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Talanta 50 (1999) 887–892

Talanta

www.elsevier.com/locate/talanta

Spectrophotometric determination of ceterizine hydrochloride with Alizarin Red S

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Received 1 June 1999; accepted 2 June 1999

Abstract

A simple, rapid and sensitive spectrophotometric method has been developed for the assay of ceterizine hydrochloride (CTZH) in bulk drug and its pharmaceutical preparations. This method is based on the ion-pair complex reaction between CTZH and Alizarin Red S in Clarks–Lubs buffer. The chromogen being extractable with chloroform, could be measured quantitatively at 440 nm. All variables were studied to optimise the reaction conditions. Regression analysis of Beer's Law plot showed good correlation in the concentration range 2.5–22 μg ml^{-1}. The method has a detection limit of 0.1328 μg ml^{-1}. The proposed method has been successfully applied for the analysis of the bulk drug and its dosage forms such as tablets and syrups. No interference was observed from common pharmaceutical adjuvants.

Keywords: Ceterizine hydrochloride; Ion-pair complex; Spectrophotometric method

1. Introduction

Ceterizine hydrochloride, CTZH, (2-(4-(4-chlorophenyl) phenylmethyl)-1-piperazinyl)-ethoxy)-acetic acid dihydrochloride is a new antihistaminic drug [1–3], currently marketed in India under the trade names cetzine, zyncet, zyrtec, cetrizet and cetiriz. It is indicated for the treatment of perennial and seasonal allergetic rhinitis and also for chronic uticaria. Currently, CTZH and its formulations are not to be found in any pharmacopoeia. Only two gas-chromatographic methods [4,5] and three high performance liquid chromatography (HPLC) methods [6–8] have been described for the determination of ceterizine in biological materials. Recently [9], El-Walily et al. have reported derivative spectrophotometric and HPLC methods for the determination of CTZH in pharmaceutical tablets. No methods based on colour formation have been reported for CTZH.

This paper describes a spectrophotometric method based on ion-association complex formation between CTZH and the acid dye, Alizarin Red S in Clarks–Lubs buffer of pH 3.2 (Fig. 1). The proposed method is simple, sensitive and the complex formed is stable for more than 24 h.

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0039-9140/99/$ - see front matter
PII: S0039-9140(99)00179-4

2. Experimental

2.1. Apparatus

An Elico Model SL 171 digital spectrophotometer with 1-cm matched glass cells was used for the absorbance measurements. pH measurements were made with an Elico Model L1-120 digital pH meter, calibrated with buffer solution (pH 4 ± 0.05).

2.2. Chemicals and reagents

All chemicals and reagents were of analytical grade. CTZH 99.62% purity (UNI-UCB, Mumbai, India) was used as the working standard. Alizarin Red S ARS (s.d. Fine Chemicals) was 0.05% w/v in Clarks–Lubs buffer of pH 3.2. Clarks–Lubs buffer of pH 3.2 was prepared by mixing 125 ml of 0.1 M potassium hydrogen phthalate and 36.75 ml of 0.1 M HCl and diluting to 250 ml. Spectroscopic grade chloroform was used.

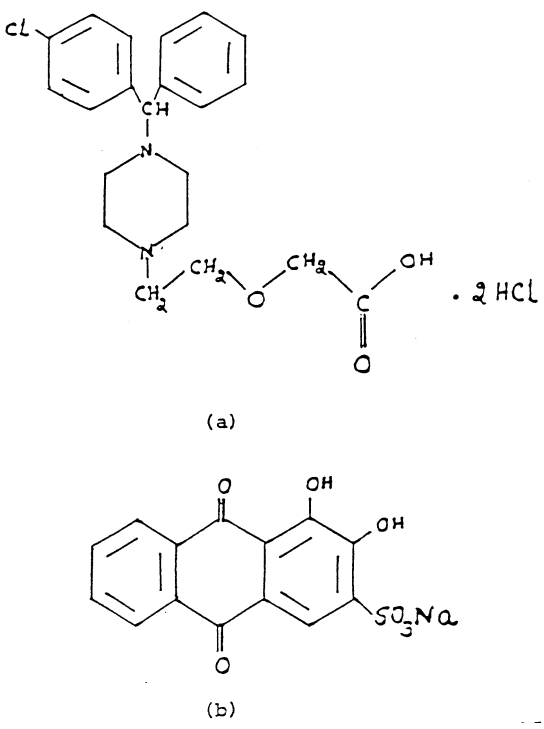

Fig. 1. Structure of (a) ceterizine dihydrochloride; (b) Alizarin Red S.

