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Preparation and Properties of Fe(III)–Sugar Complexes

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The synthesis of new Fe(III)–sorbitol, Fe(III)–glucuronic acid and Fe(III)–glucosamine complexes has been performed. The complexes were characterized by physico-chemical measurements and chemical analysis. Molecular weight determination and Mössbauer spectroscopic measurements showed that the complexes are polymeric in the solid state and also in aqueous solutions.

Introduction

A large number of works concerning the complexation of iron with sugars and polyols have been published. These complexes may have a role in the transport of iron across the cell membrane, giving considerable investigation possibilities [1–4] of iron metabolism.

It has been found that some hexoses, pentoses, tetroses, sugar alcohols and dextrans [1, 5] keep hydrolysed Fe(III) salts in solution indicating a complexation process [1]. An excess of sugar in the solution prevents Fe(III) hydroxide precipitation and low molecular weight complexes are formed [6]. Isolation of solid Fe(III)–sugar complexes was usually performed by the addition of alcohol to the solution containing the Fe(III)–sugar complexes. Isolated complexes in the solid state are mainly polymers. Molecular weights determined by ultracentrifuge, membrane osmometry or gel filtration techniques range between 2000 and 150000 [5, 7].

The preparation, isolation, analytical characterization and Mössbauer study of Fe(III)–fructose and Fe(III)–sorbose complexes have already been described [8].

The present work deals with the preparation, isolation and analytical characterization of Fe(III) complexes with sorbitol, glucuronic acid and glucosamine.

Experimental

Materials

All chemicals used were of analytical grade.

Methods of Preparation and Isolation

Reaction of sorbitol with Fe(III)

Equal volumes of water solutions of 0.1 *M* (Fe-$(NO_3)_3$ and 1.0 *M* sorbitol were mixed and the acidity of the solution adjusted to pH 9 by addition of NaOH. By addition of ethanol (the solution was made up to 80% in ethanol) a precipitate of Fe(III)–sorbitol was formed. The precipitate was separated by centrifugation, dissolved in a small volume of water and allowed to pass through a column of G-100 molecular Sephadex sieve to remove small molecules. The collected eluate was dried by lyophilization. *Anal.* Found: C, 27.76; H, 5.89; Fe, 11.16; Na, 3.87%.

Reaction of glucuronic acid with Fe(III)

Equal volumes of water solutions of 0.5 *M* Fe-$(NO_3)_3$ and 0.5 *M* glucuronic acid were mixed and the pH adjusted to 9 with NaOH. The procedure of complex precipitation and isolation was the same as described above. *Anal.* Found: C, 15.95; H, 2.56; N, 5.56; Fe, 12.24; Na, 12.26%.

Reaction of glucosamine with Fe(III)

Equal volumes of water solutions of 0.1 *M* $Fe(NO_3)_3$ and 1 *M* glucosamine·HCl were mixed and the pH of the solution was adjusted to 9 with NaOH. A brown precipitate was obtained. After a few days the precipitate dissolved leaving a deep brown solution. By the addition of ethanol (the solution was made up to 80% in ethanol) a precipitate of Fe(III)–glucosamine was formed. The precipitate was redissolved in water and reprecipitated. The complex

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TABLE I. Gel Filtration and TLC Data of Fe(III)–Sugar Complexes.

Complex	Fraction	Molecular weight	R_f
Fe(III)–sorbitol	I	>100000	–
Fe(III)–sorbitol	II	~5000	0.10
Fe(III)–glucuronic acid	I	>50000	–
Fe(III)–glucuronic acid	II	~5000	0.09
Fe(III)–glucosamine		~5000	0.07

was separated by centrifugation, washed with ethanol, acetone and ether and dried over P_2O_5. *Anal.* Found: C, 17.32; H, 4.03; N, 3.50; Fe, 25.54; Na, 3.34%.

Fe(III)–sorbitol and Fe(III)–glucuronic acid complexes were prepared using slightly modified methods from those described elsewhere [6, 8]. The optimal conditions for the preparation of the Fe(III)–glucosamine complex were found and are presented above.

Methods of Analysis

The methods of analysis used were the same as described previously [8]. Analyses of iron, carbon, hydrogen, sodium, nitrogen, IR spectroscopic analysis, molecular weight determination, thin layer chromatography and Mössbauer spectroscopy measurements were performed.

