Indirect Determination of Cetirizine Hydrochloride by ICP-AES

Wang Li-sheng, Wei Xiao-ling,* Gong Qi, Jiang zhi-liang,† Li Dong-mei, and Liang Qing

College of Chemistry and Chemical Engineering, Guangxi University, Nanning, 530004, P. R. China
†School of Environment and Resource, Guangxi Normal University, Guilin, 541004, P. R. China
E-mail: wxl1651@163.com

Indirect Determination of Cetirizine Hydrochloride by ICP-AES

Cetirizine hydrochloride reacted with BiI₄⁻ in an acidic aqueous solution to form precipitate. After centrifugation, the atomic emission intensity of Bi³⁺ contained in the supernatant solution was measured at the characteristic wavelength of 206.170 nm. The difference between the spectral signal intensity of the blank solution and that of the supernatant, ΔI, was linearly related to the concentration of cetirizine hydrochloride. As a result, a new inductively coupled plasma-atomic emission spectrometric (ICP-AES) method was developed for the analysis of cetirizine hydrochloride. The linear range was from 27.7 to 184.8 mg·L⁻¹, with a correlation coefficient (r) of 0.9961 and a detection limit of 9.6 mg·L⁻¹. This method is simple and accurate, without using toxic organic solvents, and is feasible for the quality control of cetirizine hydrochloride tablets and capsules.

Key Words: Cetirizine hydrochloride, ICP-AES, Precipitation, Indirect determination

Introduction

Cetirizine hydrochloride is an efficacious second-generation antihistamine drug with a broad range of applications. It can inhibit histamine not only at the early stage, but also at the later stage as well. It is commonly used for the treatment of allergic rhinitis, allergic skin itching, conjunctivitis, etc. Current analytical methods for cetirizine hydrochloride include ultraviolet spectrophotometry,¹² high performance liquid chromatography (HPLC),³⁻⁸ head-space-gas chromatography,⁹ capillary electrophoresis,¹⁰¹₂ chemiluminescence method¹³ and perchloric acid titration.¹⁴ Each of these methods has its own advantages and disadvantages. To our knowledge, ICP-AES has not been reported as the method for the determination of cetirizine hydrochloride. In this study, cetirizine hydrochloride reacted with BiI₄⁻ in an acidic solution to form yellow precipitate which was then separated from the liquid phase by centrifugation, and the Bi emission intensity of the supernatant was calibrated by an EDTA standard solution in order to obtain the solution concentration of 7.136 × 10⁻¹ mol·L⁻¹. A 800-type centrifuge (Shanghai Surgical Instruments Factory), HH-38 thermostatic water-bath (Changcheng Technology and Business Limited Company, Zhengzhou), Leici pHS-3C pH meter (Shanghai Precision Scientific Instrument Corporation) were used.

Preparation of BiI₄⁻ Solution.

Bi³⁺ Solution Preparation: A certain amount of solid bismuth nitrate was accurately weighed into a beaker, and then 30 mL of distilled water was added. After the mixture was stirred for a few minutes, the clear upper solution was removed. After the hydrolysis product of Bi³⁺ was washed 5 to 6 times with distilled water to remove the precipitate was dissolved in 40 mL of glacial acetic acid. This solution was then diluted to 250 mL in a volumetric flask with distilled water and was calibrated by an EDTA standard solution in order to obtain the solution concentration of 1.784 × 10⁻² mol·L⁻¹.

Preparation of KI Solution: 2.861 g of solid potassium iodide was accurately weighed, then dissolved and diluted to 250 mL in a volumetric flask with distilled water. The concentration was 7.136 × 10⁻² mol·L⁻¹.

Working Solution of BiI₄⁻: 11.20 mL of the 1.784 × 10⁻² mol·L⁻¹ Bi³⁺ solution, 30 mL of glacial acetic acid, 11.20 mL of the 7.136 × 10⁻² mol·L⁻¹ KI solution and 1 g of solid KI were

Experimental

Instruments and Reagents. An inductively coupled plasma atomic emission spectrometer (Optima 5300DV, PerkinElmer Inc., US) was used, with the operating parameters as in Table 1.

