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Transition-metal saccharide chemistry: synthesis, spectroscopy, electrochemistry and magnetic susceptibility studies of iron(III) complexes of mono- and disaccharides ☆

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Abstract

Low molecular weight, soluble and characterizable saccharide complexes of iron(III) were synthesised from MeOH using stoichiometric quantities of saccharides and sodium metal. Monosaccharides such as D-glucose, L-sorbose, D-fructose, D-mannose and D-galactose, and disaccharides such as lactose, maltose and sucrose were used for complexation. The final iron(III)–saccharide complexes were isolated, purified and characterised by various analytical, spectroscopic methods including Mossbauer, magnetic susceptibility and electrochemical methods. While half of these complexes were found to be mononuclear, the rest exhibited characteristics close to hydroxo-bridged dinuclear species. The inherent stability and hydrolytically robust nature of these complexes over a wide range of pH was demonstrated. The reductive release of iron from these complexes was shown to be better than that of the iron–dextran complex reported in the literature. Based on their demonstrated properties these may be considered as potentially important in the oral nutritional supplementation of iron.

Keywords: Transition metal–saccharide complex; Iron(III)–saccharide complex; Electrochemistry; Mossbauer spectroscopy; ESR spectroscopy; Magnetic susceptibility

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☆ This paper is dedicated to Professor C.N.R. Rao, FRS on his sixtieth birthday.

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1. Introduction

The complexation of iron with saccharides and polyols has been extensively studied because of its potential use in the treatment of iron-deficiency anemia [1–3]. Both iron(III) and iron(II) are absorbed equally well if they are properly solubilised [4]. However, the reversal to the higher oxidation state becomes increasingly favoured as the medium gets more alkaline. It is under such circumstances that chelation assumes paramount importance if precipitation (or inert polymer formation) is to be forestalled and the metal is to remain bioavailable. Although iron(III) ion interaction with carbohydrates and polyols has been a subject of several researchers [5–10], including the early work of Saltman and co-workers, quantitative information is rather scarce. If low molecular weight and soluble transition metal saccharide complexes can be synthesised and isolated, this will be of utmost importance in aspects such as catalysis, biology, medicine and material science and technology.

In view of these facts we have attempted to synthesise stable iron(III) complexes. The choice of ligands made was saccharides because of the fact that saccharides facilitate the diffusion of the complexes through membranes, though the exact mechanism is not known [11]. Our laboratory has been extensively involved in the development of transition-metal saccharide chemistry and biology of a variety of ions [12–15] including those of iron and molybdenum. In this paper we report the synthesis, isolation, characterisation and solution studies of iron(III) complexes of mono- and disaccharides.

2. Experimental methods

Iron(III)–monosaccharide complexes. — Monosaccharide (2.7 g, 15 mmol) (D-Glc, L-Sor, D-Fru, D-Man, or D-Gal), was suspended in 50 mL of methanol and stirred for 10 min. To this mixture sodium metal (0.69 g, 30 mmol) was added in small pieces with stirring until all of it was reacted to form a corresponding sodium salt. To this sodium salt, a 25 mL methanolic solution of anhydrous iron(III) chloride (0.811 g, 5 mmol) was added to give a brownish-yellow precipitate. The reaction mixture was further stirred for about 3 h in order to ensure the completion of the reaction. A solid product was obtained by filtering the reaction mixture and further washing with ether and drying under vacuum. The solid thus obtained was later purified by dissolving it in a 2:1 water–methanol mixture and reprecipitating the product with ethanol, thereby removing the free saccharide present. This procedure was repeated thrice. Further, the product was stirred in 20 mL of methanol thrice overnight. Similar purification procedure was repeated with hexane and the filtered product was dried under vacuum. These reactions resulted in products Fe–D-Glc (**1**), Fe–L-Sor (**2**), Fe–D-Fru (**3**), Fe–D-Man (**4**) and Fe–D-Gal (**5**). Preliminary results for the preparation of **1** and **3** have been reported earlier [12].

Iron(III)–disaccharide complexes. — The requisite disaccharide (Mal, Lac, Suc), (3.43 g, 10 mmol) was suspended in 100 mL of methanol and stirred for 10 min. To this mixture, sodium metal (0.92 g, 40 mmol) was added with stirring until all the sodium reacted to form the corresponding sodium salt. To the sodium salt, a 30-mL methanolic solution containing anhydrous iron(III) chloride (0.811 g, 5 mmol) was added to give a brownish-yellow precipitate. Separation and purification was carried out by the same procedure as mentioned for previous case. These reactions resulted in products Fe–Mal (**6**), Fe–Lac (**7**) and Fe–Suc (**8**).

All the Fe(III) complexes reported in this paper are found to yield products in the range 42–65% based on iron content.

