Asian Journal of Chemistry; Vol. 25, No. 3 (2013), 1730-1732

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2013.14535

Ultra Performance Liquid Chromatographic Method for the Determination of Cetirizine Dihydrochloride in Commercial Pharmaceutical Liquid Formulation

SAADET DERMIS

Department of Analytical Chemistry, Faculty of Pharmacy, Ankara University, 06100 Tandogan, Ankara, Turkey

Corresponding author: Fax: +90 312 2131081; Tel: +90 312 2033177; E-mail: dermis@pharmacy.ankara.edu.tr; Saadet.Dermis@pharmacy.ankara.edu.tr

(*Received*: 6 September 2012; *Accepted*: 28 September 2012) AJC-12200

A new ultra performance liquid chromatographic method was developed for the determination of cetirizine hydrochloride in pharmaceutical liquid formulation. The chromatographic separation was achieved on aquity ultra performance liquid chromatographic BEH C_{18} (100 × 2.1 mm, 1.7 µm) column and a mobile phase consisting of a water:acetonitrile (50:50, v/v). The flow rate was 0.3 mL min^{-1} and the detection wavelength was 235 nm. The ultra performance liquid chromatographic method shows excellent linearity over a range of 4 µg mL^{-1} to 28 µg mL^{-1}. The correlation coefficient for the cetirizine hydrochloride the linear regression equation was more than 0.999. The limit of detection and the limit of quantification for cetirizine hydrochloride were found as 0.39 and 1.30 µg mL^{-1}, respectively. This chromatographic method was validated by using validation parameters. The proposed chromatographic method can be applied to the quality control and routine analysis of cetirizine hydrochloride in pharmaceutical liquid formulation.

Key Words: Chromatographic determination, Cetirizine dihydrochloride, Pharmaceutical liquid formulation.

INTRODUCTION

Ultra performance liquid chromatographic provides the speed by using novel low micron particles that decreases chromatographic run times and also double peak capacity, resolution, reduction of the mobile phase consumption and the reduction of the flow rate, *etc*. In addition, sensitivity and speed can be achieved for chromatographic separations by minimizing the band spreading contributions of both the instrument and the column. Ultra performance liquid chromatographic system will eliminate significant time and cost per sample from analytical process while improving the quality of results and the system allows chromatographers to work at higher efficiencies with a much wider range of linear velocities, flow rates and back pressures. Ultra performance liquid chromatographic photo diode array detector detects and quantifies lower concentrations of sample analyte, trace impurities with maximum sensitivity and compares spectra across wavelengths and broad concentration ranges. It is easy to identify components that are difficult to detect by conventional HPLC-based methods.

Cetirizine hydrochloride is chemically, (2-{4-[(4-chlorophenyl)(phenyl)methyl]piperazin-1-yl}ethoxy) acetic acid (di)-hydrochloride[1] is an orally active and selective H_1-receptor antagonist, which is a potent and well-tolerated non-sedating antihistamine drug for treatment of seasonal and perennial allergic rhinits and chronic urticaria. Cetirizine hydrochloride liquid preparations are particularly susceptible to microbial growth because of the nature of their ingredients. These preparations are protected by the addition of preservatives that prevent the alteration and degradation of the product formulation[2]. The finished product release specifications should include an identification test and a content determination test with acceptance criteria and limits for each antimicrobial preservative present in the formulation. The finished product self-life specification should also include an identification test and limits for the quantity of antimicrobial preservatives[3]. Hence their antimicrobial and antifungal properties make them an integral part of the product formulation. This encourages the author for the development of new analysis technique or new stability indicating methods for the analysis of cetirizine hydrochloride to provide driving force in today's pharmaceutical industry.

In previous studies, several spectrophotometric[4-6] methods, HPLC methods[7-10], HPLC combined with tandem mass spectroscopy[11], capillary electrophoretic[12,13], electrochemical[14] methods have been also presented for analysis of cetirizine hydrochloride in pharmaceutical formulations and biological fluids.

In this study, a new ultra performance liquid chromatographic method was developed and validated for the determination of cetirizine hydrochloride in liquid pharmaceutical formulation. After analytical validation procedure, the developed

chromatographic method was applied to the quantitative analysis of cetirizine hydrochloride in a commercial pharmaceutical preparation.

