

Al(III)–Maltol Complexes, Structure and Stability

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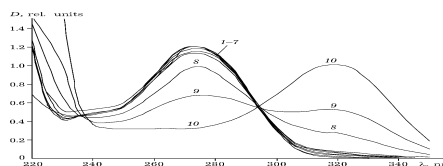
Abstract

Formation of Al(III)–maltol complexes was studied in aqueous solutions. It was shown that an increase in pH resulted in sequential transformations of the complexes in the following order: $[\text{AlMa}]^{2+}$, $[\text{AlMa}_2]^+$ and $[\text{AlMa}_3]$. The data concerning stability constants revealed the superior stability of the electrically neutral complex (formed at pH 4–8), which is also of interest regarding its application in medicine.

INTRODUCTION

Views on the role of metals in nature had changed. Contemporary investigations showed that biogenic metals are an essential part of enzymatic and metabolic processes. Nowadays there are many facts supporting harmful effects of heavy metals, or metals in exceeding concentrations on an organism.

It is well known that an increase in aluminium concentration in cerebral cortex leads to serious mental illnesses such as Alzheimer disease, dialysis encephalopathy (usually ends in madness) [1–3]. Therefore it is of great importance to solve the problem of aluminium removal from cerebral cortex. One of the possible solutions is the use of ligands: Al^{3+} cation is bound into a stable complex and removed from an organism. In order to pass through the cerebral-blood barrier, such complex have to be electrically neutral, water-soluble, stable at physiological pH [1] and have a mass about 400 Dn. These requirements are met by the six-coordinated chelate complex of Al^{3+} with 3-hydroxy-2-methyl-4-pyrone (maltol **1**) – *tris*-(3-hydroxy-2-methyl-4-pyronato) aluminium (III) **2** [4].



It was shown in previous works that maltol is water-soluble and harmless substance stable in physiological media [5]. It can be extracted from needles of silver fir tree; dry needles contain about 1–2 % (dry mass) of maltol [6].

The aim of the work was investigation of the process of Al^{3+} – maltol complex formation in a wide range of pH (1–10), as well as study of the structure and stability of the species formed.

EXPERIMENTAL

Maltol was extracted from the needles of Siberian fir tree (*Abies sibirica* L.) using the procedure described in [7]. The characteristics of the chemicals used (according to the national standards) were as follows: $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and HClO_4 – “chemically pure” (“kh. ch.”), 25 mass % solution of NH_4OH – “pure for analysis” (“ch. d. a”), water – double distilled.

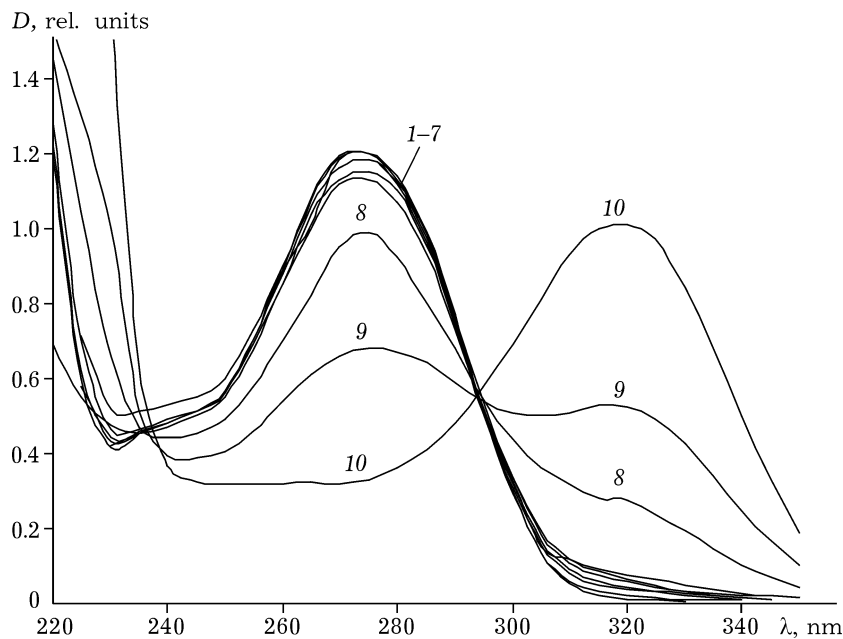


Fig. 1. Electronic spectra of the aqueous solutions of maltol ($6.87 \cdot 10^{-5}$ M).
pH values: 1 (1), 2 (2), 3 (3), 4 (4), 5 (5), 5.7 (6), 7.12 (7), 8.05 (8), 8.8 (9), 10 (10).