Iron(III)–aluminium(III)–saccharide complexes. — To the sodium salt of the appropriate monosaccharide generated in 50 mL of MeOH with 15 mmol of saccharide (D-Glc, D-Fru or D-Man) and 30 mmol sodium, a 25 mL methanolic solution containing 0.40 g (2.5 mmol) of anhydrous iron(III) chloride and 0.94 g (2.5 mmol) of aluminum nitrate was added to give a brownish-yellow precipitate. The reaction mixture was further stirred for about 3 h. Solid products were obtained: (Fe–Al–D-Glc (**1a**), Fe–Al–D-Fru (**3a**) and Fe–Al–D-Man (**4a**) by filtering the reaction mixture and further washing the product with ether and drying under vacuum.

Purity of the complexes. — The purity of the complexes were checked by silica gel TLC using a 60 : 40 : 1 : 0.5 : 20 mL butanol–acetone–HCl–acetylacetone–H_2O mixture. Sulfuric acid and potassium ferrocyanide sprays were used for identification of carbohydrates and iron, respectively. The single spot obtained in TLC experiments not only revealed the complexation between the iron and saccharide, but also its purity. The purity of complex **1** was also checked by column chromatography (alumina), where the purity of elutions were monitored by absorption spectra and were found to be essentially the same.

Characterization. — The percentage of iron and sodium present in the complexes were determined by using inductively coupled plasma–atomic emission spectroscopy (ICP–AES). The analytical and elemental analysis data are presented in the Table 1. Thermogravimetric analyses of these complexes were done in air with a heating rate of 10°C min^{-1} in the range 25–1000°C. All the characterisation methods are the same as those explained in our earlier papers [12b,13e].

3. Results and discussion

The decomposition of the complexes **1–8**, in general, resulted in a weight loss of about 75%, which corresponds to the removal of saccharide moieties and water present in the complexes. These complexes are hygroscopic and hence require special precautions in handling. Analytical data of all mono- and disaaccharide complexes **1–8** are provided in Table 1.

Absorption spectra. — Both the monosaccharide **1–5** and disaccharide **6–8** complexes of iron(III) are highly soluble in water and can be dissolved in MeOH and *N,N*-dimethylformamide using 18-crown-6 due to the complexation of sodium with the crown ether. Typical absorption spectra of the complexes **1–8** are shown in Fig. 1, and the corresponding data in three different solvents are given in Table 2. The spectra are consistent with the presence of high-spin iron(III) centres and are characteristic of the complexation of saccharides through deprotonated hydroxyl groups. The band observed

Table 1
Elemental analyses [a] of complexes (**2** and **4–8**)

Complex	Formula	Analysis [b] (%)			
		Fe	Na	C	H
2	$C_{12}H_{24}O_{14}FeNa$	o 12.20	4.98	31.08	4.90
		c 11.85	4.88	30.59	5.14
4	$C_{18}H_{37}O_{23}Fe_2Na_3$	o 13.24	7.99	26.50	4.46
		c 13.93	8.60	26.95	4.65
5	$C_{24}H_{45}O_{28}Fe_2Na_5$	o 10.54	11.48	28.66	4.11
		c 11.08	11.40	28.59	4.50
6	$C_{13}H_{26}O_{14}FeNa$	o 11.73	4.90	32.42	5.39
		c 11.51	4.74	32.18	5.40
7	$C_{12}H_{22}O_{13}FeNa$	o 12.50	5.47	31.56	5.12
		c 12.33	5.07	31.81	4.89
8	$C_{48}H_{90}O_{50}Fe_2Na_4$	o 07.02	5.30	33.88	5.77
		c 06.69	5.50	34.50	5.43

[a] Analysis could not be carried out under complete exclusion of moisture.
[b] o, Observed; c, calculated, based on formula provided.

in the region 370–390 nm may be ascribed to the formation of an iron(III)–saccharide complex as the formation of such complex was considered in the reaction between iron(III) chloride and fructose in solution by Araki and Shiraishi, prior to the photochemical oxidation of the saccharide [16]. A recent extended X-ray absorption fine-structure study [17] provided evidence for a direct coordination between iron and the ligand oxygens with an Fe–O distance in the range 1.90–1.98 Å. The two bands observed in the region 250–390 nm correspond to oxo → metal charge transfer transitions. The other

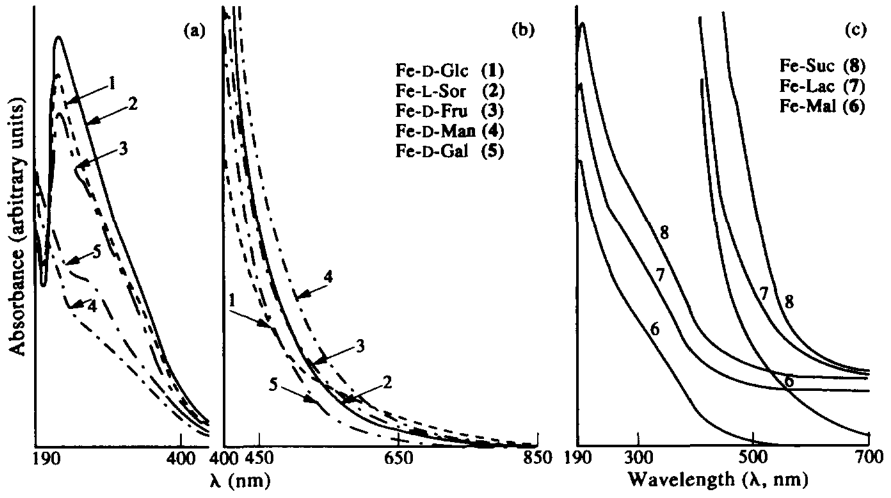

Fig. 1. Aqueous absorption spectra of the iron(III)–monosaccharide complexes, **1–5**, panels a and b; and iron(III)–disaccharide complexes, **6–8**, panel c.