For gel filtration analysis the molecular sieves G-25 and G-100 were used. Before analysis, the molecular sieves were standardized with blue dextran, dextranes (M.W. 80000, 40000 and 10000) and fructose.

Results and Discussion

Evidence for the complex formation was confirmed by physical measurements and chemical analyses of the isolated solid compounds.

The complexes are water soluble giving stable deep brown solutions with the exception of Fe(III)–glucosamine which is less stable.

Thin layer chromatography (TLC) showed the existence of the compounds containing iron and sugar, with Rf values different from sugar and iron nitrate. The fact that the complexes migrate almost to the starting position indicates that they are high molecular weight compounds. Rf values are presented in Table I. In Table I gel filtration data are presented, which show that the complexes are mainly small polymers.

The Mössbauer parameters of the solid Fe(III)–sugar complexes recorded at room temperature are shown in Table II. The values of isomer shifts and quadrupole splittings support the polymeric structure of the complexes. The Mössbauer spectra of the diluted frozen aqueous solutions of the complexes have also been recorded. The absence of magnetic hyperfine splitting has also proved [8] that there are at least two iron atoms in the complexes. However, the results of the molecular weight measurements suggest the presence of more than two iron atoms in the complex molecules. The iron atoms in the polynuclear complex are very probably linked via oxygen bridges as indicated by the Fe–O infrared band.

Infrared spectra of all complexes are rather simple and very similar. In Table III some characteristic frequencies of Fe(III)–sugar complexes, sugar used as ligands and Fe(III)–hydroxy polymer are presented.

All spectra of the Fe(III)–hydroxy polymer, sugars and Fe(III)–sugar complexes exhibit bands with maxima at 3280–3420 cm^{-1}, originating from O–H stretching vibration and can be attributed to lattice and coordinated water molecules and hydroxy groups. Spectra of the sugars and Fe(III)–sugar complexes exhibit bands with maxima between 2930–2940 cm^{-1} which can be assigned to C–H stretching vibrations and indicate the presence of sugars in the complex molecules. A weak band at 1625 cm^{-1} appears in the spectra of the Fe(III)–hydroxy polymer and is assigned to H–O–H bending modes from lattice or coordinated water molecules. In the

TABLE II. Mössbauer Parameters of the Solids Fe(III)–Sugar Complexes at Room Temperature.

Complex	$\delta_{Fe(III)}$[a] mm/s	$\Delta E_{Fe(III)}$ mm/s	$\Gamma_{Fe(III)}$ mm/s	$A_{Fe(III)}$[b] %
Fe(III)–sorbitol	0.370	0.918	0.495	–
Fe(III)–glucuronic acid	0.352	0.843	0.489	13.6
Fe(III)–glucosamine	0.356	0.774	0.461	3.0

[a] Values are referred to metallic iron. [b] A is the area of the line as percentage of whole area. The uncertainty of the results is ±0.005 mm/s.

TABLE III. Infrared Frequencies in cm^{-1}.

Fe(III)–hydroxy polymer	Sorbit	Fe(III)–sorbit	GlcCOOH	Fe(III)–GlcCOOH	$GlcNH_2$	Fe(III)–$GlcNH_2$	Assignment [12]
3360s,br	3400s,br	3400s,br	3400m	3420s,br	3280s	3310s,br	ν(O–H)asoc.
							$\nu(NH_3^+)$
	2940w	2930w	2950w	2930w	3090w	2930w	
	2900w	2860w			3030w		ν(C–H)
					2940w		
1625w	1650m	1600m,br		1625s,br	1610m	1640s,br	ν(C=O, C=C)
							ν(H–O–H)
			1710s				$\delta(COO^-)$ asym.
1387s	1415m	1390m,br	1368m	1388vs	1420m	1388s,br	$\nu(NO_3^-)(COO^-)$ sym.
							δ(C–H)
					1530s		$\delta(NH_3^+)$
	1085m	1070m	1090m	1050m,br	1090m	1090sh	δ(OH), ν(C–N)
	1030sh	1040sh	1030m		1030s	1040s,br	ν(C–O)
	890m	880w	770m		910m	790vw	region of the spectra
	750w	770w	670m		850m		in which the molecule
					770m		vibrates as a whole [9]
840vw				839m			δ(O–N–O)
450w,br		470br		490m,br		480m,br	ν(Fe–O)

spectra of all sugars and Fe(III)–sugar complexes also, bands appear but of medium or strong intensity in the region of 1600–1650 cm^{-1}. These frequencies may be attributed to water molecule vibration and C=C stretching vibration due to the formation of the enolic form of sugars in basic media [9].

