Optimization of Quantitative Analysis of Cetirizine in Bulk Drug, Dosage Formulations and Human Serum Using Spectrophotometry

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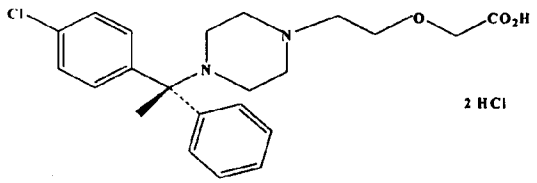
Summary: A simple spectral calibration method for the quantitative determination of cetirizine in standard and in dosage formulations has been developed for the estimation of cetirizine. The linear regression equation was used. To validate this method, analytical parameters such as selectivity, accuracy and precision have been established for different brands of tablets and have been evaluated statistically to assess its application. This method is rapid, easy, inexpensive and a powerful tool with very simple mathematical contents for systems. The method has been found to have advantage for simplicity, stability, sensitivity, reproducibility and accuracy for being used as an alternate to the existing spectrophotometric methods for the routine analysis of the drug, its pharmaceutical formulations and for clinical studies. Equivalence studies were performed for different brands of cetirizine available in Pakistan.

Introduction

Cetirizine dihydrochloride (RS)-2-[2-[4-[(4-chlorophenyl) phenyl methyl)] piperazin-1-yl]ethoxy]acetic acid dihydrochloride [1], is a second-generation H_1 receptor antagonist and an acid metabolite of hydroxyzine. It is rapidly absorbed from gastrointestinal tract after oral administration, peak plasma concentration being attained within 1 hour. Food delays the time to peak plasma concentration but does not decrease the amount of drug absorbed. It is highly bound to plasma protein and has an elimination half-life of about 10 hours. Cetirizine is excreted primarily in the urine mainly as unchanged drug and does not appear to cross the blood brain barrier to a significant extent [2,3].



Cetirizine dihydrochloride

Many procedures are described for quantitative determination of cetirizine in bulk, pharmaceutical formulations, urine and in serum. Among these methods are spectrofluorimetry [4], NMR [5], HPTLC [6,7], HPLC [8-18], potentiometry [19], colorimetry [9] and capillary electrophoresis [20]. These methods are time consuming, expensive and involve excessive use of organic solvents or are less sensitive. Furthermore analysis of cetirizine has also been studied by UV spectroscopy [4, 9, 10] but all these methods involve either a charge transfer complex or the use of internal standard. So a need was felt to devise such a method, which could be direct, less time consuming, sensitive, precise and accurate. Henceforth, in present work a method was developed and validated for the analysis of cetirizine in bulk, dosage formulations and in serum for therapeutic purposes using analytical instrument. We used this method for equivalence studies of different brands of cetirizine (available in Pakistan). The method is easy, economical and is equally applicable to the bulk drug, dosage formulations and for *in-vivo* study.

Results and Discussion

Since number of the quantitative analysis of active and dosage formulations in various departments of analytical sciences are carried out spectrophotometrically, the proposed method was applied to study the equivalency of different brands and to note the pH effect. The method was applied to the analysis of drug spiked in serum as well.

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Wavelength Selection

Most of the previous work on the spectrophotometric analysis has been carried out at 230nm, in our studies the characteristic peak of cetirizine in the UV/ visible region in buffers appeared at 231nm [19] so this wavelength was chosen for our analytical studies (Fig. 1). This method involved simultaneous use of linear regression function obtained by plotting the concentration versus absorbance in the working concentration range.

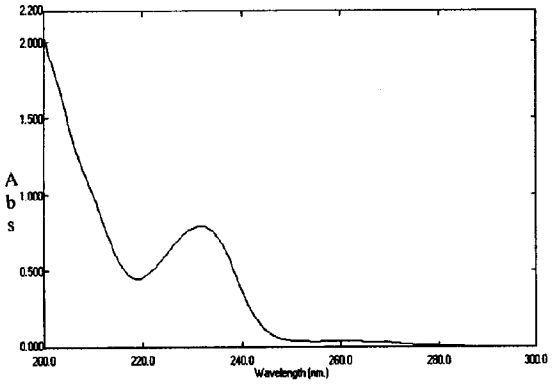

Fig. 1: UV spectra of reference cetirizine.

Method Validation

Linearity

Suitability of the method was checked by analyzing the linearity at the set concentration range in Table-1. These data sets were applied to linear regression function and results obtained are given in Table-4. The results clearly indicate that the method is suitable for all formulations. The goodness-of-fit (R^2) was found to be 0.999 at pH 1.2 and 0.999 at pH 7.4.

Accuracy and Precision

In order to determine accuracy of the method, known quantities of cetirizine was spiked in the drug product following USP 2004 standards and was analyzed in three replicates. It was observed that the method was accurate with in the given range. The method passed the test for repeatability as determined by running six replicates of the 100 % test solution according to ICH guidelines The analytical results

Table-1: % Recovery of cetirizine in buffers of pH 1.2 and 7.4.

	← Gixer →		← Zyrtec →	
Conc. *µg/ ml*	pH 1.2 231 nm	pH 7.4 231 nm	pH 1.2 231 nm	pH 7.4 231 nm
9.23	104.68	90.86	104.68	99.80
13.85	100.55	95.75	98.07	98.38
18.57	108.16	93.28	103.85	91.43
23.09	107.34	95.48	99.47	99.07
27.71	96.57	98.08	97.78	99.84
32.33	100.03	102.65	102.11	97.39
36.95	101.15	103.13	100.58	100.74
41.57	101.09	101.42	96.63	103.91
46.18	103.98	99.49	99.43	101.06

Conc. = Concentration.

Table-2: % Recovery of cetirizine in serum of pH 7.4.