<table>
<thead>
<tr>
<th>element</th>
<th>analytical line/nm</th>
<th>RF power/W</th>
<th>pumpspeed/mL/min</th>
<th>plasma gas/L/min</th>
<th>carrier gas/L/min</th>
<th>auxiliary gas/L/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bi</td>
<td>206.170</td>
<td>1300</td>
<td>1.5</td>
<td>15</td>
<td>0.8</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Table 1. Equipment operating parameters
Results and Discussion

Acidity Effect. As the procedure, the test solutions were adjusted to various pH values with 3 mol·L⁻¹ of HCl and 0.1 mol·L⁻¹ of NaOH without changing other conditions. It was found that the measured values, \( \Delta I \), remained unchanged by the addition of an acid to the test solutions with a pH of \( \leq 3.0 \). However, the measured values, \( \Delta I \), increased sharply at pH > 3.5 when an alkaline was added to the test solutions. The above results indicate that the Bi³⁺ of BiI₄ was strongly hydrolyzed at pH > 3.5 and therefore the analysis was only applicable at pH ≤ 3.0. In the preparation of the BiI₄ solution, a large volume of glacial acetic acid was added in order to prevent the hydrolysis of Bi³⁺, resulting in a pH value of approximately 2.0 which was in line with the necessary conditions for the reaction. Therefore, the pH value of the reaction system was not adjusted.

Influence of Reaction Temperature. The effect of temperature (15 - 40 °C) on the reaction of BiI₄ and cetirizine hydrochloride are shown in Figure 2. \( \Delta I \) reached the maximum value at 20 °C. The \( \Delta I \) values fell as the reaction temperature was increased above 20 °C was probably caused by decomposition of the product.

Influence of Reaction Time. Figure 3 shows that the reaction is quite rapid with the \( \Delta I \) values remaining constant after 7 min.
Unless otherwise stated, a 20 min reaction time was selected in the following study.

**Reagent Consumption.** 2.00 mL of $2.00 \times 10^{-3}$ mol·L$^{-1}$ cetirizine hydrochloride was added to various amounts of BiI$_4$ solutions respectively under the same other conditions. The data shown in Figure 4 indicate that the reaction is basically complete when the volume ratio of BiI$_4$ solution to cetirizine hydrochloride solution was 2:1. Therefore, the volume of BiI$_4$ solution must be as twice as that of the cetirizine hydrochloride standard solution.

**Linear Range.** The working curve was obtained by plotting the $\Delta I$ values for various concentrations of cetirizine hydrochloride standard solutions. The results establish that the $\Delta I$ values were proportional to the cetirizine hydrochloride concentration in the range of 27.7 - 184.8 mg·L$^{-1}$. Regression analysis yields the equation $\Delta I = 0.0353C_{\text{drug}} + 0.0926$, with a correlation coefficient of 0.9961. The detection limit (3σ) as calculated by the IUPAC method was 9.63 mgL$^{-1}$.

**Precision.** 2.00 mL of $2.00 \times 10^{-3}$ mol·L$^{-1}$ cetirizine hydrochloride and 4 mL of $2.00 \times 10^{-3}$ mol·L$^{-1}$ BiI$_4$ solutions were mixed in eleven 10-mL volumetric flasks, and the eleven $\Delta I$ values were subsequently determined and calculated to a RSD of 1.4%.

**Interference Test.** Drugs often contain additives such as glucose, dextrin, starch, magnesium stearate, calcium ions and other metal cations. Therefore, interference experiments on these substances for drug determination were conducted. The volume of cetirizine hydrochloride and BiI$_4$ solutions were fixed at 2.00 mL and 4.00 mL, respectively, and then varying amounts of the interfering substances listed above were added. The mixture was diluted to 10 mL with distilled water, and then the concentration of cetirizine hydrochloride was determined under the optimized conditions. With a measurement error of ±5%, the amount of allowable interfering substances is given in Table 2.

