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# Complexes of Hydroxamic Derivatives of Carboxymethyl- and Carboxyethylaubazidan with Some *d*-Elements

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**Abstract—**Complexes of hydroxamic derivatives of carboxymethyl- and carboxyethylaubazidan with $Fe^{3+}$, $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Mn^{2+}$ cations were synthesized. The structure and composition of the obtained compounds were studied by the IR and electronic spectroscopy and elemental analysis.

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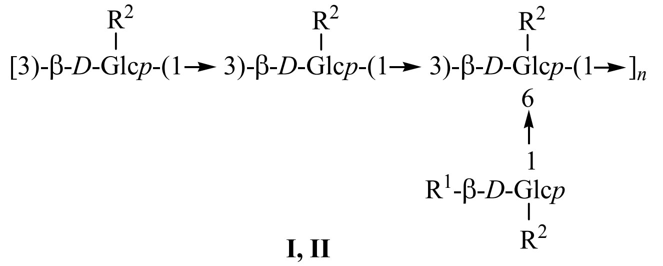
Natural polysaccharides and their derivatives often form stable complexes with metal cations, which have valuable properties and find practical application, for example, for X-ray studies, for the preparation of the plasma substitutes, and also as drugs with antianemic and antitumor activity [1].

The chemical modification of polysaccharides allows purposeful synthesis of compounds with high chelating ability with respect to a number of metals. For example, carboxymethylcellulose [2], chitosan derivatives [3], starch dialdehyde hydrazone, oxime and thiosemicarbazone were suggested as polymer ligands [4–6].

Among the complexing groups the hydroxylaminocarbonyl moiety forming strong coordination bonds should be noted.

Compounds containing this group are effective ligands and are widely used in analytical chemistry [7, 8] and they also exhibit various types of biological activity, which is important in designing polymeric drugs. Some hydroxamic derivatives of monosaccharides, like octyl-*N*-hydroxy-α(β)-*D*-glucopyranosyluronamides, are proposed as the chelating agents for the $Fe^{3+}$ ions and as surfactants [9].

Previously we have synthesized the hydroxamic derivatives of carboxymethyl- and carboxyethyldextran and their complexes with $Fe^{3+}$, $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Mn^{2+}$ cations [10, 11]. It has been shown that these hydroxamic derivatives of dextran form complexes with these cations in an acidic medium. The complexes contain 1 mol of the metal per 1 mol of the hydroxamic residues in the polyligands. The aim of this work was to obtain and study a number of metal complexes with carboxymethyl- and carboxyethylhydroxamic derivatives of aubazidan polysaccharide produced by the yeast-like fungus *Aureobasidium pullulans*. Aubazidan chemical structure is significantly different from dextran. It is a highly branched, slightly soluble in water *D*-glucan containing β-1,3-, β-1,6- and α-1,4-glycoside bonds [12].



$$[3)\text{-}\beta\text{-}D\text{-}\overset{R^2}{\mathrm{Glc}p}\text{-}(1\rightarrow 3)\text{-}\beta\text{-}D\text{-}\overset{R^2}{\mathrm{Glc}p}\text{-}(1\rightarrow 3)\text{-}\beta\text{-}D\text{-}\underset{\substack{6\\ \uparrow\\ 1\\ R^1\text{-}\beta\text{-}D\text{-}\underset{R^2}{\mathrm{Glc}p}}}{\overset{R^2}{\mathrm{Glc}p}}\text{-}(1\rightarrow]_n$$

**I, II**

$R^1 = [4)\text{-}\alpha\text{-}D\text{-}\overset{R^2}{\mathrm{Glc}p}\text{-}(1\rightarrow]_{0-2}$; $R^2 = CH_2CONHOH$ and $CH_2COOH$ (**I**); $CH_2CH_2CONHOH$ and $CH_2CH_2COOH$ (**II**).