The pH value was controlled by adding 0.2 M NH_4OH and 0.2 M HClO_4 solutions. The latter chemical was used because aluminium - ClO_4^- anion complexes are unstable in comparison with other complexes. The acidity of solutions was measured using a multi-purpose ionometer EV-74 equipped with a glass electrode (ESL-63-07). The electrode was

calibrated by means of a set of standard titre buffer solutions within pH range 1.65–9.18 (All-Union State Standard GOST 8.135–74).

Spectrophotometry was used to control the process of complex formation. Optical density was measured within the wavelength range 220–360 nm using SF-26 spectrophotometer equipped with 1 and 0.1 cm (diluting method) quartz cuvettes.

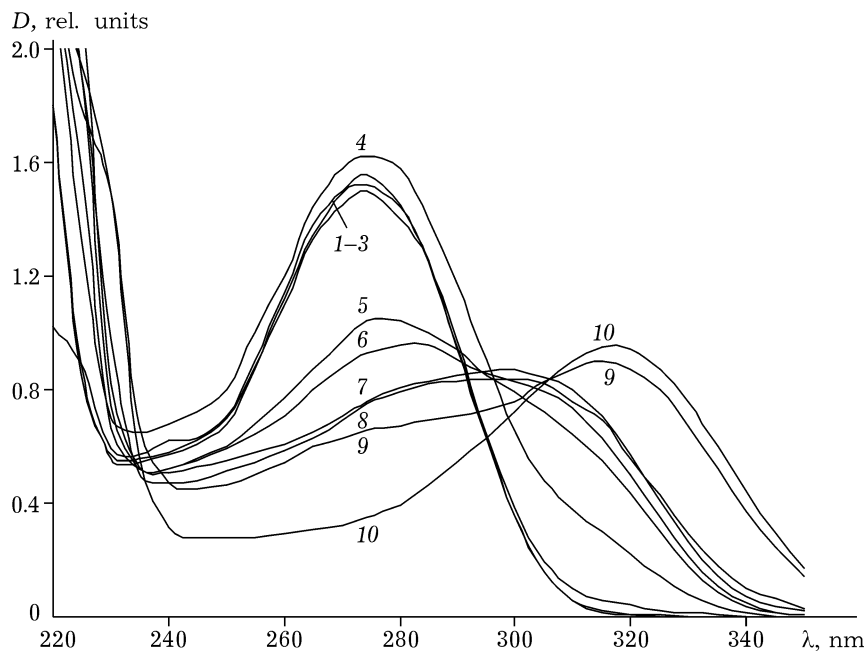


Fig. 2. Electronic spectra of the aqueous solutions of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ ($3.95 \cdot 10^{-4}$ M) and maltol (molar ratio 1 : 5).
pH values: 1.25 (1), 2 (2), 3.1 (3), 4 (4), 5.2 (5), 6 (6), 7 (7), 8 (8), 9 (9), 10 (10).

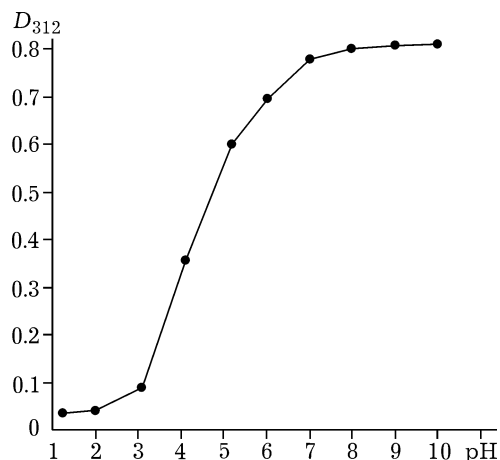


Fig. 3. pH dependence of optical density at $\lambda = 312$ nm for $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and maltol (molar ratio 1 : 5).

RESULTS AND DISCUSSION

Estimation of an appropriate wavelength range for spectrophotometric data acquisition was made in two stages. First, spectrophotometry of maltol was investigated. It was shown that maltol in the neutral form (pH 1–6) had maximum absorbance at $\lambda = 270$ nm. An increase in alkalinity (pH 7–10) resulted in the ionization of OH groups of maltol, which in turn developed a bathochromic shift of $\pi \rightarrow \pi$ electron transition, thus the absorbance maximum shifted to 320 nm (Fig. 1). Second, the electron spectra of the complexes obtained from aluminium salts and maltol with the molar ratio 1 : 5 under different conditions (pH 1–10) were recorded. One can see from Fig. 2 that the maximum absorbance of these complexes is at 305–315 nm. Therefore the optimum wavelength, at which detection was held, was 312 nm (λ_{max}).

