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GLUCOSE AND GLUCURONIC ACID INTERACTIONS WITH HYDROLYSED ALUMINIUM(III)

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Abstract—Interaction of D-glucose and D-glucuronic acid and of hydrolysed aluminium(III) has been studied in 0.6 M NaCl solution. Isolated solids were analysed and studied by means of IR and ^{13}C NMR spectroscopy. Soluble samples close to the precipitation boundary were examined with UV spectroscopy. Glucuronic acid showed higher affinity toward binding to the aluminium hydroxide matrix than glucose. It is concluded that glucose is bound via hydroxyl groups on C(4) and C(6) atoms in α- and β-pyranose forms. Glucuronic acid is bound in α- and β-pyranose forms via the carboxyl group and the hydroxyl group on the C(4) atom.

Carbohydrates, due to their wide occurrence and multihydroxy functionality, are an interesting class of chemical compounds very important in processes affecting the mobility of metal ions in biological, ecological and geochemical cycles. In the previous paper we reported on the preparation and characterization of aluminium(III) complexes with fructose and sucrose.[1] The present work was carried out to investigate the ability of aluminium(III) to form complexes with glucose, an aldohexose which occurs in nature in large amounts, and with its oxidation product glucuronic acid. The structural formulae of glucose (Glu) and glucuronic acid (GAH) are given in Fig. 1. Glucose is a monosaccharide present in small amounts in the blood serum of humans and animals, and is an integral part of various biological molecules including polysaccharides (cellulose and starch). The concentration of sugars and metal ions required for complex formation in the present work are higher than those usually found in nature but, on the other hand, reactions that occur on the surface of polysaccharides in nature might correspond to ones occurring at high concentrations. Glucuronic acid, due to the presence of the carboxyl group, is expected to show greater affinity towards complexation with metals than does corresponding

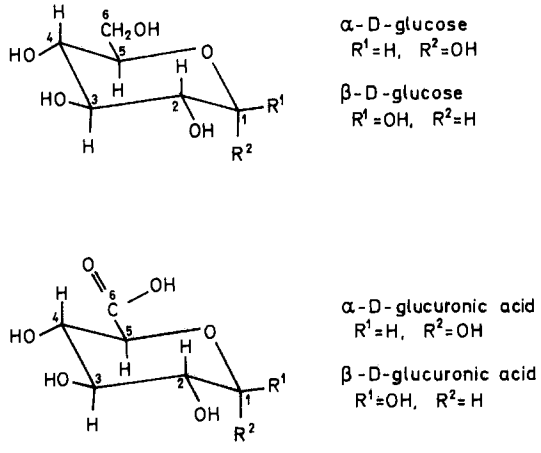

Fig. 1. Structural formulae of D-glucose and D-glucuronic acid in pyranose ring form.

aldohexose. These reactions and complexes may be important in understanding the processes which organic ligands play in the transport of aluminium in ecological and biological cycles.[2]

Although the possible role of aluminium in Alzheimer's disease (AD) is not yet clear, this element continues to be studied by AD researchers, including one of us,[3] as alumosilicates were found by Candy *et al.*[4] in brains of patients with AD.

To our knowledge, the bonding of glucose and glucuronic acid to an aluminium hydroxide matrix has not been studied. The complex of glucose with

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iron(III), isolated at very high pH values, was reported by Nagy *et al.*[5] Tajmir-Riahi studied the magnesium(II)– and calcium(II)–D-glucose adducts[6] and the complexes of glucuronic acid with Ca, Na, K, Rb, Mg, Sr, Ba and UO_2(II).[7–10] The syntheses of Ti^{4+}, V^{4+}, Cr^{3+} and Mn^{2+} complexes with glucose in non-aqueous media were also reported.[11]

In this paper the reactions of aluminium(III) with glucose and glucuronic acid in a constant ionic strength medium of 0.6 mol dm^{-3} NaCl were studied over a wide pH range and in various ligand to aluminium(III) molar ratios, with the aim of finding whether and how the organic molecules can be bound to an aluminium(III) hydroxide matrix. We are aware that the sodium chloride concentration used corresponds to the condition present in seawater; it is higher than that present in human plasma and significantly higher than in fresh water and in soil solutions. The high electrolyte concentration used was identical with that used in our previous paper,[1] in order to keep activity coefficients constant. From aluminium complexation studies, hydroxo species predominate.