Hydroxamic derivatives of aubazidan were synthesized by the previously described methods [10, 13]. We used a sample of carboxymethylaubazidanhydroxamic acid sodium salt **I** containing 0.24 mol of hydroxyaminocarbonylmethyl ($CH_2CONHOH$) units ($c_{cmg}$) and 0.86 mol of carboxymethyl ($CH_2COOH$) groups per 1 mol of monosaccharide units, and a sample of carboxyethylaubazidanhydroxamic acid potassium salt **II** containing 0.23 mol of hydroxylaminocarbonylethyl ($CH_2CH_2CONHOH$) units ($c_{ceg}$) and 0.85 mol of carboxyethyl ($CH_2CH_2COOH$) groups per 1 mol of monosaccharide units.

The potentiometric titration data showed that the p$K_a$ values for the carboxy groups in the acids **I** and **II** are about 4.9 and 5.2, respectively. For the hydroxamic CONHOH groups of both acids these values are close to 9. Therefore to evaluate the chelating ability of the polysaccharide ligand, the complexes of derivatives **I** and **II** with the $Fe^{3+}$, $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Mn^{2+}$ cations were prepared in water at room temperature and pH values of 1, 4.5, and 7.5. In these conditions at pH 1 the dissociation of the complexing groups is virtually absent. At pH 4.5 only carboxy groups of the polymer ligands are partially ionized. At pH 7.5 the hydroxamic groups are partially ionized, and the carboxy groups are completely ionized.

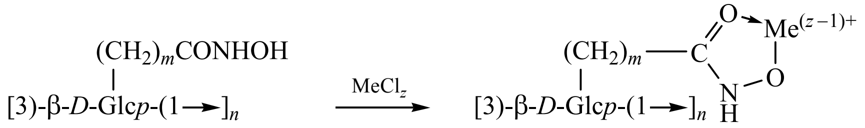
The reactions of **I** with the $Fe^{3+}$ (at pH 1, 4.5, and 7.5), $Cu^{2+}$ (at pH 4.5 and 7.5), $Co^{2+}$, $Ni^{2+}$ and $Mn^{2+}$ cations (at pH 7.5) result in the water-soluble colored precipitates. The same results were observed when the acid **II** reacted with the $Cu^{2+}$ and $Ni^{2+}$ ions at pH 7.5. In other cases, aubazidan derivatives were precipitated with alcohol from the colored solutions.

All complexes are insoluble in ethanol, acetone, and most organic solvents; their solubility in water is shown in the table. In most cases the solubility reduces as the pH increases. It may be due to the formation of the low-dissociating base forms of the cations. In general, complexes of **II** are more soluble than complexes of **I**. Like aubazidan polysaccharide [12], the $Mn^{2+}$-containing complex **In**, obtained at pH 4.5, and $Co^{2+}$-containing complexes **IIh** and **IIi**, obtained at pH 4.5 and 7.5, form stable gels, when dissolved in water.

The solid complexes were characterized by the substitution degree $c_s$, which is a number of moles of metal ions per 1 mol of the monosaccharide fragments (see the table).

The data obtained indicate that aubazidanhydroxamic acids, as well as dextranhydroxamic acids [10, 11], form complexes with the selected metals ions. Therewith, the metal content in the complexes increases as the pH value of the reaction medium increases.

The complexes of the ligands **I** and **II** with the $Co^{2+}$, $Mn^{2+}$, $Ni^{2+}$ ions formed at pH 1 contain small amounts of the metal ($c_s < 0.06$). Therefore it is not possible to elucidate the nature of the complex formation on the basis of the IR and electron absorption spectra of these compounds. The metal content in the complexes isolated at pH 4.5 and 7.5 is much higher. The $Fe^{3+}$ and $Cu^{2+}$ cations form stable complexes with a high $c_s$ value from 0.21 to 0.58 for all selected values of pH of the reaction medium. The metal ions content in the $Fe^{3+}$ (**Ia**, **IIa**) and $Cu^{2+}$ (**Id**) complexes obtained at pH 1 is close to the hydroxamic groups content in the ligands **I** and **II**. So, for these complexes the molar ratio $c_s/c_{cmg}$ or $c_s/c_{ceg}$ equals 0.88, 0.96, and 0.96, respectively. Compounds with a similar metal–hydroxamic group ratio are also formed by the reaction of the ligand **I** with the $Mn^{2+}$ ions at pH 7.5 ($c_s/c_{cmg} = 0.79$) and of the derivative **II** with the $Ni^{2+}$ ions at pH 4.5 ($c_s/c_{ceg} = 0.78$) and 7.5 ($c_s/c_{ceg} = 0.91$). Therefore, we suggest that in these compounds each metal cation is coordinated with a hydroxamic acid moiety as follows:



**I, II** **Ia–Io, IIa–IIo**

$m$ = 1 (**I**), 2 (**II**); $Me^{z+} = Fe^{3+}$ (**a–c**), $Cu^{2+}$ (**d–f**), $Co^{2+}$ (**g–i**), $Ni^{2+}$ (**j–l**), $Mn^{2+}$ (**m–o**).

The metal content of the $Fe^{3+}$ (**Ib**, **Ic**, **IIb**, **IIc**), $Cu^{2+}$ (**Ie**, **If**, **IId–IIf**), $Co^{2+}$ (**Ih**, **Ii**), $Ni^{2+}$ complexes (**Ik**, **Il**) obtained at pH 4.5 and 7.5 is higher than the content of hydroxamic groups in the ligand. This may be due to the participation of the carboxy groups in the complex formation along with the hydroxamic moities. The $c_s/c_{cmg}$ ratio is maximal (2.4) for the $Cu^{2+}$ complex **If** obtained at pH 7.5.

Physicochemical characteristics of the complexes of **I** and **II** with the $Fe^{3+}$, $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Mn^{2+}$ cations

| Comp. no. | Ligand | Cation | pH[a] | Color | Solubility in water, % | $c_s$ | IR spectrum |  | Electronic spectrum, $\lambda_{max}$, nm |
|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  | ν[C=O(NH)], $cm^{-1}$ | Δν[C=O(NH)], $cm^{-1}$ [b] |  |
| **Ia** | **I** | $Fe^{3+}$ | 1 | Dark brown | 10.4 | 0.21 | 1630 | 15 | 450 |
| **Ib** | **I** | $Fe^{3+}$ | 4.5 | Brown | 4.8 | 0.43 | 1625 | 20 | 450 |
| **Ic** | **I** | $Fe^{3+}$ | 7.5 | Brown | 4.1 | 0.46 | 1623 | 22 | 450 |
| **Id** | **I** | $Cu^{2+}$ | 1 | Pale green | 10 | 0.23 | 1629 | 16 | 340 |
| **Ie** | **I** | $Cu^{2+}$ | 4.5 | Pale green | 8.7 | 0.48 | 1625 | 20 | 340 |
| **If** | **I** | $Cu^{2+}$ | 7.5 | Pale green | 5.6 | 0.58 | 1620 | 25 | 340 |
| **Ig** | **I** | $Co^{2+}$ | 1 | Pale yellow | – | 0.03 | – | – | 480 |
| **Ih** | **I** | $Co^{2+}$ | 4.5 | Pink | 44.3 | 0.31 | 1644 | 1 | 480 |
| **Ii** | **I** | $Co^{2+}$ | 7.5 | Pink | 14.1 | 0.43 | 1630 | 15 | 480 |
| **Ij** | **I** | $Ni^{2+}$ | 1 | Pale yellow | – | 0.04 | – | – | 470 |
| **Ik** | **I** | $Ni^{2+}$ | 4.5 | Pale green | 10 | 0.41 | 1635 | 10 | 470 |
| **Il** | **I** | $Ni^{2+}$ | 7.5 | Pale green | 4.9 | 0.49 | 1630 | 15 | 470 |
| **Im** | **I** | $Mn^{2+}$ | 1 | Pale yellow | – | 0.02 | – | – | 460 |
| **In** | **I** | $Mn^{2+}$ | 4.5 | Pale pink | 100, gel | 0.11 | 1630 | 15 | 460 |
| **Io** | **I** | $Mn^{2+}$ | 7.5 | Cream | 7.9 | 0.19 | 1630 | 15 | 460 |
| **IIa** | **II** | $Fe^{3+}$ | 1 | Dark brown | 14.7 | 0.22 | 1662 | 3 | 460 |
| **IIb** | **II** | $Fe^{3+}$ | 4.5 | Brown | 14 | 0.35 | 1665 | 0 | 460 |
| **IIc** | **II** | $Fe^{3+}$ | 7.5 | Brown | 13.1 | 0.36 | 1665 | 0 | 460 |
| **IId** | **II** | $Cu^{2+}$ | 1 | Pale green | 30 | 0.31 | 1665 | 0 | 340 |
| **IIe** | **II** | $Cu^{2+}$ | 4.5 | Pale green | 24.9 | 0.38 | 1665 | 0 | 340 |
| **IIf** | **II** | $Cu^{2+}$ | 7.5 | Pale green | 8.4 | 0.41 | 1630 | 35 | 340 |
| **IIg** | **II** | $Co^{2+}$ | 1 | Pale yellow | – | 0.06 | – | – | 510 |
| **IIh** | **II** | $Co^{2+}$ | 4.5 | Pale pink | 100, gel | 0.15 | 1665 | 0 | 510 |
| **IIi** | **II** | $Co^{2+}$ | 7.5 | Pale pink | 100, gel | 0.15 | 1632 | 33 | 510 |
| **IIj** | **II** | $Ni^{2+}$ | 1 | Pale yellow | – | 0.03 | – | – | 470 |
| **IIk** | **II** | $Ni^{2+}$ | 4.5 | Pale green | 60 | 0.18 | 1660 | 5 | 470 |
| **IIl** | **II** | $Ni^{2+}$ | 7.5 | Pale green | 9.4 | 0.21 | 1659 | 6 | 470 |
| **IIm** | **II** | $Mn^{2+}$ | 1 | Pale yellow | – | 0.02 | – | – | 460 |
| **IIn** | **II** | $Mn^{2+}$ | 4.5 | Beige | 51 | 0.12 | 1660 | 5 | 460 |
| **IIo** | **II** | $Mn^{2+}$ | 7.5 | Beige | 74 | 0.12 | 1660 | 5 | 460 |

