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Short communication

Extractive spectrophotometric determination of ceterizine HCl in pharmaceutical preparations

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Abstract

Two simple, rapid and sensitive extractive spectrophotometric methods have been developed for the assay of ceterizine hydrochloride (CTZH) in bulk drug and in pharmaceutical preparations. These methods are based on the formation of chloroform soluble complexes between CTZH with bromocresol purple (BCP) or bromophenol blue (BPB) in Walpole buffer of pH 2.64 with an absorption maximum at 409 nm and at 414 nm for BCP and BPB, respectively. Reaction conditions were optimised to obtain the maximum colour intensity. The absorbance was found to increase linearly with increase in concentration of CTZH, which was corroborated by the calculated correlation coefficient value (0.9991–0.9995). The system obeyed Beer's law in the range of 1–16 and 1.5–21 μl ml^{-1} for BCP and BPB, respectively. The various analytical parameters have been evaluated. The results obtained by the proposed methods were statistically compared by means of students t-test and by the variance ratio, F-test with those of the reported method and have shown to be in excellent agreement with the reported method.

Keywords: Ceterizine hydrochloride; Bromocresol purple; Bromophenol blue; Spectrophotometry

1. Introduction

Ceterizine, a piperazine derivative and carboxylated metabolite of hydroxyzine used in the treatment of perennial and seasonal allergetic rhinitis and also for chronic uticaria, has brought forth the need for a fast, low cost and selective method for the determination of ceterizine hydrochloride (CTZH), especially for routine quality control analysis of pharmaceutical products of CTZH. The CTZH is not official in any of the pharmacopoeia. Literature mentions a few methods such as spectrophotometric [1–4], gas-chromatographic [5] and high performance liquid chromatographic [6–8] for the assay of CTZH. Some of these methods [1,3] do not explain the effects of excipients in the assay of CTZH in formulations. Only one method [2] based on colour formation has been reported. As spectrophotometric assays offer

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significant economical advantages over gas chromatography and the high performance liquid chromatographic techniques, the aim of the present investigation was to develop a new, sensitive and selective spectrophotometric methods for the determination of CTZH in bulk drug and in its pharmaceutical preparations. The proposed extractive spectrophotometric methods address these requirements.

In the present investigation, we report the development of two accurate, reproducible and adequately sensitive extractive spectrophotometric methods based on the formation of chloroform soluble ion-association complexes between CTZH with bromocresol purple (BCP) or bromophenol blue (BPB) in Walpole buffer of pH 2.64. No interference was observed in the assay of CTZH from common excipients in levels found in pharmaceutical formulations. The proposed methods are validated by the statistical data.

2. Experimental

2.1. Reagents

All chemicals were of analytical or pharmaceutical grade and quartz processed high-purity water was used throughout. Pure CTZH was obtained from Dr Reddy's laboratory, India. A 0.05% solution of BCP and BPB was prepared separately in Walpole buffer of pH 2.64. Series of buffer solutions of KCl–HCl (pH = 1.0–2.2), NaOAc–HCl (pH = 1.99–4.92), NaOAc–AcOH (pH = 3.72–5.57) and potassium hydrogen phthalate–HCl (pH = 2.2–3.6) were prepared by following the standard methods.

Different dosage forms of CTZH were obtained from different firms.

2.2. Solutions

Pure CTZH (25 mg) was accurately weighed and transferred into a 100 ml calibrated flask, dissolved in distilled water and diluted to the mark with distilled water. The solution is stable at room temperature.

2.3. Apparatus

A Hitachi UV-visible spectrophotometer model U-2001 with 1 cm matched quartz cells was used for the absorbance measurements. The pH measurements were made with Schott Gerate pH meter CG 804.

2.4. Assay procedure

An aliquot of the solution containing 10–160 or 15–210 μg of CTZH were transferred into a series of 125 ml separating funnels. A 4 or 3 ml of Walpole buffer of pH 2.64 and 5 ml of BCP or BPB were added. Chloroform (10 ml) was added to each of the separating funnels, the contents were shaken well and left at room temperature for a minute. The two phases were allowed to separate and the chloroform layer was passed through anhydrous sodium sulphate. The absorbance of the yellow coloured species was measured at 409 and at 414 nm for BCP and BPB, respectively, against corresponding reagent blank. A calibration graph was plotted.