Table 2
UV-vis absorption data of complexes **1**–**8** in H_2O, MeOH and *N*,*N*-dimethylformamide

Solvent	Complex	λ nm (ε, cm^{-1} M^{-1})				
H_2O	**1**	225 (4187)	260 (3522)	320 (2272)	470 (164)	570 (49)
	2	226 (4974)	260 (3953)	320 (2458)	460 (384)	550 (128)
	3	225 (12666)	260 (6720)	320 (6666)	460 (505)	590 (120)
	4	192 (12439)	280 (5837)	370 (5837)	470 (264)	540 (73)
	5	192 (23746)	270 (7209)	360 (3172)	470 (153)	580 (104)
	6	199 (6489)	280 (4872)	360 (2382)	470 (265)	550 (108)
	7	200 (6667)	280 (4761)	360 (1116)	490 (180)	560 (68)
	8	212 (13764)	304 (6662)	370 (2665)	480 (489)	580 (93)
MeOH	**1**	209 (6398)	250 (5483)	300 (3948)	470 (118)	570 (18)
	2	211 (6653)	280 (4808)	320 (3606)	490 (116)	590 (53)
	3	208 (15934)	230 (15158)	300 (9871)	465 (479)	545 (11)
	4	210 (11656)	250 (10724)	310 (6061)	480 (109)	580 (59)
	5	205 (17976)	270 (12505)	330 (7816)	470 (521)	540 (115)
	6	208 (5925)	270 (4083)	310 (3111)	470 (97)	590 (12)
	7	220 (4647)	260 (3468)	310 (2566)	480 (120)	550 (48)
	8	230 (14515)	300 (10161)	360 (4838)	480 (201)	590 (19)
Me_2N CHO	**1**	265 (5133)	330 (2965)	380 (1092)	470 (77)	530 (22)
	2	266 (5679)	330 (3292)	370 (1811)	470 (113)	550 (27)
	3	267 (9454)	320 (6152)	380 (2197)	470 (318)	550 (105)
	4	267 (4610)	300 (3720)	350 (2439)	470 (284)	540 (171)
	5	270 (4950)	340 (2805)	390 (1320)	470 (160)	580 (26)
	6	267 (2064)	350 (1111)	390 (347)	490 (74)	570 (16)
	7	267 (1328)	340 (719)	390 (336)	470 (144)	570 (48)
	8	270 (3080)	350 (1897)	390 (759)	490 (109)	580 (79)

two weak shoulders observed around 470 and 560 nm are characteristic of the *d*–*d* transitions for octahedral, high-spin d^5 complexes [18]. Complexes **1**–**8** exhibited ϵ_{d-d} values which are 2 to 10 times lower than iron(III) complexes of μ-oxo-μ-dicarboxylate possesing three *N*-donors [19]. The 479 nm shoulder showed marginal shift in MeOH and *N*,*N*-dimethylformamide. The marginal changes observed in the absorption spectra among the three solvents may suggest the involvement of solvent molecules in the coordination sphere. This is in accordance with our findings based on IR, TG and elemental analyses that the H_2O molecules are indeed involved in these complexes.

FTIR spectra. — FTIR spectra of **1**–**8** are quite different from their parental ligand spectra and are suggestive of complex formation. The spectra of the complexes are indicative of the breakage of extensive intermolecular hydrogen bonds existing in the solid state of the parent ligands [20], thus resulting in a broad band at 3390 ± 10 cm^{-1} ($\Delta\nu_{1/2} = 390$–410 cm^{-1}) with a small low frequency component as a shoulder at 3290 ± 10 cm^{-1} upon complex formation. The main ν(OH) band observed around 3390 ± 10 cm^{-1} may be envisaged as arising from the OH groups involved through weak lattice interactions, and the shoulder at ~ 3290 cm^{-1} may be assigned to some strong intermolecular hydrogen-bonded species. This region is further complicated due to the overlap with ν(OH) of water molecules. The bands observed between 2920 and 2940 cm^{-1} are assignable to ν(C–H) indicating the presence of saccharide moieties in the products. This spectral pattern is common with both mono- and disaccharide complexes. All the sharp bands observed in the free ligand spectra and the spectra of sugar adducts of non-transition elements [20,21] in the region of 800–1400 cm^{-1} are found to be merged and broadened upon complex formation where the individual vibrations can be noted through their shoulders. The broadening of IR bands also occured, even in the saccharide complexes of other first-row transition elements [12b,13–15]. Yet another evidence for the presence of water molecules may also be derived from the δ(H–O–H) bending vibrations observed at 1603 ± 10 cm^{-1} in all the complexes studied. All the complexes exhibited bands in the range 509–519 cm^{-1}, assignable to ν(Fe–O) vibrations [22].