[a] The pH value of the medium at the synthesis of the complex. [b] Δν[C=O(NH)] = $\nu[C{=}O(NH)]_{\mathbf{I}}$ – ν[C=O(NH)] or Δν[C=O(NH)] = $\nu[C{=}O(NH)]_{\mathbf{II}}$ – ν[C=O(NH)], where $\nu[C{=}O(NH)]_{\mathbf{I}}$ is 1645 $cm^{-1}$ for **I** and $\nu[C{=}O(NH)]_{\mathbf{II}}$ is 1665 $cm^{-1}$ **II** in the acid form.

The participation of both hydroxamic and carboxy groups in the complex formation is confirmed by the IR spectroscopy. Thus, it can be assumed that at pH 1 the carboxy groups of **I** and **II** are almost not dissociated and are not involved in the complex formation, except for the $Cu^{2+}$ ions, which interact with the acidic residues of the ligand **II**. In the IR spectra of all complexes obtained at pH 4.5 and 7.5 the absorption bands corresponding to the symmetric and asymmetric vibrations of carboxy groups $COO^-$ [1423 and 1620 cm$^{-1}$ (**I**), 1418 and 1620 cm$^{-1}$ (**II**)] are shifted to low frequencies compared with the spectra of compounds **I** and **II** indicating that they participate in the coordination.

