CHAPTER V

SECTION I

SENSITIVE EXTRACTIVE SPECTROPHOTOMETRIC METHODS FOR THE ASSAY OF CETERIZINE HYDROCHLORIDE IN PHARMACEUTICAL FORMULATIONS AND SPIKED BIOLOGICAL SAMPLES
Ceterizine hydrochloride, CTZH [(2-(4-(4-chlorophenyl)phenylmethyl)-1-piperazinyl)-ethoxy)-acetic acid dihydrochloride] is a new antihistaminic drug\textsuperscript{1-3} used in the treatment of perennial and seasonal allergic rhinitis and also for chronic urticaria. It is a second generation non-sedating, anti-histamine with strong affinity for histamine H\textsubscript{1} receptors. It does exhibit anti-cholinergic and anti-serotonergic effects. The lack of CNS effects is due to its inability to penetrate into CNS across the blood-brain barrier at therapeutic doses.

Nagesh Badwe et al\textsuperscript{4} have reported a UV method for the determination of CTZH in syrups. In this method, the parabens were separated by extraction with chloroform before the actual assay of CTZH. The system obeyed Beer's law over the concentration range of 8–20 ppm. In this method, however, the effect of excipients on the assay of CTZH in formulations was not reported.

Sastry et al\textsuperscript{5} have developed a UV method for the assay of CTZH in bulk and tablet forms in which the absorbances were measured at 230 nm. The reported Beer's law range lies in the concentration limit from 2 to 28 ppm with \%RSD value of 0.819.

Chloranil was used by El-Walily et al\textsuperscript{6} for the spectrophotometric determination of CTZH in DMF solvent. The coloured species formed was measured at 556 nm. The plot of absorbance \textit{versus} concentration of CTZH was linear over the concentration range of 120-250 ppm.

Sundarapandian et al\textsuperscript{7} have described an extractive spectrophotometric assay of CTZH in bulk and tablet formulations. The method is based on the
measurement of absorbances of an ion-association complex in phthalate buffer at $\lambda_{\text{max}} = 420$ nm. The system obeyed Beer's law in the concentration range of 4–16 ppm.

Basavaiah et al$^8$ have determined the CTZH in bulk and pharmaceutical formulations based on the formation of chloroform soluble ion-association complex using alizarin red S at $\lambda_{\text{max}} = 440$ nm. Beer's law was obeyed in the concentration range of 2.5-22 ppm.

Recently Gowda et al$^9$ have reported two spectrophotometric methods for the determination of CTZH in pharmaceutical formulations based on the formation of yellow coloured ion-pair complexes. The complexes exhibited absorption maximum in the range of 409 - 414 nm and obeyed Beer's law over the concentration range of 1-21 ppm.

Apart from the above spectrophotometric methods, gas chromatographic$^{10-11}$ and high performance liquid chromatographic$^{12-14}$ methods have been reported for the assay of CTZH.

The aim of the present investigation was to develop new, reasonably sensitive and selective spectrophotometric methods for the determination of CTZH in bulk drug, pharmaceutical formulations and in spiked biological samples.

Attempts have not been made earlier for the spectrophotometric determination of CTZH in biological samples. In the present investigation, the author reports two new and adequately sensitive extractive-spectrophotometric methods for the determination of CTZH in bulk drug, pharmaceutical
formulations and in spiked biological samples. The methods are based on the formation of chloroform soluble ion-association complexes between CTZH with bromothymol blue (BTB) or with solochrome dark blue (SDB) in acidic buffer. No interference was observed in the assay of CTZH from common excipients in levels found in pharmaceutical formulations. The proposed methods are validated by statistical data.

EXPERIMENTAL

Equipments:

As described in Chapter II and IV.

Preparation of regents and Chemicals:

All chemicals were of analytical reagent or pharmaceutical grade and quartz-processed high-purity water was used throughout.

A 0.05 % solution of each of BTB and SDB was prepared separately in distilled water. Series of buffers viz., KCl–HCl (pH 1.0–2.2), NaOAc–HCl (pH 0.65–5.2), NaOAc–AcOH (pH 3.72–5.57) and potassium hydrogen phthalate–HCl (pH 2.2–3.6) were prepared by following the standard methods.

Preparation of standard drug solution:

Stock solution of pure CTZH (Dr. Reddy’s laboratories, India) was prepared by dissolving requisite amount of CTZH in distilled water and standardised\(^\text{15}\). The aqueous solution of CTZH was found to be very stable at room temperature. It was diluted as and when needed.