EPR spectra. — The X-band EPR spectra of **1**–**8** in the solid state exhibited one sharp band at $g \sim 4.2$ and another very broad band at $g \sim 2.1$. The corresponding spectra of the complexes are shown in Fig. 2, and the numerical data are given in Table 3. While the narrow band is assignable to the isolated high-spin iron(III) (iso), the broad band is assignable to a signal arising from strong interactions between the paramagnetic, high-spin iron(III) centres (int). Similar EPR spectral parameters were also reported by Nagy et al. [23] for iron(III) complexes of sugar-type ligands, where the corresponding complexes were synthesised using high ratios of ligand to iron(III) from strongly alkaline solutions. Considering that the intensity ratio (I_{int}/I_{iso}) is proportional to the concentration ratio of the two types of iron(III) centres, it can be seen that the interacting iron(III) centres dominate in **3**–**5** and **8** (Table 3). Based on the values (I_{int}/I_{iso} = 1.3–4.7), it is logical that the complexes **1**, **2**, **6** and **7** can be grouped as one set, and the remaining can be grouped as another set (I_{int}/I_{iso} = 13.2–22.0), where the major difference between the the two sets of complexes lies in the fact that their magnetic interactions vary accordingly. This implies that there exists increased interactions between the iron(III) centres in dinuclear complexes (both intra- and intermolecular, **3**–**5** and **8**) than that of the mononuclear (only intermolecular, **1**, **2**, **6** and **7**) ones.

In such magnetically interacting systems, if the distance between the paramagnetic centres is increased, one would expect an increase in the isolated spins and correspondingly an increase in the EPR band. This will affect the intramolecular interactions considerably. In order to ascertain this, mixed metal complexes of iron and aluminium were synthesised in case of D-Glu (**1a**), D-Fru (**3a**) and D-Man (**4a**) from methanolic solutions containing 1 : 1 mole ratios of iron(III) and aluminium(III) salts. The intensity ratio, I_{int}/I_{iso} of **1a** showed almost no change as compared to its non-aluminium(III) case, **1**. The other two, **3a** and **4a**, have shown considerable changes and the value approaches 1.0. While this suggests that there is no increase in the separation between the iron centres in case of **1**, a considerable increase was noted in case of **3** and **4** as these exhibited a decrease in their magnetic interactions through diamagnetic dilution by aluminium(III). These trends indicate differences in the nuclearity of these compounds. Thus while **1** resembles the behaviour of a mononuclear species with some intermolecular interactions, **3** and **4** resemble that of dinuclear complexes with considerable intramolecular interactions.

Mossbauer spectra. — Mossbauer spectra of the complexes **1**–**8** can be fitted as a single, broad, quadrupole doublet with the isomer shift values and quadrupole splitting values given in Table 4 that are comparable to those with the high-spin ferric complexes

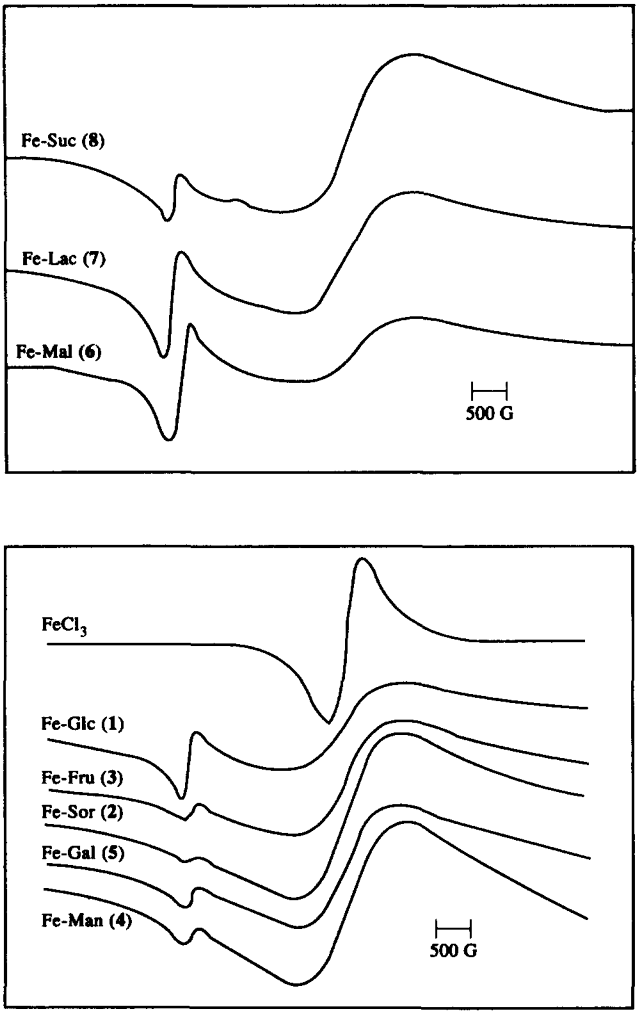

Fig. 2. Solid-state EPR spectra of (a) iron(III)–monosaccharide complexes (**1–5**) and (b) iron(III)–disaccharide complexes (**6–8**) at ambient temperature.

