Complexometric Determination of Hydroxyzinium Chloride

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The conditions of preparation of hydroxyzinium tetraiodocadmiate were elaborated. The chemical composition and solubility were determined as well as thermal analysis was performed. Basing on the spectrophotometric investigations the mechanism of hydroxyzinium tetraiodocadmiate formation was established. The method of the complexometric determination of hydroxyzinium chloride, within the concentration range 5–50 mg, has been described. The elaborated method has been checked by hydroxyzinium chloride determination in Hydroxyzinum dragees.


Hydroxyzinium chloride, 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]ethanol dihydrochloride or (4ClPh)-Ph-CH(1,4-Pip)-CH2CH2OCl1,CH2OH-2HCl, possesses anxiolytic, antihistaminic, antiemetic and sedative activities. It is used (as Hydroxyzinum or Atarax) for motion sickness, preanesthetic medication, alcohol addiction and allergic reactions.

Psychotropic drugs were determined by spectrophotometric method using their coloured compounds with complexes of some metals [1–3], with Reinecke salt [4] and picric acid [5, 6]. Complexometric [7, 8] and gravimetric [9, 10] methods have been used too for the determination of the above mentioned drugs.

The aim of the present paper was to elaborate a quick, simple as well as an exact method of complexometric determination of hydroxyzinium chloride in the matter and dragees.
EXPERIMENTAL

Reagents and apparatus

Hydroxyzinium chloride (Polfa, Rzeszów) – solutions 0.1 mol l\(^{-1}\) and 2.28×10\(^{-3}\) mol l\(^{-1}\). The content of hydroxyzinium chloride was equal to 99.6%. Concentration of the solutions was determined applying perchloric acid [11]. Cadmium nitrate – solutions 0.1 mol l\(^{-1}\) and 6.35×10\(^{-3}\) mol l\(^{-1}\). Concentrations were determined by the complexometric method [12]. Ammonia buffer (pH ca. 10.4). EDTA – solution 0.02057 mol l\(^{-1}\). Potassium iodide – 10% solution. Eriochrome Black T – 0.2% triethanolamnia solution. Hydroxyzinum dragees à 10 mg – Polfa, Rzeszów, series 011090. Spectrophotometer Specord M-80. Derivatograph MOM-OD-102.

Preparation, chemical composition, solubility and thermal stability of hydroxyzinium tetraiodocadmiate

100 ml of the 0.1 mol l\(^{-1}\) solution of cadmium nitrate were diluted to 250 ml and 10 ml of H\(_2\)SO\(_4\) (2 mol l\(^{-1}\)) and 2.5 g of solid potassium iodide were added. In agreement with calculations based on Bjerrum’s and Leden’s equation 96.97% of Cd(II) ions exist in form of [CdI\(_4\)]\(^{2-}\) when the concentration of I\(^-\) ions is equal to 1 mol l\(^{-1}\). After that 100 ml of solution of hydroxyzinium chloride (0.1 mol l\(^{-1}\)) was added portionwise with constant stirring. As a result of reaction the white precipitate was formed. This precipitate after desiccating was appropriate for physicochemical investigations.

The elementary analysis of the obtained compound was performed, using the standard semi-micro method. The content of cadmium was determined by voltammetric method, applying the microtrack heavy metal computer analyser.

The results of analysis were the following:
- calculated: 25.3% C, 2.9% H, 2.8% N, 11.3% Cd;
- found: 24.6% C, 2.6% H, 2.6% N, 11.1% Cd.

The agreement between the analysis results obtained and calculated from the formula: \((C_{21}H_{27}ClN_2O_2\cdot2H)\ [CdI_4]\, M = 996.94\), confirms that the suggested formula is correct.

The conducted thermogravimetric investigations indicate that hydroxyzinium tetraiodocadmiate is thermally stable up to temp. 233\(^\circ\). The melting point is at 175\(^\circ\). The negligible endoeffects appearing at 50\(^\circ\), 78\(^\circ\), 90\(^\circ\) and 145\(^\circ\) are probably connected with polymorphic changes of the compound obtained.

Solubility of hydroxyzinium tetraiodocadmiate in water and in some organic solvents was determined for confirmation its analytical usefulness. The saturated solutions were prepared and the content of cadmium in a well-defined volume was determined by voltammetric method. The results of investigations were the following: water – 4.46×10\(^{-5}\) mol l\(^{-1}\), ethanol – 6.23×10\(^{-3}\) mol l\(^{-1}\), methanol – 7.07×10\(^{-3}\) mol l\(^{-1}\), chloroform – 1.92×10\(^{-2}\) mol l\(^{-1}\), benzene – 1.40×10\(^{-2}\) mol l\(^{-1}\), ethyl acetate – 2.28×10\(^{-2}\) mol l\(^{-1}\).

It has been found that the investigated compound is well soluble in acetone and its solubility depends on dielectric constant of a solvent.
Spectroscopic studies of hydroxyzinium tetraiodocadmiate

Spectroscopic investigations made possible the determination of the reaction mechanism for the formation of hydroxyzinium tetraiodocadmiate. The vibrational spectra were obtained using pellets with the investigated compound and potassium bromide in the ratio of 1:120 (the crushing pressure – 150 kG cm\(^{-2}\)).