EXPERIMENTAL

Materials

Stock solutions were prepared by dissolving $AlCl_3 \cdot 6H_2O$ (Merck, Germany, reagent grade), D(+)-glucose monohydrate, NaOH and NaCl (Kemika, Croatia, reagent grade) and D-glucuronic acid (Fluka, Switzerland, purrum) in doubly distilled water.

Preparation of solid phases and chemical analyses

For batch preparation of samples, solutions of aluminium chloride, of sodium chloride and of a carbohydrate were mixed. The total volume of a sample was 0.1 dm^3. The pH value was adjusted by adding dropwise a 1 mol dm^{-3} solution of sodium hydroxide. In one series of experiments the aluminium(III) concentration (2×10^{-2} mol dm^{-3}) and pH (5.9–6.1) were kept constant, while the carbohydrate to aluminium molar ratio (N) was varied from 5 to 75 for glucose and from 1 to 10 for glucuronic acid. In another series of experiments the concentration of aluminium(III) (2×10^{-2} mol dm^{-3}) and $N = 25$ for glucose and $N = 5$ for glucuronic acid were maintained constant, while pH values were varied from 4 to 9. The precipitates formed were separated by filtration, washed with ethanol to remove traces of NaCl and dried in a desiccator over silica gel. To the aqueous solution of 2×10^{-2} mol dm^{-3} $AlCl_3$ and 1×10^{-1} mol dm^{-3} glucuronic acid, which was clear after the pH adjustment to 4.5, the same volume of acetone was added. A precipitate was formed and isolated by filtration. The solid phases were chemically analysed by conventional methods. Carbon and hydrogen were estimated by classical microanalytical techniques. Sodium was determined by flame photometry after the wet decomposition of the sample in a mixture of nitric and perchloric acids. In the same acid solution aluminium was determined titrimetrically using Titriplex III solution. The samples were amorphous as detected by X-ray diffraction.

Apparatus

IR spectra were recorded with a Perkin–Elmer spectrophotometer model 580B using KBr discs.

UV spectra were recorded with a Perkin–Elmer spectrophotometer model 124.

^{13}C NMR spectra were recorded with a Varian Gemini 300 Fourier-transform spectrometer at room temperature in 5 mm o.d. tubes at 75 MHz. The spectral width was 18,700 Hz, pulse width 5.0 μs and pulse width (90°) 13.0 μs. The samples were dissolved in CD_3COOD and D_2O. Chemical shifts were measured relative to CD_3COOD set at 178.4 ppm.

Sodium was determined using a Carl Zeiss flame photometer.

pH values were measured with a Radiometer 26 pH-meter, using a combined GK 2322 C electrode, calibrated by Titrisol buffers.

RESULTS AND DISCUSSION

Composition of precipitates

On the basis of elemental analyses the molar ratio of aluminium to carbohydrate ($1/N$) was calculated for each isolated solid phase. In Fig. 2a this value is plotted vs carbohydrate to aluminium ratio in solution (N) for constant pH. In Fig. 2b this value is plotted vs pH, for constant N in solution.

For glucose (Glu) the lowest value of $1/N$ was found to be 6 at a very high value of N (75) at pH 6.1 and at a lower value of N (25) at pH 9.1 after 2 days of ageing. The deduced formula for solid isolated at pH 9.1 and $N = 25$ is $Al_6(OH)_{18}Glu$ or $(AlOOH)_6Glu(H_2O)_6$. Found: C, 10.7; H, 3.9; Al, 25.0; loss on ignition at 800°C, 52.6%. Calc.: C, 11.1; H, 4.6; Al, 25.0; loss on ignition, 52.8%. This complex was analysed further by IR and ^{13}C NMR spectroscopy. The extended ageing (30 days) causes an increase of complexation and further binding of the glucose into aluminium hydroxide matrix.