2.5. Application of the proposed methods

2.5.1. Assay procedure for tablet dosage

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 20 mg of antiallergic drug was weighed into a 100 ml volumetric flask, 70 ml of distilled water was added and shaken thoroughly for about 15–20 min. The contents were diluted to the mark with distilled water, mixed well and filtered through a (Whatman 40) filter paper to remove the insoluble matter. A 25 ml of the filtrate was diluted to 100 ml and a suitable aliquot was used for analysis using the procedure given above. The results are shown in Table 1.

2.5.2. Assay procedure for syrup and suspension

In respect of syrup and suspension, 20 ml equivalent to 20 mg of drug, were transferred into a 250 ml separator. The sample was rendered alkaline to litmus with 6 M ammonia solution and 1 ml in excess was added. The mixture was then extracted with 3×15 ml portions of chloroform.

Table 1
Analysis of pharmaceutical preparations containing CTZH by the proposed methods and their comparison with the reported method

Pharmaceutical preparation[a]	Label claim (mg per tablet or ml^{-1})	Recovery ± S.D., % and its comparison with the reported method [2][b]		
		Reported method	Proposed methods	
			BCP	BPB
Alerid syrup[a]	1	98.12 ± 0.75	98.78 ± 1.10 $F = 1.11$, $t = 0.97$	98.89 ± 0.95 $F = 0.89$; $t = 0.75$
Alerid tablets[a]	10	97.95 ± 0.52	98.94 ± 0.75 $F = 1.01$; $t = 0.91$	98.12 ± 0.44 $F = 1.11$; $t = 1.14$
Ceterzine tablets[b]	10	97.58 ± 1.32	97.45 ± 1.12 $F = 0.97$; $t = 0.96$	97.64 ± 1.11 $F = 1.23$; $t = 1.04$
Cetzine syrup[b]	10	99.13 ± 0.85	99.38 ± 0.78 $F = 1.04$; $t = 1.19$	99.21 ± 0.86 $F = 0.86$; $t = 1.04$
Cetiriz syrup[c]	1	97.64 ± 0.95	98.06 ± 0.93 $F = 1.06$; $t = 1.11$	98.01 ± 0.55 $F = 0.78$; $t = 1.16$
Cetiriz tablets[c]	10	99.06 ± 0.97	98.83 ± 1.11 $F = 1.12$; $t = 1.11$	99.16 ± 0.65 $F = 0.91$; $t = 1.11$
Cetrizet-D tablets[d]	10	98.42 ± 0.26	98.67 ± 1.04 $F = 1{,}14$; $t = 1.04$	98.34 ± 1.13 $F = 1.11$; $t = 1.08$
Zirtin tablets[e]	10	98.73 ± 1.26	98.86 ± 0.98 $F = 1.06$; $t = 1.06$	98.77 ± 1.04 $F = 1.01$; $t = 1.06$
Zyrtec tablets[f]	10	101.54 ± 0.68	99.74 ± 0.61 $F = 0.76$; $t = 1.12$	100.76 ± 1.07 $F = 1.05$; $t = 1.15$
Zyncet tablets[g]	20	102.24 ± 0.72	101.87 ± 1.08 $F = 0.95$; $t = 1.21$	101.03 ± 0.35 $F = 1.07$; $t = 1.18$
Zyncet suspension[g]	10	96.78 ± 0.64	97.97 ± 1.04 $F = 0.47$; $t = 1.05$	97.33 ± 0.59 $F = 1.11$; $t = 1.24$
Sizon forte[h]	10	98.98 ± 0.95	99.12 ± 0.55 $F = 1.10$; $t = 1.06$	99.35 ± 0.86 $F = 1.19$; $t = 0.64$
Alzine[i]	10	99.12 ± 1.11	99.43 ± 0.67 $F = 0.96$; $t = 0.85$	98.89 ± 1.04 $F = 0.91$; $t = 0.87$
Cetrine[j]	10	101.06 ± 1.02	99.78 ± 0.75 $F = 0.58$; $t = 0.86$	99.81 ± 1.11 $F = 0.75$; $t = 1.11$
Coszin[k]	10	99.12 ± 0.86	98.97 ± 0.52 $F = 0.55$; $t = 1.08$	99.07 ± 0.55 $F = 0.99$; $t = 0.75$