Different dosage forms of CTZH were obtained commercially from different firms.
Recommended procedures

After a systematic and exhaustive study of the various parameters involved in the formation of coloured products (as described under results and discussion), the following procedures [Methods: A: BTB and B: SDB] were recommended for the assay of CTZH in bulk sample and its pharmaceutical formulations.

Analysis of bulk sample:

Method A:

Suitable aliquots of standard CTZH solutions (20–160 μg) were taken into a series of 125 ml separating flasks. To each of these solutions were added 5 ml each of NaOAc–AcOH buffer of pH = 5.0 and BTB. Ten milliliters of chloroform was added to each of the separating funnels and shaken well. The two phases were allowed to separate and the chloroform layer was dried by running through anhydrous sodium sulphate. The absorbances of the yellow coloured species were measured at 415 nm against the reagent blank. A calibration graph of absorbance versus concentration of the CTZH was plotted (Fig.5.1).

Method B:

Several aliquots of standard solution containing 20–200 μg of CTZH were transferred into a series of 125 ml separating funnels. A 4 ml of KCl–HCl buffer of pH 1.1 and 1 ml of SDB were added. A 10 ml chloroform was added to each of the separating funnels and shaken well. The two phases were allowed to separate and the chloroform layer was dried by passing
through anhydrous sodium sulphate. The absorbances of the red coloured species were measured at 515 nm against the reagent blank. A calibration graph was plotted (Fig. 5.1).

The calibration graphs were subsequently used for the determination of CTZH in pharmaceutical formulations and in spiked biological samples.

**Analysis of pharmaceutical formulations:**

**Tablets:**

After twenty five tablets were finely powdered and an amount equivalent to 20 mg of the drug was weighed into a 100 ml beaker containing 70 ml distilled water. It was stirred thoroughly for about 15–20 min and filtered through a Whatman filter paper No. 40 to remove the insoluble matter. The filtrate was diluted up to the mark with distilled water in a 100 ml calibrated flask. An aliquot was analysed using the methods A and B as described earlier.

**Syrup and suspension:**

In respect of syrup and suspension, 20 ml equivalent to 20 mg of the 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 x 15 ml portions of chloroform. The chloroform extract was evaporated to dryness and the residue was dissolved and diluted up to the mark in a 100 ml calibrated flask with distilled water. A suitable amount of aliquot was taken and analysed as described earlier for pure drug.
Analysis of biological samples:

**Urine:**

A known amount of CTZH was added to 5 ml of urine sample. To this was added 0.5 g of lead nitrate to precipitate out the chlorides. The solution was filtered and the excess of lead present in the filtrate was removed by adding 8 M sulphuric acid. It was filtered through a Whatman filter paper No. 40 and diluted the filtrate to 250 ml in a calibrated flask with distilled water. A suitable amount of an aliquot containing CTZH within Beer's law range was analysed by using the methods A and B as described earlier.

**Blood:**

A 1 ml of blood was spiked with a known amount of CTZH before the addition of sodium citrate. The citrated blood was deproteinised with trichloroacetic acid and filtered through a Whatman filter paper No. 40. The filtrate was diluted to the mark in a 250 ml calibrated flask with distilled water. An appropriate amount of an aliquot containing CTZH within Beer's law range was taken and analysed as described for pure CTZH.

**RESULTS AND DISCUSSION**

Ion-pair extraction spectrophotometry has received a considerable attention for quantitative assay of many pharmaceutical drugs\(^9,16\)\(^-\)\(^18\). The formation of ion-association complexes due to the interaction between two constituents has been explained in detail in chapter I (under theory of solvent extraction). The CTZH reacts with BTB or SDB in acidic buffer to give a chloroform soluble yellow or red coloured ion-association complex which
exhibits an absorption maximum at 415 nm or at 515 nm for BTB or SDB. Under the experimental conditions the reagent blanks showed negligible absorbance (Fig. 5.2). The probable reaction mechanism for the formation of ion-pair complexes of CTZH with BTB and SDB may be represented as shown in Scheme 5.1.

**Optimum conditions for the formation of ion-pair complexes:**

The optimum reaction conditions for the proposed methods, which were necessary for rapid formation of the coloured products with maximum stability and sensitivity were established by performing systematic investigations. For this, control experiments were carried out by measuring the absorbances of the coloured ion-association complexes at their respective $\lambda_{\text{max}}$ values.