Dosage forms used in this investigation were: cetzine tablets and syrup (Glaxo Lab); cetiriz tablets and syrup (Alchem Labs); zyncet tablets and suspension (Unichem India); cetrizet-D tablets (Sunpharm); alerid tablets and syrup (Cipla); Zyrtec tablets (UNI-UCB) and zirtin tablets (Torrent Pharm).

2.3. Preparation of standards

Twenty mg of CTZH, accurately weighed, were transferred into a 100 ml volumetric flask, dissolved in water and completed to volume with the same solvent. This solution was diluted appropriately to get a working solution of 50 μg ml^{-1}.

2.4. Assay procedure

Aliquots of solution containing 2–22 μg ml^{-1} of CTZH were transferred into a series of 125 ml of separating funnels; then 5 ml of Clarks–Lubs buffer of pH 3.2 and 2 ml of 0.05% ARS were added. The total volume was adjusted to 15 ml by adding distilled water. Chloroform (10 ml, accurately measured) was added to each separating funnel and the contents were shaken for exactly 1 min. The two phases were allowed to separate and the chloroform layer was passed through anhydrous sodium sulphate and the absorbance was measured at 440 nm against the reagent blank. The reagent blank was prepared exactly like the procedure described above, but in the absence of CTZH. A calibration graph was drawn or regression equation calculated.

2.5. Assay procedure for tableted dosage

Tablets: 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, 60 ml of distilled water were added and shaken thoroughly for about 20 min. The contents were diluted to the mark, mixed well and filtered through a quantitative filter paper (Whatman 40) to remove the insoluble matter remaining. Twenty five ml of this filtrate was

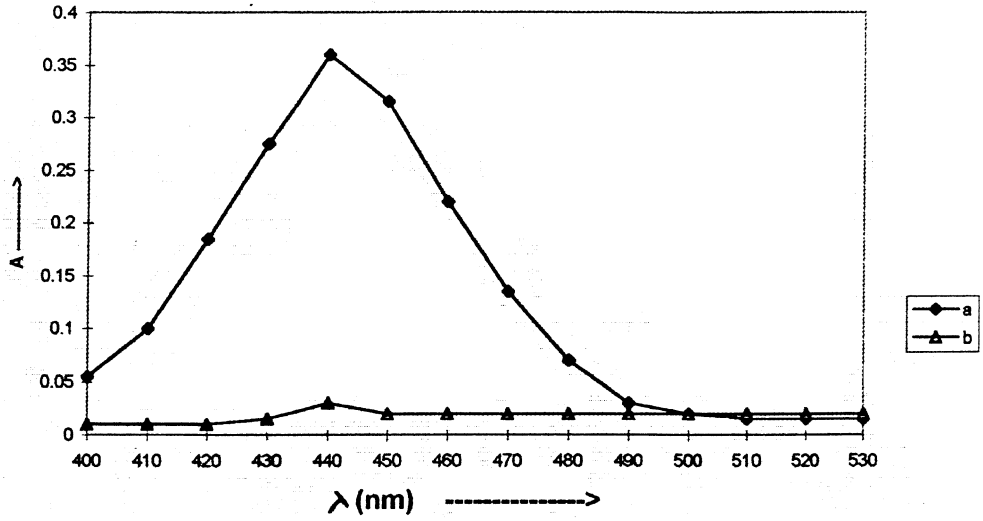

Fig. 2. Absorption spectra of (a) ceterizine (CTZ)–ARS complex; (b) reagent blank.

diluted to 100 ml and a suitable aliquot was taken for analysis using the procedure described earlier.

2.6. 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 N ammonia solution and 1 ml in excess was added. The mixture was then extracted with 3×15 ml portions of chloroform, the chloroform extracts were evaporated to dryness and the residue was dissolved in 0.1 N HCl and made upto 100 ml with distilled water. This solution was diluted to get 50 μg ml^{-1} of drug and an aliquot was analysed as above.