The data in Table 2 suggest that starch, Ca$^{2+}$ and Mg$^{2+}$ effect determining the concentration of cetirizine hydrochloride. For starch, the reason is that it has poor water solubility and forms a suspension in water which affects the formation of associated complexes. However, the starch excipient in drugs can be removed by filtration when the sample solution is processed, and therefore, it has little effect on the sample measurement. Unfortunately, Ca$^{2+}$ and Mg$^{2+}$ can interfere with the measurement of the $\Delta I$ values. This phenomenon is deduced that because these ions can inhibit the ionization of Bi$^{3+}$ in plasma flame. The result led to decrease emission spectra intensity of Bi$^{3+}$, the $\Delta I$ values between the blank solution and the supernatant of the centrifuged test solution was increased. However, Ca$^{2+}$, Mg$^{2+}$ interference eliminated by adding H$_2$C$_2$O$_4$.15

**Ion-association Ratio.** Figure 5 shows the plot of the $\Delta I$ values versus $C_{\text{Bi,4}}/C_{\text{drug}}$. The association ratio of BiI$_4$ and cetirizine hydrochloride is approximately 2:1.

**Measurement of the Solubility Product Constant and $K_{sp}$ of the Precipitate.** The working curve for Bi$^{3+}$ was obtained by using a series of BiI$_4$ standard solutions and then the linear regression analysis was conducted to generate the equation of the line. The resulting equation gives $I = 0.3143C_{\text{Bi,4}} - 1.5525$, $r = 0.9980$. Cetirizine hydrochloride and the BiI$_4$ standard solutions were added to a beaker at a 2:1 ratio of $C_{\text{Bi,4}}/C_{\text{drug}}$, allowing to form the precipitate. The precipitate was washed six times by aqueous solution of acetic acid (pH = 3). After the final wash, centrifuged and the clear upper liquid was removed for measuring emission spectra intensity, I, under the spectral line of Bi$^{3+}$, the concentration of BiI$_4$ in the supernatant was calculated.

![Graph](image)

**Figure 5.** The ratio of Associating precipitation.

<table>
<thead>
<tr>
<th>interference</th>
<th>starch</th>
<th>glucose</th>
<th>stearic acid</th>
<th>dextrin</th>
<th>Ca$^{2+}$</th>
<th>Mg$^{2+}$</th>
<th>C$<em>{2}$O$</em>{4}^{2-}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>allowed</td>
<td>multiple</td>
<td>10</td>
<td>400</td>
<td>200</td>
<td>250</td>
<td>15</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 2.** Data for interfering substances

<table>
<thead>
<tr>
<th>Sample</th>
<th>Labeled/mg</th>
<th>Measured/mg</th>
<th>Equivalent to the labeled amount ± S.D.</th>
<th>Added/mg</th>
<th>Measured/mg</th>
<th>Recovery ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1$^a$</td>
<td>1.00</td>
<td>1.02</td>
<td>102.0 ± 0.64</td>
<td>0.185</td>
<td>1.212</td>
<td>101.0 ± 0.33</td>
</tr>
<tr>
<td>2$^a$</td>
<td>1.00</td>
<td>0.999</td>
<td>99.9 ± 0.55</td>
<td>0.185</td>
<td>1.182</td>
<td>99.1 ± 1.43</td>
</tr>
<tr>
<td>3$^a$</td>
<td>1.00</td>
<td>0.992</td>
<td>99.2 ± 0.21</td>
<td>0.185</td>
<td>1.170</td>
<td>97.4 ± 0.024</td>
</tr>
<tr>
<td>4$^a$</td>
<td>1.00</td>
<td>0.992</td>
<td>99.2 ± 0.38</td>
<td>0.185</td>
<td>1.177</td>
<td>97.5 ± 3.2</td>
</tr>
</tbody>
</table>