These optimum conditions were incorporated in the procedures.

**Method A:**

*Effect of buffer/pH:*

The effect of buffers was studied by extracting the coloured complex in the presence of various buffers *viz.*, KCl−HCl (pH 1.0–2.2), NaOAc−HCl (pH 0.65–5.2), NaOAc−AcOH (pH 3.72–5.57) and potassium hydrogen phthalate−HCl (pH 2.2–3.6). It was noticed that the quantitative extraction of the complex was possible in NaOAc−AcOH buffer of pH 5.00 (Fig. 5.3).

*Effect of reagent:*

From the studies, it was found that the constant and maximum absorbance readings were observed over the range of 4.5-6.0 ml of 0.05 % of BTB (Fig.5.4). The sensitivity of the complex was affected for more than
6.0 ml of the reagent while effective extraction was not achieved with the reagent volume below 4.5 ml. Hence a volume of 5 ml was employed throughout the study.

**Method B:**

*Effect of buffer/pH:*

The formation of an ion-association complex and its effective extraction depends on the type of buffer used and its pH. Hence various buffers as mentioned above were tried to optimize the reaction conditions. It was noticed that the maximum colour intensity and constant absorbances were observed in KCl–HCl buffer of pH 1.1 (Fig. 5.5).

*Effect of reagent:*

From experiments it was observed that a volume of 0.5 ml of 0.05 % SDB was necessary for achieving maximum colour intensity and longer stability of the ion-association complex. Below a volume of 0.5 ml of SDB effective extraction of the complex was not achieved. It was also noticed that no change in colour or stability of the complex was observed even if a little excess of the reagent was used (Fig. 5.6). However a large excess of the reagent affected the stability and sensitivity of the complex. Hence a volume of 1 ml of SDB was used for the study.

**Choice of extractant for Methods A and B:**

Several organic solvents were tried for the effective extraction of the ion-pair complexes from aqueous phase. Chloroform was found to be the most suitable solvent as it was observed that only one extraction was adequate to
achieve a quantitative recovery of the complex. Shaking times of 0.5 to 1.5 min produced a constant absorbance and hence a shaking time of 1 min was used throughout.

Order of addition of reagents:

From experiments in which the reactants were added in all possible sequences, it was found that there was no appreciable change in \( \lambda_{\text{max}} \), sensitivity or stability of the coloured species even if the order of addition was varied.

Precision and accuracy:

Analysis of known amounts of CTZH within Beer's law limits checked the precision and accuracy of the proposed methods. The low percentage error and percentage relative standard deviation values (Table 5.1) for the analyses of five replicates of CTZH highlighted good accuracy and precision of the proposed methods.

Optical characteristics of ion-pair complexes:

In order to test whether the yellow or the red coloured ion-association complexes formed in the proposed methods (A and B) adhere to Beer's law or not, the absorbances at their respective \( \lambda_{\text{max}} \) values were recorded under optimum reaction conditions for a series of solutions containing different amounts of CTZH. A linear relationship was found between absorbance at respective \( \lambda_{\text{max}} \) and the concentration of the coloured species in the concentration range of 2 - 16 ppm for BTB and 2 - 20 ppm for SDB. The optimum photometric range, molar absorptivity and Sandell's sensitivity values
were calculated. Least squares regression analysis was also carried out for evaluating the slope, intercept and correlation coefficient.

The results are given in Table 5.1.

Effect of temperature:

The effect of temperature on the stability of the complexes was studied. It was found that the complexes were stable in the temperature range 5 - 35 °C. The drug concentration was increased due to volatile nature of chloroform at higher temperatures. As a result, the absorbance values increased. Hence the studies were carried out at room temperature.

Stability of the coloured species:

In order to study the stability of the complexes, the absorbances were measured with respect to time. From the experiments, it was observed that the coloured ion-association complexes were stable for more than 15 h.

