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Complex Formation of 5-Hydroxyorotic Acid with Copper(II) Ions in Water Solutions

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Abstract—Complex formation of 5-hydroxyorotic acid with copper(II) chloride in water solution is studied by electron spectroscopy. The composition of the complex was established spectrophotometrically by molar ratio method and confirmed by elemental analysis. The constant of complex formation was calculated. By the IR spectroscopy the electron-donating centers of 5-hydroxyorotic acid taking part in coordination with metal ion were established. The structure of the obtained complex was suggested.

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Orotic acid is the precursor of pyrimidine bases of nucleic acids in the course of their biosynthesis. Reactions of orotic acid proceed in the presence of enzymes. For the activation and normal functioning of the latter metal ions are necessary. Besides, complexes of orotic acid are suggested as the biological carriers of metal ions, which is important for curing syndromes connected with the deficit of various metals [1]. Recently a series of papers appeared [2, 3] where complex formation of orotic acid with ions of metals of the varied valence was studied.

Despite the interest to metal complexes of orotic acid the reported data on the coordination chemistry of the derivatives of orotic acid are scarce [4, 5]. From our point of view the greatest interest presents 5-hydroxyorotic acid which has several electron-donating centers. The coordination of a metal ion may take place at the nitrogen atoms of the heterocycle, at the two exocyclic carbonyl oxygen atoms, at the hydroxy and the carboxy groups. The introduction of a hydroxy group in the position 5 of the pyrimidine ring might significantly amplify the effectiveness of orotic acid as a drug which was shown by an example of preparations of 6-methyluracyl and 6-hydroxy-6-methyluracyl [6]. That is why the investigation of complex formation of 5-hydroxyorotic acid with metal ions presents interest not only for the chemistry of coordination compounds, but also for medicine.

The complex formation of copper(II) ions with 5-hydroxyorotic acid was studied by electronic and IR spectroscopy. For the evaluation of composition of the complex the method of molar ratios was used. In the visible part of spectrum the maximum of absorption of copper(II) aquacomplex is located at about 790 nm. At the addition of orotic acid the maximum of the absorption of solution suffers a blue shift till 740 nm. At the same time the intensity of the absorption band increases. In the UV spectrum of water solution of 5-hydroxy orotic acid the absorption band with maximum at 310 nm is observed. Its intensity gradualy decreases at the increase in the ratio of copper(II) ions and the acid. The maximum of absorption band of the solution undergoes a red shift. In Fig. 1 dependences of variation in optical density for the aquacomplexes of copper(II) (Fig. 1a) and the ligand (Fig. 1b) are presented. It follows from these data that the complex of copper(II) with 5-hydroxyorotic acid has the composition 1:2. The elemental analysis of the complex isolated from water solution agrees with the above-presented data. The absorption in the range 740–790 nm shows the octahedral surrounding of copper(II) ion [7].

We established which of the electron-donor centers of the ligand took part in the complex formation using the IR spectroscopy.

In the IR spectrum of the obtained complex new weak absorption bands appear at 543 cm^{-1} [ν(COO–Cu)] and at 650 cm^{-1} [ν(OH-Cu)] (see the table). The appearance of absorption bands at 1616 and 1311 cm^{-1} shows the monodentate coordination of copper ion

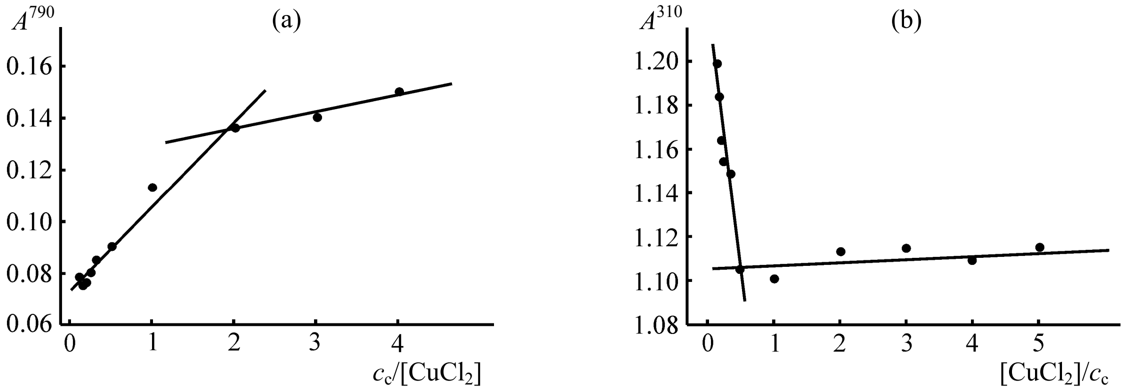
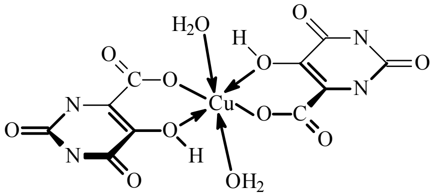


Fig. 1. Dependence of optical density of solutions (a) on the concentration of 5-hydroxyorotic acid at constant concentration of copper(II) chloride (1 mM) and (b) on concentration of copper(II) chloride at constant concentration of 5-hydroxyorotic acid (1 mM).

with the carboxylate. Binding by the hydroxy group is characterized by the shift of absorption band at 1273 cm^{-1} [ν(C^5–O^5)] by 35 cm^{-1} to the low frequency range. The strong absorption band at 3440 cm^{-1} indicates the presence of coordinated water. Hence, on the basis of the obtained data it was established that the coordination of copper(II) ion proceeds via the hydroxy and carboxy groups. The octahedral coordination sphere of copper(II) ion is completed by two water molecules.