EXPERIMENTAL

The chromatographic analysis were performed by using Waters Corporation Milford, USA) equipped with photo diode array, ternary solvent manager and auto sampler system. The autput signals were monitored and processed using empower 2 software.

Cetirizine hydrochloride was obtained from Hoechst Marion Roussel without prior purification. Cetryn® pharmaceutical liquid formulations (syrups) containing a (5 mg CTZ/5 mL) dose were obtained from local drugstores. HPLC grade acetonitrile and Merck grade methanol were purchased from Merck & Co. All chemicals were of analytical reagent grade and were used as received.

Standard solution preparation: Standard solution of cetirizine hydrochloride (20 mg/100 mL) was prepared in the solvent system consisting of water and methanol (40:60, v/v). Standard series of cetirizine hydrochloride in the concentration range of was 4-28 μg mL^{-1} prepared. An independent validation samples were prepared by using the stock solution.

Analysis procedure: 0.5 mL of liquid formulation was taken into the 25 mL volumetric flask. This solution was sonicated in an ultrasonicated in ultrasonic bath for 5 min. It was then filtered through 0.22 μm PVDF syringe filter. The filtrate was diluted into the working concentration range. This sample preparation procedure was repeated seven time. All the sample preparation steps were carried out by using a solvent system containing water and methanol (40:60, v/v).

RESULTS AND DISCUSSION

Method development and optimization: The main aim of this study is to develope a new ultra performance liquid chromatographic method for the determination of cetirizine hydrochloride in a liquid pharmaceutical preparation. The separation of cetirizine hydrochloride in liquid pharmaceutical preparation was carried out by using a mobile phase consisting of water and acetonitrile (50:50, v/v) on Waters ultra performance liquid chromatographic column (Acquity™ ultra performance liquid chromatographic BEH C_{18} 100 × 2.1 mm, 1.7 μm) with the isocratic flow program. In this work the flow rate of 0.3 mL/min was selected with regards to the back pressure and analysis time as well. During this study column oven tempe-rature was capped at 30 ºC.

Detection wavelength was selected as 235 nm for the recording the cetirizine hydrochloride chromatograms (Fig. 1). In this investigation, optimized ultra performance liquid chromatographic conditions by using 2 μL sample injection volume were; flow rate 0.3 mL/min; column oven temperature 30 ºC; a mobile phase containing water and acetonitrile (50:50, v/v). In this chromatographic analysis, the retention time for cetirizine hydrochloride was found as about 0.6 min (Fig. 2). Calibration graph was calculated by using the chromatographic areas and analyte concentration. Calculation results of linear regression analysis was presented in Table-1.

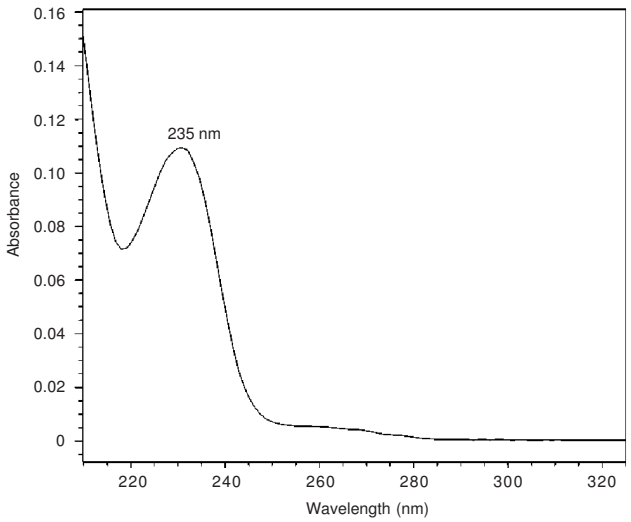

Fig. 1. UV spectra of cetirizine hydrochloride for the selection of the detection wavelength

TABLE-1
STATISTICAL RESULTS FOR THE CETIRIZINE HYDROCHLORIDE CALIBRATION

Calibration parameter							
m	n	r	SE (m)	SE (n)	SE (r)	LOD	LOQ
12458.26786	47598.7	0.9991	240.00	4293.17	5079.74	0.39	1.30

m = slope; n = intercept; r = correlation coefficient; SE (m) = Standard error of slope; SE (n) = Standard error of intercept; SE (r) = Standard error of correlation coefficient; LOD = Limit of dedection; LOQ = Limit of quantitation