This wavelength was used to measure the optical density (D_{312}) of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and maltol aqueous solutions depending on pH (Fig. 3). It can be inferred from the curve that there were three complex forms: the first one formed at pH 2–3, second one at pH 3–5 and the last complex at pH 5–8.

The structures of the complexes were studied utilizing the isomolar series method [8]. For that purpose, three series of solutions were made containing $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and maltol at pH 2.2, 3.4 and 6.5. These particular conditions were chosen because at these values of pH there

were sufficient amounts of Al^{3+} cations in unbound state. At the plot (Fig. 3) this condition corresponds to an increase in optical density at the part of the curve in charge of a certain complex form. As the position of maximum absorbance of pure maltol and the complex form are similar, every experiment at $\lambda_{\text{max}} = 312$ nm was made in comparison with a

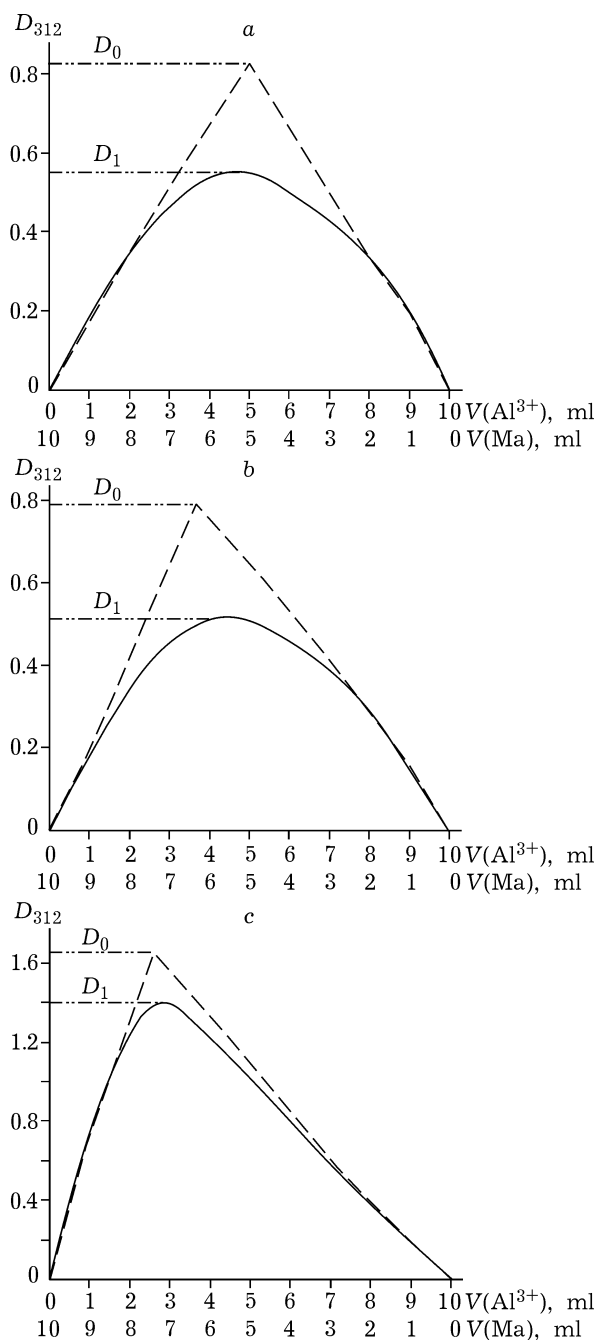


Fig. 4 Optical density vs. component ratio (aqueous solutions of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and maltol). Isomolar series: a - $C = 1.49 \cdot 10^{-3}$ M, pH 2.2; b - $C = 3.73 \cdot 10^{-4}$ M, pH 3.4; c - $C = 3.73 \cdot 10^{-4}$ M, pH 6.5.