reported in the literature [24–26]. The close range of isomer shift values observed for **1–8** indicates that the binding nature of the iron centres through saccharide oxygens are similar. The large quadrupole splitting values reflect the distortion in the octahedral metal centre caused by the coordination of the deprotonated hydroxyl groups in the complex. This also suggests asymmetry in the coordination sphere of the complexes as manifested through the binding of OH and O^- groups to different extents.

Magnetic measurements. — The plot of $1/\chi_M$ vs T of the complexes **1–8** does not give a straight line and deviates from the behaviour of a pure paramagnetic substance. Based on the 10–300 K data for **1**, **2** and **3**, **1** and **2** exhibited negative deviation from

Table 3
EPR data of complexes **1–8**

Complex [a]	Narrow band		Broad band		Intensity ratio (based on area)
	g_{iso}	$\Delta\nu_{1/2}$(mT)	g_{int}	$\Delta\nu_{1/2}$(mT)	I_{int}/I_{iso}
1	4.168	10.0	2.112	62	4.7
1a	4.197	6.5	2.112	50	4.2
2	4.223	11.0	2.095	51	2.7
3	4.209	7.0	2.095	60	15.5
3a	4.292	5.5	2.138	62	3.8
4	4.193	5.0	2.087	50	15.3
4a	4.250	6.5	2.082	60	1.0
5	4.252	7.5	2.112	50	22.0
6	4.182	10.5	2.070	45	1.3
7	4.205	9.5	2.112	50	2.8
8	4.171	6.5	2.157	55	13.2

[a] **1a**, **3a** and **4a** are the iron–aluminium complexes corresponding to **1**, **3** and **4**, respectively.

the straight line at 50 K and **3** goes through a minimum around 40 K. The data are thus suggestive of an antiferromagnetically coupled interaction in **3** and only some intermolecular magnetic interactions in **1** and **2**. This suggestion is supported by the EPR intensity ratio (I_{int}/I_{iso}) where **1** and **2** indeed have weak interactions and **3** has a strong interaction between the centres. For complexes **4–8** the magnetic data is available only in the range 80–300 K. Extension of the EPR results to all these complexes resulted in the proposal that the complexes **3–5** and **8** are dinuclear. The experimental molar susceptibility per iron centre (χ_M) has been fitted for complexes **3–5** and **8** as a function of temperature with the theoretical one as per the standard equation [27]. The dinuclear iron(III) complexes of μ-OH showed $-J$ in the range 7–17 cm^{-1} and those of μ-oxo showed $-J$ in the range 65–195 cm^{-1} for a large number of compounds in the literature [26]. Thus the rather low antiferromagnetic coupling constants obtained for complexes **3–5** and **8** ($-J \sim 26$, 20, 25 and 23 cm^{-1}) may be explained as due to the hydroxo-bridging in these complexes [26,28]. The fact that these complexes did not

Table 4
Mossbauer data of complexes (**1–8**)

Complex	Isomer shift δ (mm s^{-1})	Quadrupole splitting ΔE_q (mm s^{-1})
1	0.3187	0.8473
2	0.3109	0.8807
3	0.3286	0.8951
4	0.3156	0.8765
5	0.3124	0.8629
6	0.3246	0.8585
7	0.2992	0.8549
8	0.3174	0.7634

Table 5
Fe(III) → Fe(II) reduction potentials of complexes **1–7** at Pt and HMDE working electrodes in H_2O, MeOH and *N,N*-dimethylformamide

Complex	Electrode potentials (mV), w.r.t., Ag/AgCl					
	H_2O		MeOH		Me_2NCHO	
	Pt	HMDE	Pt	HMDE	Pt	HMDE
1	−378	−1202	−400	−1360	−400	−1575
3	−401	−1300	−400	−1497	−400	−1528
4	−620	−1350	−630	−1530	−950	−1800
5	−421	−1300	−477	−1486	−990	−1700
6	–	–	−640	−1030	−940	−1547
7	–	–	−655	−1400	−1100	−1450

show any considerable change in their absorption spectra even at pH ~ 2 indicate that these are not likely to possess μ-oxo bridging, an aspect that supports the presence of bridging OH group.