The IR spectra of the coordinated ligand **I** contain the same shift to low frequencies of the absorption band ν[C=O(NH)] compared with the spectrum of the free acid, which is associated with a decrease in the electron density on the nitrogen atom of the hydroxamic group at the formation of coordination bonds. In the spectra of the free acids **I** and **II** the absorption bands of the C=O(NH) groups are observed at 1645 and 1665 cm$^{-1}$, respectively. For the complexes the values of Δν[C=O(NH)] = ν[C=O(NH)]$_{\mathrm{I}}$ – ν[C=O(NH)] are 15–22 cm$^{-1}$ (Fe$^{3+}$, **Ia**–**Ic**), 16–25 cm$^{-1}$ (Cu$^{2+}$, **Id**–**If**), 1–15 cm$^{-1}$ (Co$^{2+}$, **Ih**, **Ii**), 10–15 cm$^{-1}$ (Ni$^{2+}$, **Ik**, **Il**), 15 cm$^{-1}$ (Mn$^{2+}$, (**In**, **Io**). For complexes of **II** the values of Δν[C=O(NH)] = ν[C=O(NH)]$_{\mathrm{II}}$ – ν[C=O(NH)] are 0–3 cm$^{-1}$ (Fe$^{3+}$, **IIa**–**IIc**), 0–3 cm$^{-1}$ (Cu$^{2+}$, **IId**–**IIf**), 0–33 cm$^{-1}$ (Co$^{2+}$, **IIh**, **IIi**), 5–6 cm$^{-1}$ (Ni$^{2+}$, **IIk**, **III**), 5 cm$^{-1}$ (Mn$^{2+}$, **IIn**, **IIo**).

The electron absorption spectra of the diluted (10$^{-2}$–10$^{-3}$ mol l$^{-1}$) aqueous complexes contain weak (except for the Fe$^{3+}$ complex) absorption peaks in the visible region at λ > 300 nm (see the table), which are absent in the spectra of sodium and potassium salts of the acids **I** and **II**, respectively, as well as in the spectra of carboxymethyl- and carboxyethylaubazidan in the presence of metal salts. These data indicate the presence of the characteristic peaks due to the complexation of cations with hydroxamic moiety. The spectra of the free acids obtained from the derivatives **I** and **II** contain only the absorption maxima of the carbonyl groups in the ultraviolet region at λ 210–225 nm. Moreover, for all complexes the hyperchromic effect and red shift of the maximum are observed.

## EXPERIMENTAL

The IR spectra were recorded on a FSM 120 Fourier spectrometer from KBr pellets. The electron absorption spectra of aqueous solutions of the substances obtained were taken on an Ocean Optics PX-1 spectrometer ($l$ = 1 cm) at room temperature. Photometric measurements were made on a KFK-3-01 spectrophotometer ($l$ = 1 cm) at room temperature. The gravimetric dissolution test was carried out according to the procedure described in [4, 5]. The metal content of the obtained complexes was calculated from the analysis results using spectrophotometric techniques. After the complexes decomposition in a strongly acidic medium the content of the Fe$^{3+}$ ions was determined by the photometry of its complex with sulfosalicylic acid in an aqueous ammonia solution, the Cu$^{2+}$ ions, by the photometry of an ammonia complex, the Co$^{2+}$ ions, by the photometry of a thiocyanate complex in acetone, the Mn$^{2+}$ ions, by the photometry of a formaldoxime complex in an alkaline medium, the Ni$^{2+}$ ions, by the photometry of a dimethylglyoxime complex in an alkaline medium in the presence of iodine [14, 15].

**Complexes of hydroxamic derivatives of carboxymethyl- (I) and carboxyethylaubazidan (II) with Fe$^{3+}$, Cu$^{2+}$, Ni$^{2+}$, Co$^{2+}$, Mn$^{2+}$ cations.** To a solution of 0.1 g of the polyligand **I** or **II** in 5 ml of distilled water acidified with 4 N HCl solution was added dropwise the freshly prepared aqueous 10% solution of the corresponding metal chloride under stirring until the metal excess of 1.5 mol per 1 mol of the monosaccharide units was reached. The solution pH was adjusted to the desired value with 0.1 N HCl solution. The resulting reaction mixture was stirred at room temperature for 30 min, the colored precipitate was filtered off, washed thoroughly with a water–alcohol mixture to remove the low-molecular salts. The soluble reaction products were fractionally precipitated from the reaction mixtures with ethanol. The resulting product was dried in a vacuum (20–25 mm Hg) at 61°C to a constant weight.

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