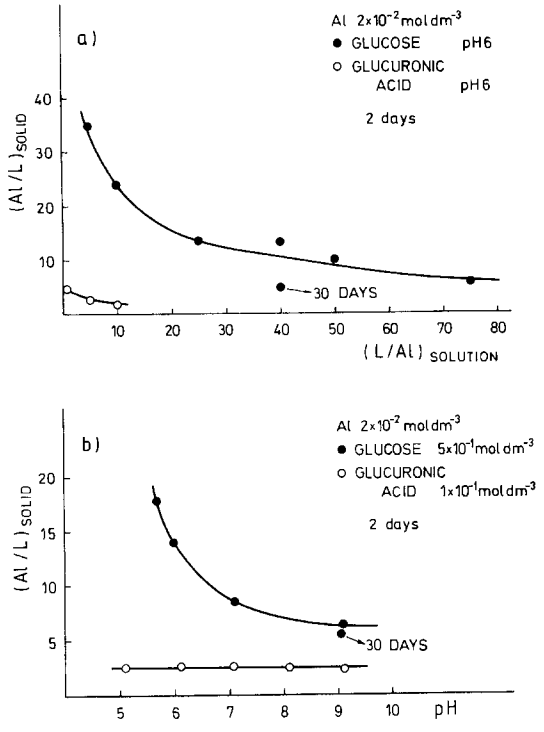

Fig. 2. Results of chemical analyses of studied precipitates presented in the form of $(Al/L)_{solid}$ plotted: (a) vs $(L/Al)_{solution}$ at constant value of pH 6, (●) glucose, (○) glucuronic acid; (b) vs pH, at constant $(L/Al)_{solution}$, 25 for glucose (●), 5 for glucuronic acid (○).

Glucuronic acid (GAH) was found to be much better bonded to aluminium hydroxide matrix than glucose, as was expected due to the presence of one carboxyl group. The data were collected with $N = 1$, 5 and 10 and variable pH values. The lowest value of aluminium to ligand ratio in solid (1.13) was obtained for the sample isolated from solution containing 2×10^{-2} mol dm^{-3} $AlCl_3$ at $N = 5$ and pH 4.5. This solid phase was precipitated by addition of acetone to clear solution just prior to formation of precipitate in aqueous solution. The deduced formula was $Al(OH)_2(GA)(H_2O)$. Found: C, 25.6; H, 4.5; Al, 11.1; loss on ignition at 800°C, 79.5%. Calc.: C, 26.5; H, 4.8; Al, 9.9; loss on ignition, 81.3%. GA is the glucuronate ion. At pH 8.1 and $N = 5$, the precipitated solid has a deduced formula $Al_7(OH)_{19}(GA)_3(Na)(H_2O)_7$. Found: C, 16.7; H, 4.6; Al, 15.2; Na, 2.2; loss on ignition at 800°C, 66.4%. Calc.: C, 17.4; H, 4.8; Al, 15.2; Na, 1.9%; loss on ignition, 66.9%. It is interesting to note from Fig. 2 that the ratio of aluminium to ligand in the solid phase has not changed considerably by varying the pH; it is dependent preferably on the ligand to aluminium ratio in solution.

UV spectral characteristics of soluble complexes

The difference UV spectra of soluble aluminium–glucose and aluminium–glucuronic acid complexes were measured. Samples were prepared with aluminium chloride solution (2×10^{-3} mol dm^{-3}), at a constant ligand to aluminium ratio of 5 and adjusting pH values in acid and alkaline regions close to the precipitation region. Solution containing the same concentration of a ligand and identical pH was used as a blank. Glucose alone shows a single peak at 190 nm, measured against doubly distilled water. This glucose peak is found to be pH independent up to 10.6. The aluminium–glucose complex shows a weak maximum at a similar position (e.g. 193 nm) at pH 3.9, which is shifted to 210 nm at pH 10.6. This red shift of about 20 nm we ascribe to a complexation reaction. Because there is no absorbance between 290 and 310 nm, in which region the broad band was found for a number of saturated aldehydes, it can be concluded that the glucose molecule preserved its ring form. Glucuronic acid shows a single peak, slightly pH dependent, at 198 nm for pH 2.9 and 204 nm for pH 10.7, measured against doubly distilled water. The aluminium–glucuronic acid complex shows a weak and broad maximum at shifted position, e.g. at 213 nm for pH 2.9 and at 217 nm for pH 10.7.

IR spectral characteristics of solid samples

IR spectra of representative samples and corresponding free ligands are presented in Fig. 3a for glucose and in Fig. 3b for glucuronic acid. All the sharp bands observed in the case of glucose and glucuronic acid are merged and become broad due to complex formation. Based on the assignments reported in the literature,[6,10,12] the most characteristic features of the IR spectra can be assigned as follows: the free glucose O—H stretching vibrations in the 3400–3000 cm^{-1} region are overlapped in the spectra of aluminium–glucose complex by the band of O—H stretching vibrations of coordinated water molecules. The C—H stretching vibrations at about 2900 cm^{-1} found in the ligand exhibited no major changes on aluminium–glucose complex formation. The medium band at about 1640 cm^{-1} found in the aluminium–glucose complex is due to the H_2O bending mode, which is absent in the free D-glucose spectrum. The weak band at 1520 cm^{-1} arises from the matrix of aluminium hydroxide. The bands of free glucose appearing in the region of 1460–1200 cm^{-1} are due to O—C—H, C—C—H and C—O—H bending vibrations. They are of medium or weak intensity. In the spectrum of the aluminium–glucose complex,