[a] Marketed by: a, Cipla; b, Glaxo Lab; c, Alchem; d, Sun Pharmaceuticals; e, Torrent Pharmaceuticals; f, UNI-UCB; g, Unichem, h; Systopic Laboratories Limited; i, Core Healthcare Ltd.; j, Dr Reddy's labs. Ltd.; k, CFL pharmaceuticals Ltd.
[b] Average of five determinations.

The chloroform extracts were evaporated to dryness and the residue was dissolved in 0.1 M HCl and made upto 100 ml with distilled water. The solution was diluted to get 100 μg ml^{-1} of drug and an aliquot was analysed as above. The results are represented in Table 1.

3. Results and discussion

3.1. Absorption spectra

CTZH reacts with BCP or BPB in an acidic buffer to give a chloroform soluble yellow

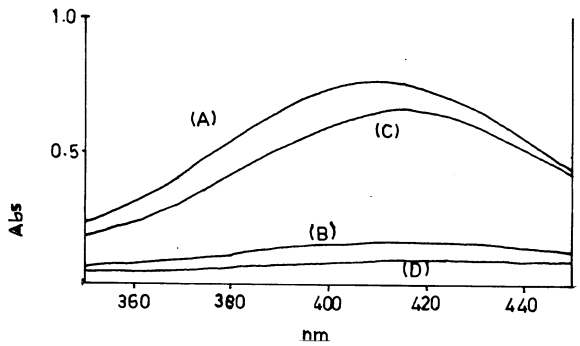

Fig. 1. Absorption of (A) BCP-CTZH (B) reagent blank (for BCP) (C) BPB-CTZH (D) reagent blank (for BPB).

coloured ion-association complex which exhibits an absorption maximum at 409 nm for BCP or at 414 nm for BPB. Under the experimental conditions, the reagent blank showed negligible absorbance as shown in Fig. 1.

3.2. Optimum reaction conditions

The optimum reaction conditions for quantitative determination of the ion-pair complex were established via a number of preliminary experiments. The optimum volume of the reagent was studied. It was observed that 5 ml of 0.05% of BCP or BPB was necessary for maximum colour development of the complex. The effect of pH was studied by extracting the coloured complex in the presence of various buffers such as KCl–HCl (pH = 1.0–2.2), NaOAc–HCl (pH = 1.99–4.92), NaOAc–AcOH (pH = 3.72–5.57) and potassium hydrogen phthalate–HCl (pH = 2.2–3.6). It was noticed that the maximum colour intensity and constant absorbance were observed in Walpole buffer (NaOAc–HCl) of pH 2.64 with a buffer volume of 4 and 3 ml for BCP and BPB, respectively. At pH values greater than 2.64, the decrease in absorbances of the complexes were observed while low absorbances were observed below pH 2.64. Hence a buffer of pH 2.64 was used in all subsequent work. Several organic solvents were tried for effective extraction of the coloured species from aqueous phase. Chloroform was found to be the most suitable extractant as it was observed that only one extraction was adequate to achieve a quantitative recovery of the complex. Shaking times of 0.5–2 min produced a constant absorbance and hence a shaking time of 1 min was used throughout. There was no appreciable change in the absorbance or colour of the product if the order of addition of the reactants is varied. The absorbances of the complexes were found to be stable for more than 18 h. The drug-reagent ratio was found to be 1:1 as evaluated from Job's method.

