. 41 Whatman filter paper and then pipette 5 ml in 50 ml volumetric flask. By using a spectrophotometer with a wavelength of 230.60 nm, all brand absorbance was determined.

2.6.4. Photolytic degradation at 254 nm (UV-light)

The tablets of each of the brands have been weighed individually. Powdered was administered equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) were carefully weighed and transferred to the petri dishes in the U.V light chamber at 254 nm for 3 hours. The tablets of each of the brands were weighed individually. Powdered was given equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) were carefully weighed and transferred to the petri dish in the U.V light chamber at 254 nm for 3 hours.

2.6.5. Thermal degradation

The tablets of each of the brands have been weighed individually. Powdered was administered equal to 15 mg of Levocetirizine. Okacet-L (372 mg), LECOPE (480.36 mg), Levocet (387.86 mg), 1-AL (306.90 mg) were carefully weighed in each 100 ml volumetric flask, all of which were transferred individually. Add 10 ml of the diluent and 10 ml of the water. Place in a water bath for 3 hours at a temperature of 80°C, then cooled the flask and add the volume with diluent up to the mark. Filtered through the 41 Whatman filter paper, then pipette 5 ml in 50 ml volumetric flask. By using a spectrophotometer with a wavelength of 230.60 nm, all brand absorbances have been determined.

3. Results and Discussion

The aim of degradation studies is to obtain shelf-life, investigate improvements to the drug product and suggest

Table 1: Manufacturing and Expiry date of various brands of Levocetirizine Dihydrochloride 5 mg

S. No	Brand Name	Mfg. Date	Exp. Date
1	Okacet-L	March, 2019	February, 2021
2	LECOPE	November, 2019	October, 2021
3	Levocet	April, 2019	March, 2021
4	1-AL	August,2019	July, 2021

Table 2: Absorbance of each brands in different parameters

S. No.	Brand Name	Avg. Mean Abs. inUntreated cond.	Avg. Mean Abs. in Acidic cond.	Avg. Mean Abs. in Basic cond.	Avg. Mean Abs. in Oxidation cond.	Avg. Mean Abs. in Photolytic cond.	Avg. Mean Abs. in Thermal Cond.
1	Okacet-L	0.544	0.474	0.507	0.481	0.403	0.502
2	LECOPE	0.487	0.463	0.476	0.473	0.434	0.461
3	Levocet	0.492	0.469	0.480	0.465	0.441	0.477
4	1-AL	0.491	0.447	0.467	0.453	0.421	0.461

Table 3: Acidic degradation of different brands (0.1 M HCl)

S. No.	Brand Name	% Assay	% Degradation
1	Okacet-L	87.10	12.90
2	LECOPE	95.07	04.93
3	Levocet	95.32	04.68
4	1-AL	91.03	08.97

Table 4: Alkali degradation of different brands (0.1 M NaOH)

S. No.	Brand Name	% Assay	% Degradation
1	Okacet-L	93.10	06.90
2	LECOPE	97.74	02.26
3	Levocet	97.56	02.44
4	1-AL	95.11	04.89

Table 5: Oxidation degradation of different brands (0.3% H_2O_2)

S. No.	Brand Name	% Assay	% Degradation
1	Okacet-L	88.40	11.60
2	LECOPE	97.12	02.88
3	Levocet	94.51	05.49
4	1-AL	92.26	04.74

Table 6: Photolytic degradation of different brands (254 nm UV-light)

S. No.	Brand Name	% Assay	% Degradation
1	Okacet-L	74.00	24.00
2	LECOPE	89.11	10.89
3	Levocet	89.63	10.37
4	1-AL	85.74	14.26

Table 7: Thermal degradation of different brands (Heat liquid at 80°C)

S. No.	Brand Name	% Assay	% Degradation
1	Okacet-L	92.20	07.80
2	LECOPE	94.66	05.34
3	Levocet	96.95	03.05
4	1-AL	93.89	06.11

its storage conditions, which will apply to all future lots of the drug product tested manufactured and packaged under similar circumstances.[13,14]

No literature was found to use U.V spectrophotometer to test compared degradation of the various Levocetirizine dihydrochloride tablet brands. We have therefore tried this research to compare the degree of degradation of Levocetirizine dihydrochloride in four separate brands using Okacet-L 5 mg tablets of Cipla Ltd., LECOPE 5 mg tablets of Mankind Pharma Ltd., Levocet 5 mg tablets of Hetero Healthcare Limited, 1-AL 5 mg tablets of FDC Limited. And active form of Levocetirizine dihydrochloride. Table 2 shows the absorbance variation after different degradation parameters have an effect. In the acidic condition, the % degradation of tablet Okacet-L (12.90) is very high than the tablet Levocet (04.93) Table 3. In basic condition, the % degradation of tablet Okacet-L (06.90) is more than the tablet LECOPE (02.26) Table 4. In oxidation condition, the % degradation of tablet Okacet-L (11.60) is more than the tablet LECOPE (02.88) Table 5. In photolytic condition, the % degradation of tablet Okacet-L (24.00) is very high than the tablet Levocet (10.37) Table 6. In thermal degradation condition, the % degradation of tablet Okacet-L (07.80) is more than the tablet Levocet (03.05) Table 7.

4. Conclusion

Studies of degradation of different tablet brands containing 5 mg of Levocetirizine dihydrochloride were used to test as per ICH guidelines. In almost all types of stress conditions, levocetirizine dihydrochloride was found to be degraded and in alkaline condition was found to be less degraded. The method was used is accurate, precise, reproducible and economical. It was concluded that the Levocet and LECOPE brands degraded less than the Okacet-L and 1-AL brands in all stress conditions.

5. Acknowledgement

The authors are very grateful, H. R. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule, for the supports of valuable tools and equipment during laboratory work.

6. Source of Funding

None.

7. Conflict of Interest

Authors declare no conflict of interest.

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Cite this article: Patil GB, Sonawane JK, Khan ZG, Patil DA. Forced degradation study of different brands of levocetirizine dihydrochloride by UV-spectroscopy. *Int J Pharm Chem Anal* 2020;7(2):69-73.