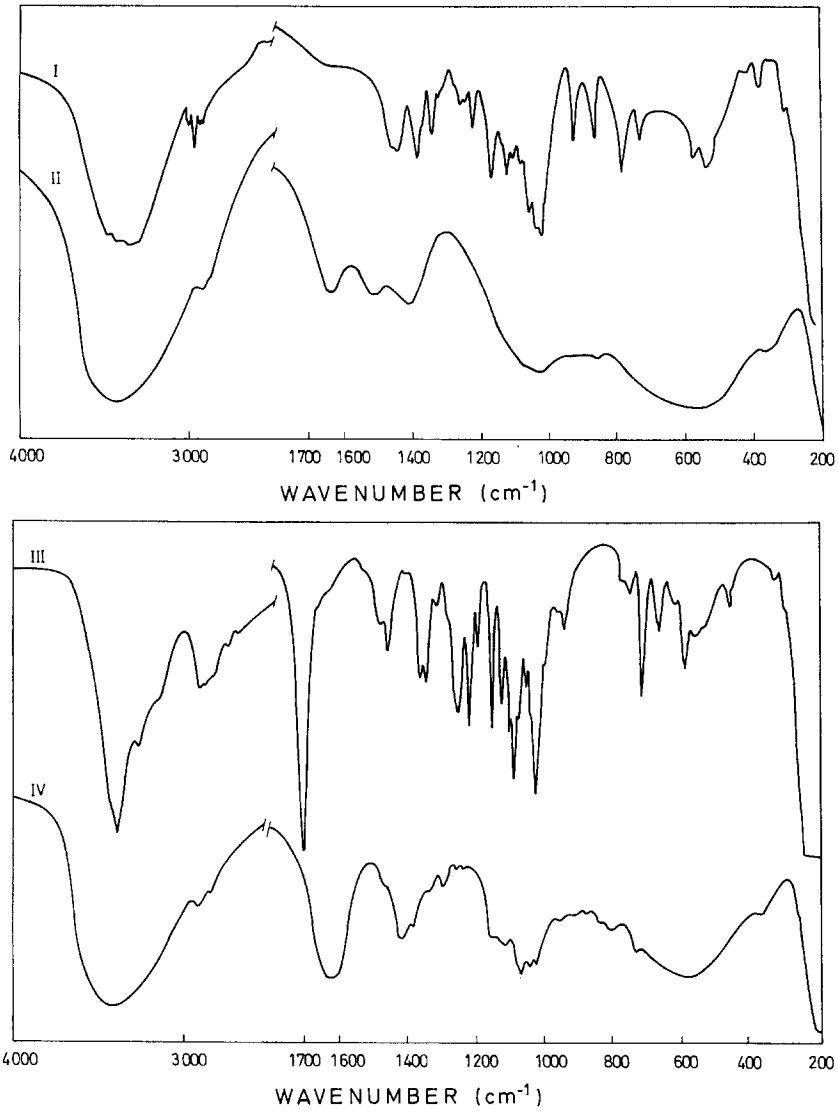

Fig. 3. IR spectra of free ligands and corresponding aluminium complexes: (a) I, glucose; II, $Al_6(OH)_{18}Glu$; (b) III, glucuronic acid; IV, $Al(OH)_2(GA)(H_2O)$.

only the band at 1420 cm^{-1} is present. The bands observed in the 1160–900 cm^{-1} region in the ligand, assigned to C—O and C—C stretching modes, show alteration upon aluminium–glucose complex formation; only a broad band of medium intensity at 1030 cm^{-1} is present. The bands below 900 cm^{-1} are due to the C—C—H and C—H bending modes, C—C and C—O stretching modes, and skeletal deformation and internal rotation. The band observed in the spectrum of aluminium–glucose complex at 860 cm^{-1} (due to C—H and C—C—H bending and C—C stretching) shows a decrease in intensity. The other bands in this region are overlapped with a strong and broad band at about 560 cm^{-1}, which is assigned to Al—O stretching vibrations.[13] The weak band at 350 cm^{-1} could be assigned to aluminium–oxygen stretching vibrations, according to the tentative assignment of Finnegan *et al.*[14] These two bands are present in the spectra of $Al(OH)_3$ isolated at various pH values. The two spectra presented in Fig. 3b can be compared as follows: in the spectrum of the aluminium–glucuronic acid complex, it is noteworthy that the strong and sharp absorption band of free acid at 1705 cm^{-1}, related to the COOH stretching vibration, shifts to lower frequency and splits into two absorption bands at 1620 and 1415 cm^{-1}, assigned to COO^- antisymmetric and symmetric stretching vibrations, respectively.[15] There is an overlap resulting in a broad and strong band at 1620 cm^{-1} due to the water bending mode. The splitting and shifting of the COOH stretching vibration of glucuronic acid upon complexation indicate the participation of the carboxylic oxygen