Interference studies:

In order to assess the possible analytical applications of the proposed methods, the effect of wide range of excipients and other additives, usually present in the formulations of CTZH, were investigated under optimum conditions. The colour was developed following the procedure described earlier. It was observed that the talc, magnesium stearate, starch, gelatin, dextrose, lactose and sucrose did not interfered with the determination at the levels found in dosage forms. Hence, the proposed methods are free from interferences by various substances.
Recovery studies:

Recovery studies were conducted by analysing each pharmaceutical formulation in the first instance for the active ingredient (CTZH) by the proposed methods. Three different amounts of pure CTZH were added to the previously analysed formulations and the total amount of the drug was once again determined by the proposed methods after bringing the CTZH concentration within Beer's law range. The amount of the added drug was calculated by difference. The results were found to be in good agreement.

Stoichiometry of the complexes:

The drug to reagent ratio was found to be 1:1 in both the methods as evaluated from Job’s method of continuous variation and mole ratio method (Fig. 5.7-5.8). The elemental analysis of the isolated ion-association complexes in solid form also confirmed the composition to be 1:1 for drug to reagent ratio. The tentative reaction mechanism for the formation of ion-pair complexes of CTZH is shown in Scheme 5.1

Applicability of the proposed methods:

In order to check the reliability and suitability of the developed methods, dosage forms marketed under different trade names (Table 5.2) and spiked biological samples (Table 5.3) were analysed. The results of the assay of pharmaceutical preparations of CTZH compare favorably with those of reported method8 (Table 5.2). The results of analysis of CTZH in biological samples by the proposed method could not be compared as no spectrophotometric method for the assay of CTZH in biological samples is
reported so far. The percentage RSD values for the analyses of biological samples were found to be in the range of 0.41-0.77.

Statistical analysis of the results in comparison with the reported method:

The results of analysis of various dosage forms of CTZH obtained by the proposed methods were compared statistically by Student t-test and by the variance ratio F-test with those obtained by the reported method. The results are recorded in Table 5.2. The Student t-values at 95% confidence level did not exceed the theoretical value indicating no significant difference between the two methods. It was also observed that 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.

CONCLUSIONS

The proposed methods are economical, simple, sensitive and accurate. The methods more practicable as the ion-pair complexes are stable for a sufficient interval of time at room temperature. Among the two reagents suggested, BTB was found to be more sensitive for the assay of CTZH. The validity of the proposed methods for the assay of CTZH is well demonstrated by analysing various dosage forms and spiked biological samples. The results of the analysis of medicaments revealed that the proposed methods are suitable for their analysis with virtually no interference from the additives. Statistical analysis of the results indicated good precision and accuracy of the methods. Hence the proposed methods could be adopted for routine quality control.
REFERENCES


7. M. S. Prakash, M. Sundarapandian, S. Meena and M. S. Nagarajan, Indian Drugs, 2000, 37, 211.


15. European Pharmacopoeia, 1997, 578


Scheme 5.1: Reaction mechanism of formation of ion-pair complexes of CTZH
Fig. 5.1 Beer's law plots of CTZH for ■ BTB and ▲ SDB
Fig. 5.2: Absorption spectra of ion-pair complexes of CTZH.

1. CTZH (11 ppm) + NaOAc-AcOH buffer + BTB
2. NaOAc-AcOH buffer + BTB reagent blank
3. CTZH (17 ppm) + KCl-HCl buffer + SDB
4. KCl-HCl buffer + SDB reagent blank
Fig. 5.3 Effect of NaOAc-AcOH buffer on the absorbance of CTZH (8 ppm)-BTB complex.

Fig. 5.4 Effect of volume of BTB (0.05 %) on the absorbance of ion-pair complex, CTZH(12 ppm)-BTB.
Fig. 5.5  Effect of KCl-HCl buffer on the absorbance of CTZH (16 ppm)-SDB complex

Fig. 5.6  Effect of volume of SDB (0.05 %) on the absorbance of the ion-pair complex, CTZH (18 ppm)-SDB
Fig. 5.7 Composition of the ion-pair complexes of
- CTZH-BTB ▲ CTZH-SDB by Job's method
[CTZH] = [BTB] = [SDB] = 1.0 x 10^{-3} M

Fig. 5.8 Composition of the ion-pair complexes of
- CTZH-BTB ▲ CTZH-SDB by Mole ratio method
[CTZH] = [BTB] = [SDB] = 1.0 x 10^{-3} M
Table 5.1 Optical characteristics, precision and accuracy data

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<th>Parameter</th>
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<tr>
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<td>Relative standard deviation ($%$)$^c$</td>
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<td>% Range of error ($95 %$) (95 % confidence limit)</td>
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$^a$ $Y=a+bX$ where $X$ is the concentration of the drug in ppm