Conc. (*µg/ ml*)	*% Recovery*
32.33	103.95
36.95	102.2
41.57	100.04

Conc. = Concentration.

obtained from these investigations for both methods are summarized in Table-5.

Detection and Quantification Limit

The detection limit or (LOD) and limit of quantification (LOQ) for cetirizine was checked at two pH levels *i.e.* pH 1.2 and pH 7.4. LOD for cetirizine at pH 1.2 was found to be 0.04 *µg/ ml* and 0.03 *µg/ ml* at pH 7.4. LOQ values were found to be 0.14 *µg/ ml* at pH 1.2 and 0.11 *µg/ ml* at pH 7.4 for raw material. The LOD and LOQ values in serum were found to 0.04 *µg/ ml* and 0.15 *µg/ ml* respectively.

Tablet Analysis

Equivalence study was performed using different brands of cetirizine tablets available in Pakistan. The availability of cetirizine from commercially available dosage forms was calculated (Table-2) results were found to be in agreement with the labeled claims. Moreover, no pronounced effect was observed in case of pH 1.2 and 7.4 and the results were found to be pH independent *i.e.*, same at pH 1.2 and pH 7.4.

Quantification in Serum

Three concentration levels in pH 7.4 (simulating blood pH) were selected for

quantification of cetirizine in serum. The recovery values so obtained are given in Table-3 indicating suitability of method.

Table-3: % Recovery of cetirizine in different formulations of pH 7.4.

Conc.	← % Recovery →				
μg/ ml	Avec tablet	Cerizine tablet	Zanlan tablet	Ronex tablet	Zanlan tablet
9.2	100.5	100.3	98.48	96.28	98.48
13.9	100.8	98.38	95.75	97.25	95.75
18.5	97.9	97.27	92.12	84.26	92.12
23.1	105.8	103.88	102.78	90.73	102.78
27.7	107.7	99.84	98.47	99.84	98.47

Conc. = Concentration.

Apparatus

Shimadzu 1601 double beam UV–visible spectrophotometer possessing a fixed slit width (2 nm) with quartz cells of 10-mm path length. The spectrophotometer was connected to a P IV computer loaded with Shimadzu UVPC version 3.9 software and a HP DeskJet 1200 printer was used to record the absorption spectra.

Preparation of Solutions

Stock solution of cetirizine reference standard (100 *μg/ ml*) was prepared by dissolving 10 mg of cetirizine in 100 ml of buffers of pH 1.2 (KCl/ HCl) and 7.4 (phosphate). Nine different serial dilutions were made in the two buffer mediums having 9.23–46.1 *μg/ ml* concentration range. These dilutions were scanned in the UV/ visible region and were found to give a distinct peak at 231 nm. The absorbances for all these solutions were measured at 231 nm and were run in triplets to improve result statistically. Moreover, in order to find out if there is any hypsochromic or bathochromic shift, we studied the effect on different pH.

Table-4: Linear regression functions and their statistical parameters.

Active	*λ*	Regression equation	*r*	S. E.	S. E. E	LOD (*μg/ ml*)	LOQ (*μg/ ml*)
pH 1.2	231	A = 0.02Cx - 0.003	0.998	0.42	0.62	0.04	0.14
pH 7.4	231	A = 0.02Cx + 0.003	0.999	0.42	0.32	0.03	0.11

Table-5: Accuracy and precision of the proposed method.

Actual Concentration (*μg/ ml*)	Found Concentration (*μg/ ml*)	% recovery	%R.S.D
18.47	18.96582	102.684476	
	18.96013	102.653636	0.01
	18.96076	102.657063	
23.09	23.06646	99.8980325	
	23.05949	99.8678808	
	23.06266	99.8815861	0.02
	23.0724	99.9237765	
	23.0587	99.8646167	
	23.0755	99.9372023	
27.7	27.95	100.866113	
	27.94937	100.863829	0.03
	27.96456	100.918647	

Experimental

Materials

The cetirizine dihydrochloride reference standard was kindly provided by Ali Gohar Pharmaceuticals (Pakistan) Karachi. It was utilized after confirming its purity by melting point and IR spectra. Different commercially available tablets *i.e.* Avec (Platinum Pharmaceuticals), Cerizine (Pharm Evo Pharmaceuticals), Gixer (Barrett Hodgson), Rigix (Ali Gohar Pharmaceuticals Pakistan), Ronex (Hilton), Zanlan (Sandoz Novartis), Zyrtec (UCB) were purchased from market.

Assay of Formulations

In case of cetirizine formulations, different brands of tablets were dissolved in 100 ml volumetric flasks and volume was made up with respective buffers. The sample was filtered through Whattman filter paper; dilutions (9.23–27.71 μg/ ml) were made in 25 ml volumetric flask following the same procedure as for reference standard studies.

Assay in Serum

One volume of plasma was deproteinated by nine volume of acetronitrile and filtered through Whattman filter paper. 10 ml of this filtered solution was transferred to 100 ml volumetric flask and volume was made up by phosphate buffer pH 7.4. From this stock solution, dilutions of cetirizine (32.33-41.57 *μg/ ml*) were made. Three measure-

ments were carried out for each concentration; the satisfactory correlation coefficient and intercept values were obtained for each concentration.

Solutions for Accuracy of Assay

Accuracy of the method was checked by analyzing six replicate samples each of cetirizine at three different concentration levels 80 % (18.47), 100 % (23.06) and 120 % (27.70) and calculating relative standard deviation %RSD.

Conclusion

The result of the above study indicates the suitability of the method to estimate cetirizine in bulk drug as well as in dosage formulations and in serum. This method is more reliable than other UV spectrophotometric methods and it encourages one to apply this method for routine analysis.

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