In the IR spectrum (Fig. 1) of hydroxyzinium chloride as well as hydroxyzinium tetraiodocadmiate the characteristic bands of free vibrations occur within the range 400–1700 cm\(^{-1}\). The wide, multiple band of N–H vibration of hydroxyzinium chloride, characteristic for tertiary amine within the range 2450–2650 cm\(^{-1}\), is shifted towards lower energetic region 2880–3060 cm\(^{-1}\) in IR spectra of hydroxyzinium tetraiodocadmiate. This effect is connected with the appearance of the strong interactions: Cd–I...H–N–CH\(_2\)–. Hydrogen bond which occurs in the crystal lattice reduces the N–H bond strength causing the above mentioned band shift [13, 14].

The spectroscopic investigations indicate that formation of hydroxyzinium tetraiodocadmiate is the result of the exchange of chloride ion in organic base for the greater tetraiodocadmiate ion.

Figure 1. Absorption spectra: 1) hydroxyzinium chloride, 2) hydroxyzinium tetraiodocadmiate
Complexometric determination of hydroxyzinium chloride

20 ml of standard solution of cadmium nitrate \((6.35 \times 10^{-3} \text{ mol l}^{-1})\), 5 ml of 2 mol l\(^{-1}\) sulfuric acid and 20 ml of 10% potassium iodide were added to 100 ml of water. An excess of iodide ions does not interfere with complexometric determination of Cd(II). Next, suitable amounts of aqueous solution of hydroxyzinium chloride were added (5–50 ml, which corresponded to 5.1–51 mg of the pure substance). The white precipitate was formed as a result of the reaction. This precipitate was filtered into a sintered glass crucible G-4 to a clean filtering flask vol. 300 ml and was washed several times with water. Next 20 ml of ammonia buffer \((\text{pH ca. 10.4})\) and 5–10 drops of Eriochrome Black T were added to the filtrate and cadmium ions were back titrated with EDTA solution to the colour change from red to blue. The content of hydroxyzinium chloride in a sample was calculated as a difference between the amounts of cadmium introduced and back-titrated. The automatic microburette type KB1 was used.

1 ml of 0.02057 mol l\(^{-1}\) EDTA solution corresponds to 9.22 mg of hydroxyzinium chloride. The results of determinations are collected in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Complexometric determination of hydroxyzinium chloride</th>
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<tr>
<td>Comparative method</td>
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Complexometric determination of hydroxyzinium chloride in Hydroxyzinum dragees

In order to prove the usefulness of the elaborated method hydroxyzinium chloride determination in Hydroxyzinum dragees was carried out. Dragees Hydroxyzinum with the declared content of 10 mg were used for the determinations. Before dissolving dragees were powdered in the agate mortar. Four solutions were prepared in measuring flasks, containing 4, 8, 12 and 16 dissolved dragees. 25 ml of the prepared solutions were sampled to analysis. The further procedure was analogous as described above.

The results of determinations are collected in Table 2.
Table 2. Complexometric determination of hydroxyzinium chloride in dragees Hydroxyzinum

<table>
<thead>
<tr>
<th>Sample</th>
<th>Found by the described method (n = 5) x, mg</th>
<th>Standard deviation s</th>
<th>Standard deviation of the mean s</th>
<th>Confidence interval $U_{0.05} = x \pm t_{0.05}s$</th>
<th>Relative standard deviation $s_r$</th>
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<tbody>
<tr>
<td>10 (1 dragee)</td>
<td>9.94</td>
<td>1.94x10^{-2}</td>
<td>8.66x10^{-3}</td>
<td>9.94±2.41x10^{-2}</td>
<td>1.95x10^{-3}</td>
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<tr>
<td>20 (2 dragees)</td>
<td>19.89</td>
<td>4.33x10^{-2}</td>
<td>1.95x10^{-2}</td>
<td>19.89±5.42x10^{-2}</td>
<td>2.18x10^{-3}</td>
</tr>
<tr>
<td>30 (3 dragees)</td>
<td>29.83</td>
<td>8.93x10^{-2}</td>
<td>3.99x10^{-2}</td>
<td>29.83±1.11x10^{-1}</td>
<td>2.99x10^{-3}</td>
</tr>
<tr>
<td>40 (4 dragees)</td>
<td>39.79</td>
<td>1.17x10^{-1}</td>
<td>5.21x10^{-2}</td>
<td>39.79±1.45x10^{-1}</td>
<td>4.27x10^{-3}</td>
</tr>
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RESULTS AND DISCUSSION

The elaborated method of complexometric determination of hydroxyzinium chloride is quick and simple as well as exact. It is suitable for the determination of hydroxyzinium chloride within the concentration range of 5–50 mg of the pure substance. For the greater concentrations the results are too high because of difficulties with exact washing of the large amounts of precipitate from the excess of $[\text{CdI}_4]^{-}$ ions. It has been confirmed that an excess of iodide ions does not interfere with the quantitative precipitation of hydroxyzinium tetraiodocadmiate as well as has no effect on complexometric determination of cadmium ions. The coloured envelope does not interfere with the complexometric determination. The very best results were obtained using EDTA of the concentration of 2x10^{-2} mol l^{-1}.

The elaborated method of hydroxyzinium chloride determination is suitable for the use in drug-checking laboratories and makes an appendix to the methods currently in use.

REFERENCES


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