3. Results and discussion

Ion-pair extraction spectrophotometry has received considerable attention for quantitative estimation of many pharmaceutically important compounds [10–14]. CTZH reacted with ARS in an acidic buffer to form a yellow ion-pair complex which was extracted into chloroform. This complex has an absorption maximum at 440nm against reagent blank, hence this wavelength was used for all subsequent measurements. Under the same experimental conditions the reagent blank gave negligible absorbance (Fig. 2).

3.1. Optimum conditions for complex formation

The optimum conditions for quantitative determination of the associated ion-pair formed were established via a number of preliminary experiments. The effect of pH was studied by extracting the coloured complex formed in the presence of various buffers of different acidic pH values. Of the various buffers tried, Clark–Lubs (pH 2.2–3.8) was found to be more suitable compared to Walpole or Sorenson buffer in terms of sensitivity. In order to establish the optimum pH range, CTZH was mixed with ARS in selected buffer of pH 2.2–3.8, and the absorbance of the ion-associated complex was measured. Fig. 3 shows that the absorbance increases and reaches a maximum and a constant value at 3.0–3.4 pH range. At pH values greater than 3.4, the decrease in absorbance of the complex and increase in absorbance of the blank were observed. Hence, a pH of 3.2 was used in all subsequent experimental work. The shape of the absorption spectrum and maximum position did not vary with pH, so, it was concluded that only one complex was formed in this pH range.

The optimum volume of the dye used was also studied. Fig. 4 revealed an increase in the absorbance readings with the increase of volume of ARS upto 3.0 ml. However, a significant increase in the absorbance value of the blank was observed at volumes larger than 3 ml. Therefore, 3 ml of 0.05% w/v ARS was found to be quite adequate in a total volume of 15 ml of aqueous phase. Several organic solvents were tried to provide an effective extraction of the drug-dye complex from the aqueous phase and chloroform was preferred for its selective extraction. A ratio of 3:2 of aqueous to chloroform phases was required for efficient extraction of the coloured species. Shak-

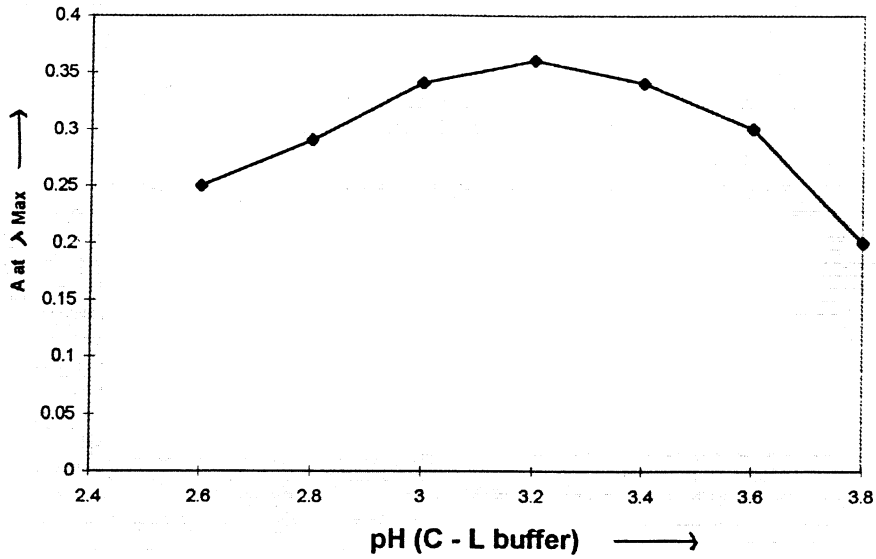

Fig. 3. Effect of pH on the absorbance of the ceterizine hydrochloride (CTZH)–ARS complex (final concentration of CTZH was 10 μg ml^{-1}).

