Simultaneous UV Spectrophotometric Determination of Cetrizine and Dextromethorphan in Tablet Dosage Form

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Abstract: Two accurate, precise, sensitive and economical procedures for simultaneous estimation of cetrizine and dextromethorphan in tablet dosage forms have been developed. First method employs formation and solving of simultaneous equations using 230 nm and 280 nm as two analytical wavelengths for both drugs in methanol. The second method is *Q*-analysis based on measurement of absorptivity at 224 nm (as isobestic point) and 280 nm ($\lambda_{\max}$ of CTZ). Cetrizine and dextromethorphan at their respective $\lambda_{\max}$ 280 nm and 230 nm and at 224 nm (isobestic point) shows linearity in a concentration range of 10-30 mcg/mL for both the drugs. The recovery studies confirmed accuracy of the proposed methods and low values of standard deviation confirmed precision of the methods. The methods were validated as per ICH guidelines.

Keywords: Cetrizine, dextromethorphan, Simultaneous-equations method, *Q*-analysis.

Introduction

Cetrizine hydrochloride is a piperazine derivative and its chemical name is $(\pm)$ - [2-[4-[(4-chlorophenyl) phenyl methyl]-1-piperazinyl]ethoxy]acetic acid, dihydrochloride. It is a non-sedating antihistamine or histamine (*H*-1) receptor blockers. The mechanism of action of CT is block the ability of histamine to promote the allergic reactions in the body. Cetrizine is used in the treatment of perennial and seasonal allergic rhinitis and also for chronic urticaria. Few methods have been used for quantitative determination of cetrizine. These methods include fluorimetry², spectrophotometry^{1,3-8}, titrimetry and conductimetry⁹, gas chromatography¹⁰, high-performance liquid chromatography^{8,11-13}, liquid chromatography^{14,15} and ion-selective electrodes¹⁶, based on the formation of ion pair complex of cetrizine with tetraphenylborate.

Dextromethorphan hydrobromide (DEX), [(+)-3-2-6 Methoxy-17-methyl-9 α , 13 α , 14 α -morphinan hydrobromide monohydrate] is a cough suppressant used for the relief of non-productive cough. It has a central action on the cough centre in the medulla. DEX is rapidly adsorbed from the gastro intestinal tract. It is metabolized in the liver and excreted in the urine as unchanged DEX and demethylated metabolites including DEX, which has some cough suppressant activity¹⁷. Different methods have been reported for the determination of DEX in the bulk drug, in the dosage forms with other drugs in cough cold products and in biological samples which include HPLC¹⁸⁻²², the first and second-derivative technique uv spectrophotometry²³⁻²⁶, capillary electrophoresis²⁷⁻²⁹, GC³⁰⁻³², LC³³⁻³⁶ and TLC³⁷⁻³⁸ methods.

Experimental

Elico UV-Visible spectrophotometer (SL 164) was used for spectral measurements with 1 cm matched quartz cells.

Method 1

Employing simultaneous equations using crammer's rule

Pure drug samples of cetrizine and dextromethorphan were dissolved separately in methanol, so as to give several dilutions of standard in the concentration range of 10 to 30 mcg/mL for both drugs. All dilutions were scanned in the wavelength range of 200-400 nm.

Two wavelengths selected for the formation of simultaneous equations were 280 nm ($\lambda_{\max}$ of CTZ) and 230 nm ($\lambda_{\max}$ of DXM). Similarly, mixed standard solutions were also used and the drugs showed linearity in the range of 10-30 mcg/mL for (CTZ) and (DXM). The absorptivities for the two drugs were presented in the Table 1. Figure 1 represents the overlain spectra of both drugs. The method employs solving of simultaneous equations using crammer's rule and matrices. The simultaneous equations formed were

$$A_1 = 443.3 \times C_1 + 25.6 \times C_2 \quad (1)$$

$$A_2 = 350.4 \times C_1 + 113.2 \times C_2 \quad (2)$$

Figure 1. Zero order overlain spectra of CTZ (10 mcg/mL) and DXM (10 mcg/mL)

Where A_1 and A_2 are absorbances of sample solution at 230 nm and 280 nm respectively. C_1 and C_2 are the concentrations of DXM and CTZ respectively in sample solution. By substituting the value of C_1 from equation (1) into equation (2), the value of C_1 can be obtained. Similarly C_2 can also be obtained.