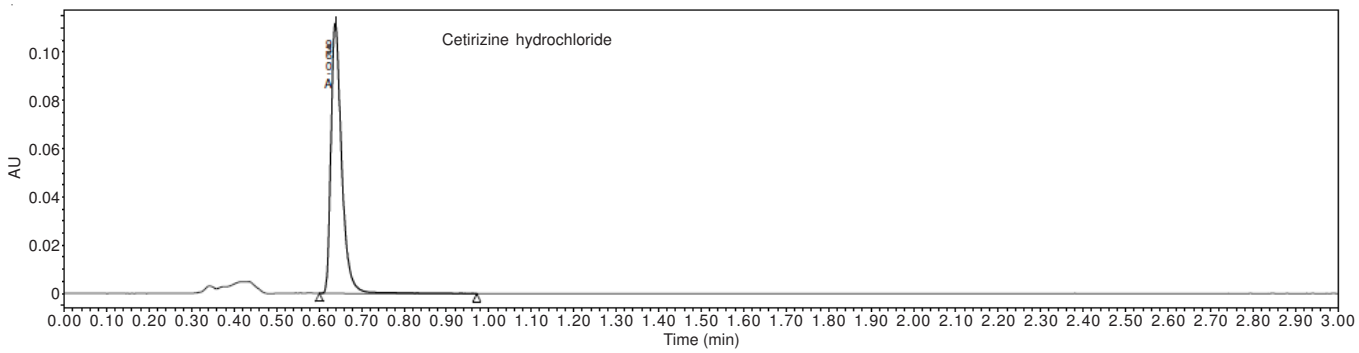

Fig. 2. Chromatogram of 30 μg mL^{-1} cetirizine hydrochloride

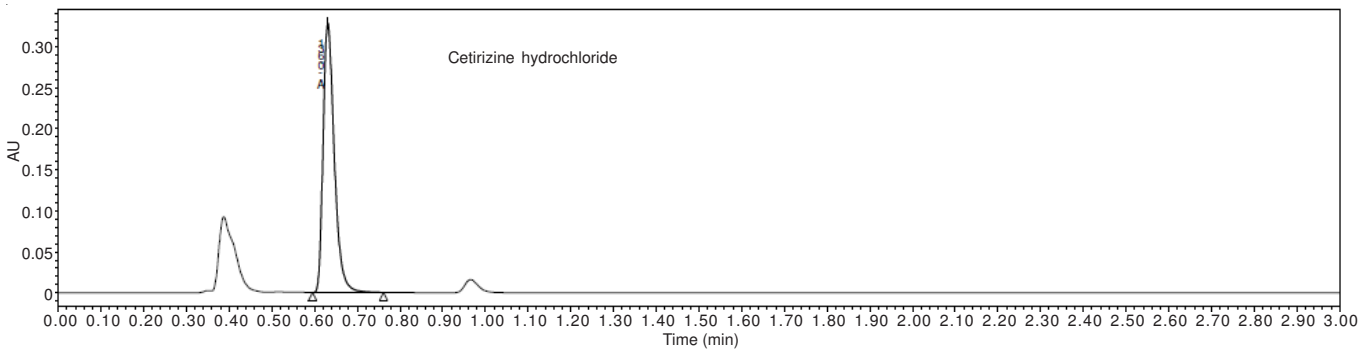

Fig. 3. Chromatogram of cetirizine hydrochloride in commercial pharmaceutical liquid formulation

Method validation: The proposed ultra performance liquid chromatographic method was validated by analyzing standard addition sample in the working concentration range of 4-28 μg mL^{-1}. Method validation was performed in accordance with established international conference on harmonization guidelines. For this procedure, recovery, standard deviation and relative standard deviation results were presented in Table- 2. As it can be seen from this table, the results obtained show the applicability of the ultra performance liquid chromatographic method to the analysis of cetirizine hydrochloride in samples. All validation procedures were carried out by using the regulation in accordance with ICH[15].