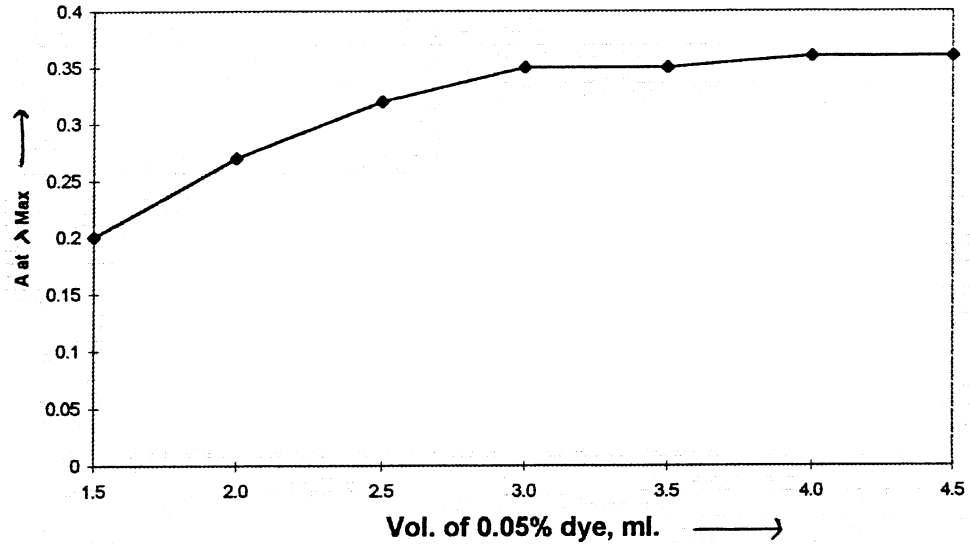

Fig. 4. Effect of concentration of ARS (final concentration of ceterizine hydrochloride, CTZH, was 10 μg ml^{-1}).

Table 1
Analysis of pharmaceutical preparations containing ceterizine hydrochloride (CTZH) by the proposed method

Preparation*	Label claim (mg tablet^{-1} or ml^{-1})	Recovery by the proposed method (%)	RSD (%)
Ceterzine tablets[a]	10	97.58	1.32
Cetzine syrup[a]	1	103.26	0.84
Cetiriz tablets[b]	10	98.35	1.06
Cetiriz syrup[b]	1	97.64	0.95
Zyncet tablets[c]	10	102.14	0.72
Zyncet suspension[c]	1	96.58	0.64
Cetrizet-D tablets[d]	10	98.42	0.26
Alerid tablets[e]	10	97.95	0.52
Alerid syrup[e]	1	98.12	0.75
Zyrtec tablets[f]	10	101.54	0.68
Zirtin tablets[g]	10	98.73	1.26

* Marketed by: a, Glaxo Lab; b, Alchem; c, Unichem; d, Sun Pharmaceuticals; e, Cipla; f, UNI-UCB; g, Torrent Pharmaceuticals.

ing times of 0.5–5 min produced a constant absorbance, and hence a shaking time of 1 min was used throughout. Only one extraction was adequate to achieve a quantitative recovery of the complex. Absorbances of the separated extracts were stable for more than 24 h. The drug-dye ratio as evaluated from the slope-ratio method was 1:2.

3.2. Quantification

A linear correlation was found between absorbance and concentration of CTZH in the range 2–22 μg ml^{-1}. The equation for one representative calibration curve is:

$A_{440} = (0.0115 + (0.035)C)$, where A and C correspond to absorbance and CTZH concentration in μg ml^{-1}, respectively. The correlation coefficient, $r = 0.9995$ ($n = 8$), indicates excellent linearity. The molar absorptivity coefficient was 1.60×10^4 l mol^{-1} cm^{-1}, and Sandell sensitivity was 0.3019 ng cm^{-2}. The method has a detection limit of 0.1328 μg ml^{-1}.

The precision of the proposed method was excellent as indicated from the relative standard deviation (S.D. $< 1\%$) calculated from eight replicate analysis of 10 μg ml^{-1} of pure CTZH.

3.3. Application

The applicability of the method to the assay of dosage forms was examined by analysing tablets, syrups and suspension marketed under different trade names. Table 1 shows the quantities obtained by the proposed method and labelled amount. The relative S.D.s are lower than 1% indicating good precision and the independence of the matrix effect over the absorbance. The method is simple and inexpensive as compared to the currently available methods [4–9] which are tedious and involve expensive experimental set-up which ordinary laboratories cannot afford.

Acknowledgements

The authors thank M/s UNI-UCB Ltd., Mumbai, India, for gifting pure sample of ceterizine hydrochloride.

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