The μ_{eff} of the complexes **1**, **2**, **6** and **7** are found in the range 5.1–5.6 BM at 298 K and are close to the expected value of 5.9 BM based on mononuclear, high-spin iron(III) complexes. On the other hand, low values are observed for **3–5** and **8** (4.7–5.3 BM). Based on a large number of compounds reported in the literature [26], it is noted that μ-OH compounds have μ_{eff} in the range 4.0–5.3 BM and μ-oxo compounds have μ_{eff} in the range 1.6–2.0 BM. Based on the comparison of the μ_{eff} values of our complexes with those reported in the literature, a μ-oxo can be ruled out for **3–5** and **8**, and hence a μ-OH is a better fit.

Cyclic voltammetry. — Cyclic voltammetric studies were carried out with **1–7** in water–methanol and in Me_2NCHO using Pt or HMDE as the working electrode. All the complexes showed an irreversible cathodic reduction peak for the process Fe(III) → Fe(II). The data are shown in Table 5. The reduction potentials showed shifts to more negative values in non-aqueous solvents as expected.

Solution stability. — A cyclic voltammetric study was carried out with complexes, **1–7** as a function of pH using HMDE as working electrode. Representative voltammograms are shown in Fig. 3 for complex 1. All the complexes showed a single, irreversible cathodic reduction, Fe(III) → Fe(II) peak at all pH values. The reduction potentials are found to be shifted to more negative values with increase in pH. The relation between the cathodic potentials (E_p^c) and pH was found to be linear in all the cases (Fig. 4), indicating that there are no major changes observed in the species present except for the changes in protonation and deprotanation states of these. Neither precipitation nor hydrolytic breakage of the metal centre was noted even at extreme pH conditions (pH 2 and 12) studied. The complexes have thus exhibited a robust behaviour, which is important for any iron complex to be considered for its applicability as an oral supplement. From the slopes of these straight lines, it can be found that the order of complexity for various saccharide complexes are as follows: Fe–D-Gal, **5** (40) > Fe–Mal, **6** (33) > Fe–D-Glc, **1** (29) > Fe–D-Man, **4** (28) > Fe–L-Sor, **2** (22) > Fe–D-Fru, **3**, (20) > Fe–Lac, **7** (8) with the values in the brackets indicating the slope,

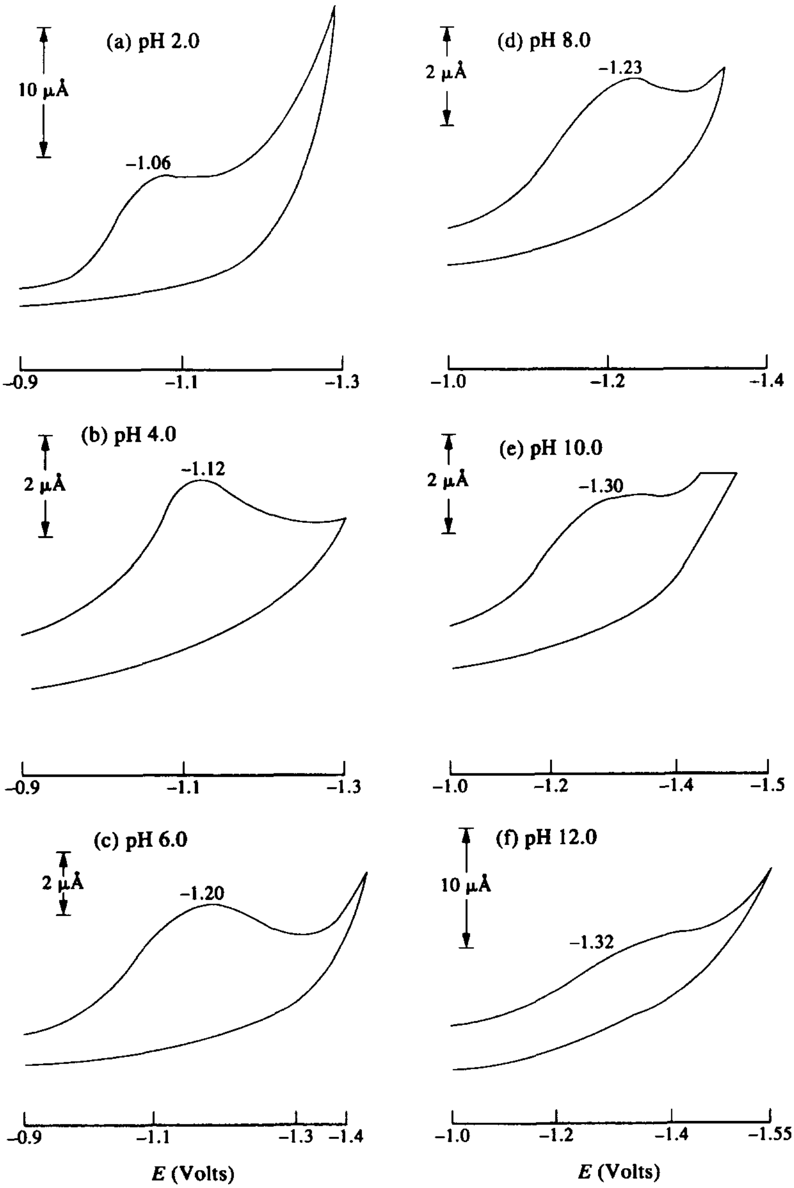

Fig. 3. Cyclic voltammograms of Fe–D-Glc (1) at various pH values. Working electrode, HMDE; scan rate, 100 mV s^{-1}; auxiliary electrode, Pt; reference electrode, Ag/AgCl.