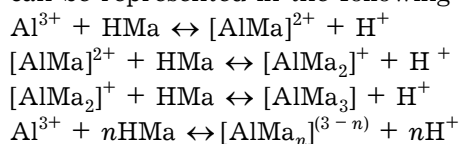
TABLE 1

Partial instability constants (k) and overall instability constants (β) of aluminium-maltol complexes, obtained by different methods

Complex formula	pH	Isomolar series method		Buger–Lambert–Berr’s law imaginary deviation method	
		k , mol/l	$\log \beta$	k , mol/l	$\log \beta$
[AlMa] ²⁺	2.2	$2.66 \cdot 10^{-4}$	3.58	$2.60 \cdot 10^{-4}$	3.58
[AlMa ₂] ⁺	3.4	$7.14 \cdot 10^{-5}$	7.72	$7.10 \cdot 10^{-5}$	7.73
[AlMa ₃]	6.5	$1.06 \cdot 10^{-5}$	12.70	$1.20 \cdot 10^{-5}$	12.64

standard solution. The latter contained the same amount of pure maltol and had the same pH as the solution under investigation. The results of these experiments are plotted in coordinates: ΔD_{312} versus the composition of the complex (Al³⁺ : Ma). One can see from Fig. 4 that the maximum of isomolar curves is observed for the molar ratios 5.0 : 5.0 (see Fig. 4, a), 3.3 : 6.6 (see Fig. 4, b) and 2.5 : 7.5 (see Fig. 4, c). The structure of the complexes was obtained from these values, *i.e.* (Al³⁺ : Ma) 1 : 1, 1 : 2 and 1 : 3.

A consequent scheme of complex formation can be represented in the following way:



where HMa is maltol molecule; Ma is maltol anion.

Partial instability constants of the complexes were found from the obtained isomolar series using Babko’s method, [8, 9]. Extrapolation of the initial regions of every curve yielded us a value of the optical density for the complex without dissociation (D_0). Then the instability constant was evaluated from equation $k = \alpha^2 C / (1 - \alpha)$, where C is solution concentration, mol/l; α is degree of transformation that can be derived from equation $\alpha = (D_0 - D_1) / D_0$ (D_0 is optical density of the complex without dissociation; D_1 is optical density corresponding to a maximum of isomolar series curve).

The instability constants (k) of [AlMa_{*n*}]^(3-*n*) complexes are given in Table 1. In order to confirm estimations of k , we used Buger–Lambert–Berr’s law imaginary deviation method [8, 9].

Three mixtures of reactants with molar ratios (Al³⁺ : Ma) 1 : 1 (pH 2.2; initial concentration equaled to overall concentration $1.49 \cdot 10^{-3}$ M), 1 : 2 (pH 3.4; $C = 3.73 \cdot 10^{-3}$ M) and 1 : 3 (pH 6.5; $C = 3.73 \cdot 10^{-4}$ M) were used. These ratios corresponded to [AlMa]²⁺, [AlMa₂]⁺ and [AlMa₃] complexes. The UV spectra of solutions were recorded within the range 295–350 nm in a 0.1 cm cell, thus the amount ΔD_1 was obtained. Then the solutions were diluted 10 times and their optical density (ΔD_{10}) was measured in a 1 cm cell. The relative change in the optical density Δ was calculated according to equation $\Delta = (D_1 - D_{10}) / D_1$. Dissociation degree (α) was derived from equation $\alpha = \Delta / (10^{1/2} - 1)$.

Considering two values: α and C , one can evaluate instability constants: $k = \alpha^2 C$. Using these constants we can calculate overall stability constants of complexes β : $\beta = 1/K$, where K is overall instability constant, which is equal to a product of all partial instability constants.

As one can see from the results represented in Table 1, there is a good consistency between the values obtained by means of Buger–Lambert–Berr’s law imaginary deviation and isomolar series methods.

CONCLUSIONS

It was shown that an increase in pH from 1 to 10 resulted in consequent formation of aluminium-maltolate complexes, with stability increasing in the following row: [AlMa]²⁺ (pH 2–3), [AlMa₂]⁺ (pH 3–4), [AlMa₃] (pH 4–8). The prevailing form at pH 4–8 is an electrically neutral, water-soluble, sufficiently stable aluminium complex ($\log \beta = 12.7$). These results are in agreement with the literature data [1],

where the hydrolytic stability of 3-hydroxypyron (maltol, pyromeconic, kojic and chlorkojic acids) complexes with Al(III) and Ga(III) was studied. In that work, the superior stability of Al(Ma)₃ complex (at pH 4.5–8) was shown. It was also noted that, for the octanol/water mixture (model lipid solubility system), this complex had the highest ($c = 0.67$) distribution coefficient, thus one can expect high brain capillary permeability.

Basing on the obtained results one can suggest maltol as a chelate ligand to form strongly bound complexes with aluminium. The properties of the complex adhere to the requirements of a substance intended to remove excess aluminium from a human organism.

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