The value of complex formation constant *K* of copper(II) with 5-hydroxyorotic acid calculated from the spectrophotometry data for the solutions with various ratio of 5-hydroxyorotic acid and copper(II) was 15.5±3.1.

Hence, by the molar ratio method the composition of complex of copper(II) ion with 5-hydroxyorotic acid equal to 1:2 was established. It was shown that the coordination bonds in this complex were formed between copper(II) ion and the hydroxy and carboxy groups of the ligand. The constant of complex formation was evaluated from the spectrophotometry data.

EXPERIMENTAL

Electron absorption spectra were registered on a Specord M-40 UV-Vis spectrophotometer in the range 200-800 nm using quartz cells of *l* = 0.2 and 5 cm against bidistilled water. IR spectra were recorded on a Specord M-80 spectrometer in the range 4000–250 cm^{-1} for the mulls in mineral oil. The attribution of absorption bands was carried out on the basis of the reported data [3, 5].

Copper(II) chloride dihydrate of "chemically pure" grade was used.

5-Hydroxyorotic acid was synthesized according to the procedure [8].

Attribution of bands in the IR spectrum of 6-hydroxyorotic acid and of its complex with copper(II) ions

Wave no., cm^{-1}		Attribution of vibration
5-hydroxyorotic acid	complex	
3535 s	3535 m	ν(O–H)$_{\text{cryst.water}}$
3439 m	3437 m	ν(O–H)$_{\text{coord.water}}$
3194 m	3196 m	ν(N^1–H^1)
3105 sh	3115 sh	ν(N^3–H^3)
2476 w		ν(O–H)$_{\text{acid}}$
1745 s	1743 s	ν(C^2=O) + ν(C=O)$_{\text{acid}}$
1697 s	1701 s	ν(C^4=O^4)
1647 s	1647 s	ν(C=C)
	1616 s	ν_{as}(COO$^-$)
1525 w	1520 sh	Vibration of the ring
1454 m	1458 m	δ(N^1–H^1)
1427 m	1427 m	δ(N^3–H^3)
	1311 m	ν_s(COO$^-$)
1273 m	1238 m	ν(C^5–O^5)
1047 m	1047 m	ν(C^6–C^7)
975 w	977 w	Vibration of the ring
870 s	873 s	Δ[$C^{2(4)}$=$O^{2(4)}$]
820 s	820 s	δ(C^6–C^7)
	659 w	ν(Cu–O^5)
	543 w	ν(Cu–O^1)

Solutions of 5-hydroxyorotic acid and copper(II) chloride were prepared from the accurately weighed batches.

Studies of complex formation of 5-hydroxyorotic acid with copper(II) chloride. The composition of obtained complex was established spectrophotometrically using the molar ratio method at room temperature. To this end a series of solutions with different ratio of concentrations of 5-hydroxyorotic acid and $CuCl_2$ was prepared. Optical density of solutions was measured at the maximum of the absorption band of aquacomplex $Cu(H_2O)_6^{2+}$ at 790 nm and also at the maximum of the absorption band of 5-hydroxyorotic acid at 310 nm.

The value of complex formation constant K of copper(II) ion with 5-hydroxyorotic acid was calculated using spectrophotometric method [9]. Visible (790 nm) spectra of solutions containing 5-hydroxyorotic acid and copper(II) chloride with a constant concentration of copper(II) chloride and the varied concentration of second component were recorded. For each ratio the constant of complex formation was calculated according to the formula.

$$K = \frac{[CuL_2][H^+]^2}{[Cu^{2+}][HL]^2}. \quad (1)$$

At the assumption that when optical density of the solution becomes independent of concentration of 5-hydroxyorotic acid because all copper(II) ions are involved in complex formation, the molar absorption coefficient of complex was calculated according to the following relationship.

$$\varepsilon(CuL_2) = \frac{A}{c_{Cu^{2+}}l}. \quad (2)$$

The equilibrium concentration of complex was found from the equation:

$$[CuL_2] = \frac{\Delta A}{\varepsilon(CuL_2)l}. \quad (3)$$

Here Δ is the variation in optical density at the complex formation. L is the thickness of the cell.

Equilibrium concentrations of 5-hydroxyorotic acid and copper(II) ion were found as:

$$[HL] = c_L - 2[CuL_2], \quad (4)$$

$$[Cu^{2+}] = c_{Cu^{2+}} - [CuL_2]. \quad (5)$$

The concentration of hydrogen ions was measured by the OR-211/1 pH-meter with the combined glass electrode. From the obtained values of complex formation constant the average value was calculated.

Synthesis of complex of copper(II) with hydroxyorotic acid. To a solution of 0.104 g of 5-hydroxyorotic acid dihydrate in 50 ml of water 0.043 g of $CuCl_2 \cdot 2H_2O$ was added. The obtained solution was stirred for 20 min in a temperature-controlled cell at room temperature. The obtained yellowish green precipitate was filtered off and dried in air. Yield 0.082 g (94%). Found, %: C 30.41; H 1.85; N 14.02. $C_{10}H_6CuN_4O_{10}$. Calculated, %: C 29.56; H 1.48; N 13.79.

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