$^c$ For 5 replicate analysis within Beer's law limits
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** Average of five determinations
Table 5.3 Analysis of CTZH in spiked urine and blood samples

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<th>CTZH found* ppm ± RSD, %, ppm BTB SDB</th>
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<td>Urine 3</td>
<td>15.0</td>
<td>14.94 ± 0.57 14.84 ± 0.68</td>
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* Average of five determinations
CHAPTER V
SECTION II

A NEW SPECTROFLUORIMETRIC METHOD FOR THE DETERMINATION OF CETERIZINE HYDROCHLORIDE IN VARIOUS DOSAGE FORMS
Ceterizine dihydrochloride (CTZH), a piperazine derivative and carboxylated metabolite of hydroxyzine, is a potent, multifunctional antihistaminic that works beyond histamine antagonism. The analytical methods reported for the assay of CTZH are given in the first section of chapter V.

From the literature mentioned in the first section, it is very clear that the methods reported for the assay of ceterizine (CTZH) described either direct measurement of the absorbance of CTZH in the UV region (around 230 nm) or based on the extraction of ion-pair complexes into chloroform. No spectrofluorimetric method for the determination of CTZH has been reported so far.

The goal of the present investigation is to develop a rapid, sensitive and selective fluorimetric method for the assay of CTZH. The proposed method is based on the measurement of fluorescence intensity of CTZH at 297 nm after exciting at 230 nm in hydrochloric acid medium.

EXPERIMENTAL

Equipments:

As described in chapter III, section II.

Preparation of reagents and chemicals:

All chemicals were of analytical reagent or pharmaceutical grade and quartz-processed high-purity water was used throughout.

A 0.05 M HCl was used for the study.
Preparation of standard drug solution:

A stock solution of CTZH was prepared in 0.05 M HCl and standardised as described in the first section. It was diluted with 0.05 M HCl as and when needed.

Recommended procedures

After a systematic and thorough study of various parameters involved in the formation of fluorescent species, the following procedures were recommended for the assay of CTZH in pure and pharmaceutical preparations.

Analysis of pure drug:

Suitable amounts of aliquots of CTZH containing 0.125-80.0 μg were transferred into a series of 5.0 ml calibrated flasks and diluted with 0.05 M HCl. The fluorescence intensity of the solution was measured in a 1.0 cm quartz cell at an emission wavelength of 297 nm after excitation at a wavelength of 230 nm. The reagent blank was also prepared similarly without CTZH.

A calibration graph was drawn which was used subsequently for the analysis of pharmaceutical formulations.

Analysis of pharmaceutical formulations:

Tablets:

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 10 mg of the drug was weighed into a 100 ml beaker, stirred well for about 15-20 min and filtered to remove the insoluble matter. The filtrate together with washings was diluted to the mark with 0.05 M HCl in a 100 ml
calibrated flask and mixed well. It was further diluted as required. A suitable aliquot was taken and analysed following the procedure outlined earlier.

Syrup and suspension:

In respect of syrup and suspension, 10 ml equivalent to 10 mg of CTZH were transferred into a 100 ml separating funnel. The sample was rendered alkaline with 3.0 M ammonia solution and 2.0 ml in excess was added. The mixture was then extracted with three 10 ml portions of chloroform. The chloroform extracts were evaporated to dryness and the residue was dissolved in 0.05 M HCl and made up to 100 ml with 0.05 M HCl. The solution was diluted as and when required and a suitable aliquot was analysed as above.

RESULTS AND DISCUSSION

Spectral characteristics:

In order to ascertain the optimum wavelength of maximum absorption of CTZH in hydrochloric acid medium, 10 ppm of CTZH was taken and the absorption spectrum was scanned on a spectrophotometer in the wavelength region of 190-500 nm. The species showed an absorption maximum at 230 nm, which was chosen as an excitation wavelength for further study.

In order to obtain an emission maximum, the CTZH species was excited at 230 nm and it showed an emission maximum at 297 nm.

The spectra are shown in figures 5.2a and 5.3a.
Optimum reaction conditions:

The optimum reaction conditions for the quantitative determination of CTZH were established via a number of preliminary trials by measuring the emission intensity at 297 nm after exciting at 230 nm of a series of solutions.