Procedure for analysis of tablet formulation

The average weight of twenty tablets were determined and then ground to a fine powder. A quantity equivalent to 50 mg of CTZ and 50 mg of DXM were transferred to a 100 mL volumetric flask. The contents were dissolved by using 50 mL of methanol, filtered and made up to volume with the same. The solutions were further diluted with methanol to give concentrations of 5 mcg/mL of CTZ and DXM. Absorbances of these solutions were measured at 280 nm and 230 nm as A_1 and A_2 respectively and concentrations of these two drugs in the sample were calculated using equation (1) and equation (2). Results of the analysis of the tablet formulations were reported in Table 2. The recovery studies were depicted in Table 3.

Method 2

Absorbance ratio or q-analysis method

From the overlain spectrum of CTZ and DXM, two wavelengths were selected, one at 224 nm, isobestic point for both the drugs and the other at 280 nm ($\lambda_{\max}$ of CTZ). The absorbances of the standard and sample solutions were prepared in the same manner as in the previous method. The absorptivities for both drugs at the selected wavelength were presented in Table 1. The method employs Q values; the concentrations of drugs in sample solution were determined by using the following formula. Results of the analysis of the tablet formulations were reported in Table 2. The recovery studies were depicted in Table 3.

For CTZ

$$C_1 = \frac{Q_0 - Q_2}{Q_1 - Q_2} \times \frac{A}{a_1} \quad \text{for DXM} \quad C_2 = \frac{Q_0 - Q_1}{Q_2 - Q_1} \times \frac{A}{a_2}$$

$$Q_0 = \frac{\text{Absorbance of sample at 224 nm}}{\text{Absorbance of sample at 280 nm}}$$

$$Q_1 = \frac{\text{Absorptivity of CTZ at 224 nm}}{\text{Absorptivity of CTZ at 280 nm}}$$

$$Q_2 = \frac{\text{Absorptivity of DXM at 224 nm}}{\text{Absorptivity of DXM at 280 nm}}$$

A = Absorbance of sample at isobestic point a_1 and a_2 -absorptivities of CTZ and DXM respectively at isobestic point.

Table 1. Absorptivity values for cetirizine and dextromethorphan

Concentration mcg/mL		Absorptivity at 230 nm		Absorptivity at 280 nm		Absorptivity at 224 nm	
CTZ	DXM	CTZ	DXM	CTZ	DXM	CTZ	DXM
10	10	350	444	113	26	36	360
15	15	350	443	113	26	37	360.7
20	20	350.5	444	114	26	37.5	360.5
25	25	350.8	442	113	26	37.2	360.4
30	30	351	443	113	25	38	360.7
mean	mean	350.5	443.2	113.2	25.8	37.1	360.5

Table 2. Results of commercial formulation analysis

Method	Label Claim, mg/TAB	%Label Claim estimated* (Mean±S.D)	% R.S.D
I	CTZ, 10 mg	100.03±0.550	0.850
	DXM, 10 mg	99.92±0.650	0.845
II	CTZ, 10 mg	99.69±0.850	0.967
	DXM, 10 mg	99.58±0.750	0.958

*Mean of six determinations, R.S.D. is relative standard deviation

Table 3. Recovery studies of CTZ and DXM

Drug	Conc. Of drug added		% Recovery * ((Mean±S.D)	
	µg/mL	% level	Method I	Method II
CTZ	5	50	99.55±0.561	99.00±0.380
	10	100	99.80±0.489	99.64±1.001
	15	150	99.61±0.450	99.98±0.897
DXM	5	50	100.09±0.651	100.38±0.644
	10	100	101.57±0.126	99.74±0.932
	15	150	100.62±0.345	100.54±0.659

*Average of three determinations

Results and Discussion

The proposed methods for simultaneous estimation of CTZ and DXM in combined dosage forms were found to be simple, accurate, economical and rapid. In both the methods, the values of coefficient of variation were satisfactorily low and recovery was close to 100% for both the drugs.

Conclusion

The proposed methods are simple, precise, accurate and rapid for the determination of CTZ and DXM in combined tablet dosage forms. These methods can be adopted as an alternative to the existing spectrophotometric methods. Analysis of authentic samples containing CTZ and DXM showed no interference from the common additives and excipients. Hence, recommended procedure is well suited for the assay and evaluation of drugs in pharmaceutical preparations. It can be easily and conveniently adopted for routine quality control analysis.

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