Table 1. ^{13}C NMR chemical shifts (ppm) of ligands and aluminium complexes

Compound			C(1)	C(2)	C(3)	C(4)	C(5)	C(6)
D-Glucose (pyranose form)		α	92.6	72.1	73.5	70.4	71.9	61.5
		β	96.5	74.8	76.4	70.3	76.4	61.5
$Al_6(OH)_{18}Glu$		α	92.4	71.9	73.3	70.1	71.8	61.2
($N = 25$, pH 9.1)						69.6		64.5
		β	96.3	74.6	76.7	70.1	76.7	61.2
						68.2		63.6
D-Glucuronic acid (pyranose form)	pH 1.8	α	93.2	72.0	73.4	72.4	71.4	172.9
		β	96.9	74.7	76.3	72.2	75.4	173.8
	pH 7.8	α	92.9	72.2	73.5	73.0	76.9	176.9
		β	96.7	75.0	76.5	72.7	72.6	177.6
$Al(OH)_2(GA)(H_2O)$		α	93.4	72.5	73.7	72.9	77.2	181.8
($N = 5$, pH 4.5)		β	97.1	75.1	76.6	73.2	72.5	181.8
$Al_7(OH)_{19}(GA)_3(Na)(H_2O)_7$		α	93.4	72.5	73.7	72.9	77.2	181.8
($N = 5$, pH 8.1)		β	97.1	75.1	76.7	73.2	72.5	181.9

Glu = glucose, GA = glucuronate ion.

atoms in the aluminium–glucuronic acid bonding. The bands at 870 and 835 cm^{-1} assigned to bending modes of β- and α-anomers respectively indicate that both anomers are included in the bonding to the aluminium hydroxide matrix. The other assignments are almost the same as in the aluminium–glucose complex.

Aluminium-induced chemical shifts in the ^{13}C NMR spectra of glucose and glucuronic acid

Complexation of aluminium(III) with glucose and glucuronic acid was studied on selected samples for each ligand in order to obtain information about the possible binding sites for aluminium. As the ^{13}C chemical shifts of glucose and glucuronic acid are known,[16] these data were used to assign the carbon atoms in the studied compounds and to observe the changes. The results are given in Table 1. In the aluminium–glucose complex $Al_6(OH)_{18}Glu$, the changes in chemical shift took place at C(4) (upfield) and C(6) (downfield) of α- and β-glucopyranose. It is an indication that both configurations can form complexes with aluminium hydroxide matrix via hydroxyl groups on C(4) and C(6) atoms. The existence of both glucopyranose anomers in aluminium(III) complexes could be expected, as in aqueous solution glucose is in the pyranose form (>99%) and the equilibrium solution contains 36% α-pyranose and 64% β-pyranose.[17] Aluminium(III) with glucose behaves completely differently from calcium and magnesium studied by Tajmir-Riahi.[6] He suggested that the α-anomeric configuration is favoured by calcium and magnesium and that binding possibly occurs via the hydroxyl groups on C(1) and C(2) atoms.

In the two aluminium–glucuronic acid complexes $Al(OH)_2(GA)(H_2O)$ and $Al_7(OH)_{19}(GA)_3(Na)(H_2O)_7$, the changes in chemical shift took place at C(6) (downfield) of the α- and β-pyranose ring forms. These shifts are related to the ionization of the carboxyl group[18] with $pK = 3.07$ and to bonding to the aluminium hydroxide matrix via this group. The shifts at C(5) (downfield for α-anomer, upfield for β-anomer) and at C(4) (α- and β-anomer, downfield) suggest that the D-glucuronic acid molecule is also bonded to the aluminium hydroxide matrix through the hydroxyl group on the C(4) atom. The participation of the hydroxyl group on the C(4) atom in the binding to metal ions was observed in the complexation of D-glucuronic acid to bivalent cations such as Ca, Mg, Sr, Ba and UO_2(II), but in these complexes either α- or β-anomer dominated in isolated solids. Both anomers are present in the aluminium(III)–glucuronic acid complexes.

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