Effect of diluent:

The fluorescence intensity of the fluophore depends on the nature of the medium. A precipitate was observed in alkaline medium. Hence different acids viz. hydrochloric, sulphuric, phosphoric and acetic acids were tried in order to achieve maximum fluorescence intensity of CTZH. Low fluorescence intensity values were observed in sulphuric, phosphoric and acetic acid media. However maximum fluorescence intensity was observed with 0.05 M HCl.

Precision and accuracy:

The precision and accuracy of the proposed method was checked by analysing six replicates of 10 ppm of CTZH. The low percentage relative standard deviation (0.91) and percentage error (0.84 at 95 % confidence limit) values indicate good precision and accuracy of the proposed method.

Analytical features:

The fluorescence intensity of the fluorophore was recorded under optimum reaction conditions. It was found to be linearly related to the CTZH concentration over the range 0.025 - 16 ppm (r = 0.999). The detection limit calculated based on the reported method1 was found to be 0.3076 μg ml⁻¹.
Interference studies:

In order to assess the possible analytical applications of the proposed method, the effects of wide range of excipients and other additives usually present in the formulations of CTZH were investigated by following the procedure described earlier. It was observed that the talc, magnesium stearate, starch, gelatin, dextrose, lactose and sucrose were not interferred with the determination at the levels found in dosage forms. Thus, the proposed method is free from interferences by various excipients.

Recovery studies:

Recovery studies were carried out to justify the proposed method by assaying each pharmaceutical formulation in the first instance for the active ingredient (CTZH). Three different amounts of pure CTZH solution were added to the previously assayed formulations and the total amount of the drug was once again determined by the proposed method. The amount of the added drug was calculated by difference. The percentage recovery of CTZH was in the range of 99.62 - 101.12.

Application of the method:

The applicability of the method was examined by analysing various pharmaceutical formulations (tablets, syrups and suspension) marketed under different trade names. The results are presented in Table 5.1a. The RSD values were found to be lower than 1.1 % indicating good precision of the proposed method.
CONCLUSIONS

The method is simple and accurate compared to the currently available methods\textsuperscript{2-5}, which are tedious and hence can be used routinely for quality control. The developed method has advantages over the reported spectrophotometric methods\textsuperscript{6,7}, which do not explain the effects of excipients in the assay of CTZH in formulations.
REFERENCES


Fig: 5.2 a Absorption spectra of CTZH

1. 5 ppm CTZH in 0.05 M HCl
Fig: 5.3 a Emission spectra of CTZH
<table>
<thead>
<tr>
<th>Preparation*</th>
<th>Taken (mg/ tablet or mg/ml)</th>
<th>Found ** ± SD, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alerid syrup</td>
<td>1.0</td>
<td>0.9943 ± 0.78</td>
</tr>
<tr>
<td>Alerid tablet</td>
<td>10</td>
<td>9.886 ± 0.98</td>
</tr>
<tr>
<td>Ceterzine tablet</td>
<td>10</td>
<td>9.898 ± 0.86</td>
</tr>
<tr>
<td>Cetzine syrup</td>
<td>10</td>
<td>9.913 ± 0.85</td>
</tr>
<tr>
<td>Cetiriz syrup</td>
<td>1.0</td>
<td>0.9864 ± 0.93</td>
</tr>
<tr>
<td>Cetiriz tablet</td>
<td>10</td>
<td>9.906 ± 1.09</td>
</tr>
<tr>
<td>Cetrizet-D tablet</td>
<td>10</td>
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</tr>
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<td>Zirtin tablet</td>
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<td>9.912 ± 0.49</td>
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<tr>
<td>Zyrtec tablet</td>
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<td>9.868 ± 0.86</td>
</tr>
<tr>
<td>Zyncet tablet</td>
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<td>19.79 ± 1.05</td>
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<tr>
<td>Zyncet suspension</td>
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<tr>
<td>Sizon forte</td>
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<td>9.898 ± 0.98</td>
</tr>
<tr>
<td>Alzine tablet</td>
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<td>9.912 ± 1.08</td>
</tr>
<tr>
<td>Cetrine tablet</td>
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<td>10.11 ± 0.83</td>
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<tr>
<td>Coszin tablet</td>
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<td>9.912 ± 1.08</td>
</tr>
</tbody>
</table>

* Manufactured by *Cipla, *Glaxo Lab, *Alchem, *Sun Pharmaceuticals,

** Average of five determinations