$^a$Tablets from Suzhou Dawnrays Pharmaceutical Co., Ltd. Labeled amount, 10 mg/tablet. $^b$Tablets from Kunshan Dragon Reddy Pharmaceutical Co., Ltd. Labeled amount, 10 mg/tablet. $^c$Tablets from Chongqing Winbond Pharmaceutical Co., Ltd. Labeled amount, 5 mg/tablet. $^d$Capsules from Zhuhai Phoenix Pharmaceutical Co., Ltd. Labeled amount, 10 mg/grain.
calculated against the working curve equation shown above. Finally, the $K_{sp}$ value was calculated as $5.73 \times 10^{-13}$ according to the formula $K_{sp} = [\text{BiI}_4^-][\text{drug}] ([\text{drug}] = 1/2 [\text{BiI}_4^-])$. The results indicate that the association complex is stable.

**Analysis of Samples.**

**Pre-treatment of Sample:** It is known from the specifications that the tablets of cetirizine hydrochloride contain magnesium stearate. The previous interference tests revealed that Mg$^{2+}$ had a significant influence on the determination of the cetirizine hydrochloride. Therefore, some H$_2$C$_2$O$_4$ must be added to eliminate the interference of Mg$^{2+}$ during sample preparation.

Twenty tablets of cetirizine hydrochloride were accurately weighed and ground into powder. An amount of powder equivalent to 50 mg of cetirizine hydrochloride was weighed and added to a small beaker, added 0.2 g H$_2$C$_2$O$_4$, and some water, stirred well, then transferred to 100 mL volumetric flask with distilled water diluted to volume 100 mL. The solution was filtered to yield the filtrate for the following test.

**Sample Concentration and Percentage of Recovery:** 2.00 mL of sample solution and 4.00 mL of $2.00 \times 10^{-3}$ mol L$^{-1}$ of Bi$^{3+}$ solution were added to a 10-mL volumetric flask, mixed and measured five times individually using the method. The concentration of cetirizine hydrochloride in the tablets and the percentage recovery of a known quantity of cetirizine hydrochloride were determined. The concentration of cetirizine hydrochloride determined by the experimental method was compared to the given concentration stated by the manufacturer as determined by inductively coupled plasma atomic emission spectrometry. The optimal conditions for this method were developed experimentally as follows: pH of the solution to be ≤ 3.0, a reaction temperature of 20 °C, reaction time of 20 min, and the ratio of $C_{\text{BiI}_4^-}/C_{\text{drug}} = 2:1$.

The method used in these experiments has the following characteristics: an obvious reaction phenomenon, simple steps, low-cost, accurate results and the elimination of toxic solvents in the detection process. It is therefore safer and more environment-friendly compared to the current methods for analyzing cetirizine hydrochloride content. Most importantly, this method has extended the scope of applications for ICP-AES which has mainly been used for metallic, non-metallic element analysis only.

**Conclusions**

In this paper, based on the precipitation reaction of Bi$^{3+}$ anion and cetirizine hydrochloride, the concentration of cetirizine hydrochloride in real samples was determined indirectly by inductively coupled plasma atomic emission spectrometry. The optimal conditions for this method were developed experimentally as follows: pH of the solution to be ≤ 3.0, a reaction temperature of 20 °C, reaction time of 20 min, and the ratio of $C_{\text{BiI}_4^-}/C_{\text{drug}} = 2:1$.

The method used in these experiments has the following characteristics: an obvious reaction phenomenon, simple steps, low-cost, accurate results and the elimination of toxic solvents in the detection process. It is therefore safer and more environment-friendly compared to the current methods for analyzing cetirizine hydrochloride content. Most importantly, this method has extended the scope of applications for ICP-AES which has mainly been used for metallic, non-metallic element analysis only.

**References**