3.3. Quantification

A linear correlation was found between absorbance and concentration of CTZH in the range of 1–16 μg ml^{-1} for BCP and 1.5–21 μg ml^{-1} for BPB. The equations for one representative calibration curve for each method are $A_{409\ nm} = 0.026C + 0.1463$ and $A_{414\ nm} = 0.025C + 0.0472$ for BCP and BPB, respectively, where A and C refers to absorbance and concentration of the drug in μg ml^{-1}. The slope, intercept and correlation coefficient obtained by linear least squares treatment of the results, molar absorptivity and Sandell's sensitivity values are presented in Table 2. The precision and accuracy of the proposed method was checked by using 10 μg ml^{-1} of CTZH and the R.S.D. value was found to be less than 1.0%.

To determine the accuracy and reproducibility of the proposed methods, recovery experiments were performed using the method of addition. A fixed amount of pure sample solution was added to one of the three different concentrations of the standard drug solution. The total amount of the drug was then determined using the proposed methods and the amount of the added drug was calculated by difference.

3.4. Interference studies

The extent of interference by commonly associated excipients such as magnesium stearate, starch, talc, gelatin, dextrose, lactose and sucrose was determined by measuring the absorbance of a

Table 2
Optical characteristics, precision and accuracy data

Parameter	Value	
	BCP	BPB
λ_{max} (nm)	409	414
Beer's law limits (μg ml^{-1})	1–16	1.5–21
Molar absorptivity (l mol^{-1} cm^{-1})	1.89×10^4	1.21×10^4
Sandell's sensitivity (ng cm^{-2})	28.5	32.2
Stability (h)	18	20
Correlation coefficient (r)	0.9995	0.9991
Regression equation (Y)[a]		
Slope, b	0.026	0.025
Intercept, c	0.1463	0.0472
Relative standard deviation (%)[b]	0.85	0.93
% range of error (95% confidence limit)[b]	0.54	0.42

[a] $Y = a + bX$ where X is the concentration in μg ml^{-1}.
[b] For six replicate analysis within Beer's law limits.

solution containing 10 μg ml^{-1} of CTZH. An error of $\pm 2\%$ in the absorbance readings was considered tolerable. The proposed method was found to be free from interferences by the excipients in levels found in dosage forms. In order to test the accuracy of the method, the recovery experiments were performed on synthetic mixtures prepared in the laboratory and the results of analysis are given in Table 3.

3.5. Analysis of practical samples

The application of the proposed methods to the assay of dosage forms was examined by analysing tablets, syrups and suspension marketed under different trade names. The results obtained were compared statistically by Student's t-test and by the variance ratio F-test with those obtained by the reported method [2]. The Student's t-values at 95% confidence level did not exceed the theoretical value indicating no significant difference between the two methods. On the other hand, the variance ratio F-values, calculated for $P = 0.05$, did not exceed the theoretical value, indicating that there was no significant difference between the precision of the proposed methods and the reported method. The results are tabulated in Table 1.

4. Conclusion

A significant advantage of the extractive spectrophotometric method is that it can be applied for the determination of individual compounds in a multi component mixture. Unlike the gas chromatographic and HPLC procedures, the instrument is simple and is not of high cost. The importance lies in the chemical reactions upon which the procedures are based rather than upon the sophistication of the instrument. This aspect of spectrophotometric analysis is of major interest in analytical pharmacy since it offers distinct possibility in the assay of a particular component in a complex dosage formulations. The reagents utilised in the proposed methods are cheaper, readily available and the procedures do not in-

Table 3
Recovery of CTZH from various excipients

Reagent used	Amount added (mg)	Excipients (mg)						Recovery (%)[a]	R.S.D.
		Talc	Sucrose	Starch	Gelatin	Lactose	Mg-stearate		
BCP	10	30	40	40	10	40	20	99.68	0.84
BPB	10	30	40	40	20	40	30	99.46	0.91

[a] Average recovery from five determinations.

volve any critical reaction conditions or tedious sample preparation. The method is unaffected by slight variations in experimental conditions such as pH, reagent concentration or temperature. The wide applicability of the new procedures for routine quality control is well established by the assay of CTZH in pure form, as well as in pharmaceutical preparations.

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