mV/pH. The study further implies that there exists no substantial changes in the structures of these complexes. In the pH 2–12 range, none of these complexes showed hydrolysed products, indicating their robust nature. Similar behaviour was noted with

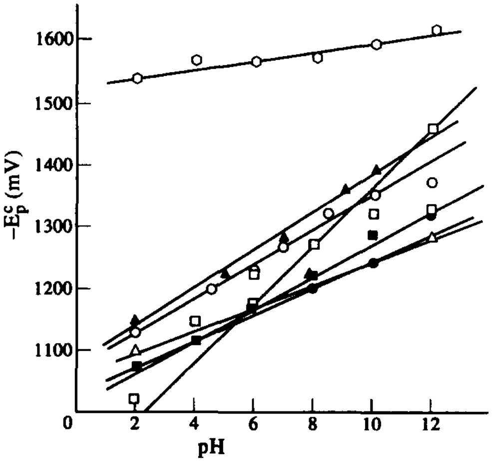

Fig. 4. Reduction potentials E_p^c vs pH plots for complexes (1–7). Legends: ■, 1; ●, 2; △, 3; ○, 4; □, 5; ▲, 6; ○, 7.

chromium(III)–saccharide complexes. The solution stability of these complexes **1–8** was also studied by absorption spectroscopy as reported earlier [12a].

Reductive release of iron. — Studies on the reductive release of iron(II) of the complexes **1–8** by sodium dithionite by absorption spectra revealed that three equiv of this reducing agent were needed per equiv of iron. Comparison of this result with that reported in the literature regarding the iron–dextran complex [29], where a high concentration of dithionite was required for the reductive release, it is understood that the complexes reported in this paper may represent better iron-releasing agents.

4. Conclusions

The absorption and FTIR spectra indicated the complexation between the iron(III) and saccharides. The variable temperature magnetic susceptibility measurements indicated a monomeric structure in the case of complexes **1**, **2**, **6** and **7** and a μ-hydroxo dimeric iron(III) centre for **3–5** and **8**. The presence of μ-oxo bridging in the dinuclear complexes has been ruled out based on the low value of $-J$ and high value of μ_{eff}. This is further supported by the stability of the complexes at pH ~ 2.0. The large quadrupole splitting of the complexes showed non-symmetric environments around the iron centre. All these data reported, together with elemental analyses, can be fitted with molecular formulae as shown in Table 6. The observed conductivities (Table 6) of the complexes **1–5** are consistent with 2:1, 1:1, 3:1, 3:1 and 5:1 electrolytes, respectively. The intensity ratios ($I_{\text{int}}/I_{\text{iso}}$) calculated from the EPR spectra supported the formulation in terms of the mono- and dinuclear nature of these complexes. Since these complexes are paramagnetic, the proton NMR spectra were broad and not resolved enough to assign specific hydroxyl groups involved in iron(III) coordination.

Table 6
Proposed molecular formulae for the complexes **1**–**8**

	Complex	Proposed formulae	Molar conductivity (cm^2 ohm^{-1} M^{-1})
1	Fe–D-Glc	$Na_2[Fe(OH)(D\text{-}Glc)_2(H_2O)]$	140
2	Fe–D-Sor	$Na[Fe(L\text{-}Sor)_2(H_2O)_2]$	76
3	Fe–D-Fru	$Na_3[Fe_2(OH)(D\text{-}Fru)_4(H_2O)_2]$	188
4	Fe–D-Man	$Na_3[Fe_2(D\text{-}Man)_3(OH)_3(H_2O)_2]$	193
5	Fe–D-Gal	$Na_5[Fe_2(D\text{-}Gal)_4(OH)_3(H_2O)]$	349
6	Fe–Mal	$Na[Fe(Mal)(MeO)(H_2O)_2]$	86
7	Fe–Lac	$Na[Fe(Lac)(H_2O)_2]$	64
8	Fe–Suc	$Na_4[Fe_2(Suc)_4(OH)_2(H_2O)_4]$	251

The literature reports based on photochemical studies of saccharides in the presence of iron(III) chloride favour the binding of C-2 and C-3 hydroxyls of the saccharide to iron. Even in the reduction of chromium(VI) by saccharides to form chromium(III) complexes, the presence of the 2-OH was found to be important, thereby supporting the involvement of $2\text{-}O^-$ in binding to the metal [30]. Further the EXAFS studied carried out on the iron–sugar complexes suggested bidentation by the saccharides through hydroxy groups [17]. Although there is no direct evidence for the μ-hydroxo bridging in these complexes, the rather low magnetic coupling constants and high μ_{eff} values observed with these, in comparison with those reported in the literature, rule out the possibility of μ-oxo bridging and are suggestive of their dinuclear nature with μ-OH bridging.