Glucuronic acid exhibits a strong maximum at 1710 cm^{-1} which is assigned to the free carboxylic group. In spectra of the Fe(III)–glucuronic acid complex this band disappears and two new bands occur at 1625 cm^{-1} and 1388 cm^{-1}. A strong band at 1625 cm^{-1} can be assigned as H–O–H bending modes from water molecules and antisymmetric stretching vibration of the carboxylate group. A very strong band at 1388 cm^{-1} is assigned to symmetric stretching vibration of the carboxylate group which indicates a sodium carboxylate bond. The maximum at 1530 cm^{-1} in the spectrum of free glucosamine disappears in the Fe(III)–glucosamine complex indicating complexation through the amino group.

Absorption bands in the region of 1030–1090 cm^{-1} present in spectra of all sugars and Fe(III)–sugar complexes may be assigned to C–O stretching vibration and O–H bending vibration which indicates the presence of sugars in complexes.

In the Fe(III)–hydroxy polymer and Fe(III)–glucuronic acid spectra maxima occur at about 840 cm^{-1} attributable to nitrate bending. The frequency at 1388 cm^{-1} can be attributed to nitrate bending as well, but in the spectra of Fe(III)–glucuronic acid this band is overlapped by the symmetric stretching vibration of the carboxylate group. The presence of nitrate was also proved by chemical microanalysis.

Infrared spectra of all complexes exhibit bands in the region of 470–490 cm^{-1} which can be assigned

TABLE IV. Elemental Analysis.

Complex	Molar ratio				Fraction
	C/Fe	N/Fe	Sugar/Fe	Na/Fe	
Fe(III)–sorbitol	11.56	–	1.92	0.84	II
Fe(III)–glucuronic acid	6.07	1.81	1.01	2.43	II
Fe(III)–glucosamine	3.16	0.55	0.53	0.32	–

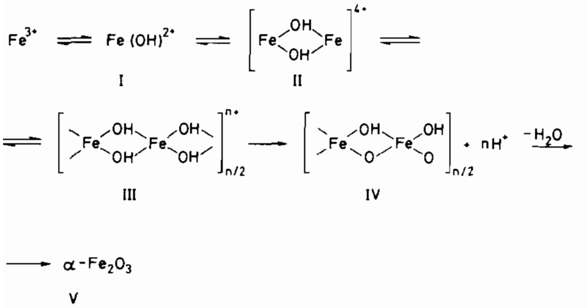

Fig. 1. Formation of Fe(III)–hydroxy polymer.

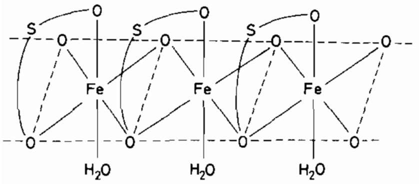

Fig. 2. Fe(III)–sugar polymer [15].

to Fe–oxy and –hydroxy bent bridge vibrations [10, 11].

Table IV presents elemental analysis data in terms of ratio to iron as unit. The compounds with molecular weights larger than 10000 (fraction I) were isolated in an insufficient amount for chemical analysis. From the results presented in Table IV it can be seen that polymeric complex units are composed of one and two sugar molecules bonded to one iron atom, and one sugar molecule bonded to two iron atoms respectively.

The formation of a solid Fe(III)–hydroxy polymer in the process of hydrolysis of $Fe(NO_3)_3$ was studied by Mössbauer spectroscopy [13] and the mechanism of reaction is given in Fig. 1.

It seems possible that complexation of sugars with Fe(III) takes place in the III and IV phases of polymer formation, preventing precipitation of the Fe(III)–hydroxy polymer. Oxo and hydroxo bridging is proposed by several authors [6, 14–17].

The structures of newly prepared complexes are probably similar to those presented in Fig. 2 but with some differences in the composition of polymer units (see Table IV). The real structure of the complexes can be found only by X-ray structure analysis, but as the complexes obtained were amorphous this type of analysis was not performed.

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