TABLE-2
RECOVERY RESULTS FOR STANDARD SAMPLES USING THE PROPOSED UPLC METHOD

Sample no.	Added (μg/mL)	Found (μg/mL)	Recovery (%)
1	4	4.14	103.6
2	8	8.06	100.8
3	12	11.61	96.8
4	16	15.54	97.1
5	20	19.82	99.1
6	24	24.04	100.2
7	28	28.44	101.6
		Mean	99.87
		SD	2.43
		RSD	2.44

SD= Standard deviation, RSD = Relative standard deviation

Sample analysis: The developed ultra performance liquid chromatographic technique was successfully applied to the commercial samples liquid formulation. Sample analysis treatments were repeated seven time. As seen from Fig. 3, a good chromatographic separation was performed to eliminate the effects of the excipients on the analysis of cetirizine hydrochloride in commercial liquid preparation. Determination results for the liquid formulation were illustrated in Table-3. As a result a good agreement was found for the application of the ultra performance liquid chromatographic to the analysis of commercial samples.

Conclusion

A new ultra performance liquid chromatographic method was successfully developed for the quantitative analysis of cetirizine hydrochloride in liquid pharmaceutical formulation. The developed method is selective, precise, accurate, linear, filter compatible and robust. Forced degradation data proved that the method is specific for the analytes and free from the interference of placebo/known impurities/degradation products and unknown degradation products. The run time (about 0.6 min) enables for rapid determination of drug. Also it can be utilized for determination of assay, blend uniformity and content uniformity of pharmaceutical products (CTZ syrup), where sample load is higher and high throughput is essential for faster delivery of results.

TABLE-3
DETERMINATION RESULTS OF CTZ IN PHARMACEUTICAL LIQUID PREPARATION BY THE PROPOSED UPLC METHOD

Sample no.	mg/ 5 mL
1	5.09
2	5.16
3	5.20
4	5.10
5	4.91
6	4.89
7	5.03
Mean	5.05
SD	0.12
RSD	2.34

SD = Standard deviation; RSD = Relative standard deviation

REFERENCES

1. S.C. Sweetman, Martindale, The Complete Drug Reference, The Phamaceutical Press, London, edn. 33, p. 411 (2002)
2. Reminghton: The Science and Practice of Pharmacy. Lippincott Williams and Wilkins, Philadelphia, edn. 21 (2006).
3. European Medicines Agency. Guideline on Excipients in the Dossier for Application for Marketing Authorization of a Medicinal Product, Doc. Ref. EMEA/CHMP/QWP/396951/2006. London, 6 November.
4. M.S. Prakash, M. Sundarapandian, S. Meena and M.S. Nagarjan, *Indian Drug*, **37**, 211 (2000).
5. K.C. Ramesh, M.B. Melwanki, B.G. Gowda, J. Seetharamappa and J. Keshavayya, *Indian J. Pharm. Sci.*, **64**, 455 (2002).
6. A.F.M. El Walily, M.A. Korany, A. El Gindy and M.F. Bedair, *J. Pharm. Biomed. Anal.*, **17**, 435 (1998).
7. M.F. Zaater, Y.R. Tahboub and N.M. Najib, *J. Pharm. Biomed. Anal.*, **22**, 739 (2000).
8. A.M.Y. Jaber, H.A. Al-Sherife, M.M. Al-Omari and A.A. Badwan, *J. Pharm. Biomed. Anal.*, **36**, 341 (2004).
9. O.C. Sun, H.L. Seok, S.K. Hak, J.K. Eun and P.C. Hae-Young, *J. Chromatogr. B.*, **744**, 201 (2000).
10. M.T. Rosseel and R.A. Lefebvre, *J. Chromatogr.*, **565**, 504 (1991).
11. S. Rudaz, S. Souverain, C. Schelling, M. Deleers, A. Klomp, A. Norris, T.L. Vu, B. Ariano and J.L. Veuthey, *Anal. Chim. Acta*, **492**, 271 (2003).
12. E.A. Van and Y. Michotte, *Electrophoresis*, **27**, 2376 (2006).
13. M. Peter, V. Iva and H. Emil, *J. Sep. Sci.*, **28**, 1278 (2005).
14. S.D. Güngör, *Die Pharmazie*, **59**, 929 (2004).
15. International Conference on Harmonization. Validation of Analytical Procedure, Text and Methodology Q2(R1). IFPMA, Geneve, Switzerland (2005).