The hydrolytic stability of these complexes in the range of pH 2–12 without any precipitation may make these complexes better candidates for oral nutritional supplements. Further, the easy release of iron(II) observed with these complexes by the addition of sodium dithionite may add to their suitability as oral supplements of iron. Hence, further detailed biological studies on these complexes can lead to the development of a better suited drug for the treatment of iron-deficiency anemia. On the other hand, the iron(III) complexes of sugars and their derivatives reported in the literature [23], though synthesised from large iron-to-sugar ratios, the final products seem to possess metal-to-sugar ratios in the range 1 : 0.66–1 : 1 and high metal-to-hydroxide ratios of 1 : 1–1 : 5. Due to the low ratio of saccharide and the high ratio of hydroxide, their complexes tend to oligomerise. As their complexes were synthesised from highly alkaline solution, the presence of iron hydroxide and/or oxide cannot be ruled out. However, the solution behaviour of these complexes was not reported. In contrast, the complexes reported by us were synthesised from stoichiometric ratios using MeOH as a solvent, and a thorough solution behaviour has been ascertained. Thus the present paper not only provides new synthetic directions to make low molecular weight iron(III)–saccharide complexes of characterizable nature, but it also demonstrates the properties required for these to be considered as potential oral supplements of iron.

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References

[1] J.S.G. Cox, R.F. King, and G.F. Reynolds, *Nature*, 207 (1965) 1202–1203.
[2] J. Briggs, P. Finch, M.C. Matulewicz, and H. Weigel, *Carbohydr. Res.*, 97 (1981) 181–188.
[3] S.A. Barker, P.J. Somers, and J. Stevenson, *Carbohydr. Res.*, 36 (1974) 331–337.
[4] D.A. Brown and M.V. Chidambaram, in H. Sigel (Ed.), *Metal Ions in Biological Systems*, Vol. 14, Marcel Dekker Inc., New York, 1982, p 159.
[5] P.J. Charley, B. Sarkar, C.F. Stitt, and P. Saltman, *Biochem. Biophys. Acta.*, 69 (1963) 313–321.
[6] P. Saltman, *J. Chem. Educ.*, 42 (1965) 682–687.
[7] M. Tonkovic, S. Music, I. Hadzija, A. Nagy-Czeko, and A. Vertes, *Acta. Chim. Hung.*, 110 (1982) 197–202.
[8] K. Burger, I. Zay, and G. Takacsi Nagy, *Inorg. Chim. Acta*, 80 (1983) 231–235.
[9] S. Wolowiec and K. Drabent, *J. Radioanal. Nucl. Chem. Lett.*, 95 (1985) 1–12.
[10] K. Araki and S. Shiraishi, *Bull. Chem. Soc. Jpn.*, 59 (1986) 3661–3662, and references cited therein.
[11] C. Stitt, P. Charley, E. Butt, and P. Saltman, *Proc. Soc. Exp. Biol. Med.*, 10 (1962) 70–75.
[12] (a) C.P. Rao, K. Geetha, and R.P. Bandwar, *BioMed. Chem. Lett.*, 2 (1992) 997–1002; (b) C.P. Rao, K. Geetha, and M.S.S. Raghavan, *BioMetals*, 7, (1994) 25–29.
[13] (a) C.P. Rao, P.S. Sarkar, S.P. Kaiwar, and S. Vasudevan, *Proc Indian Acad. Sci. (Chem. Sci.)*, 102 (1990) 219–230; (b) C.P. Rao and S.P. Kaiwar, *Carbohydr. Res.*, 237 (1992) 195–202; (c) S.P. Kaiwar and C.P. Rao, *Carbohydr. Res.*, 237 (1992) 203–210; (d) C.P. Rao and S.P. Kaiwar, *Inorg. Chim. Acta.*, 186 (1991) 11; (e) C.P. Rao, S.P. Kaiwar, and M.S.S. Raghavan, *Polyhedron*, 13 (1994) 1895–1906; (f) S.P. Kaiwar, R.P. Bandwar, M.S.S. Raghavan, and C.P. Rao, *Proc. Indian Acad. Sci. (Chem. Sci.)*, 106 (1994) 743–752; (g) S.P. Kaiwar, M.S.S. Raghavan, and C.P. Rao, *J. Chem. Soc., Dalton Trans*, in press.
[14] R.P. Bandwar, M.S.S. Raghavan, and C.P. Rao, *BioMetals*, 8 (1995) 19–24.
[15] A. Sreedhara, M.S.S. Raghavan, and C.P. Rao, *Carbohydr. Res.*, 264 (1994) 227–235.
[16] K. Araki and S. Shiraishi, *Bull. Chem. Soc., Jpn.*, 59 (1986) 229–234.
[17] L. Nagy, H. Ohtaki, H. Yamaguchi, and M. Nomura, *Inorg. Chim. Acta.*, 159 (1989) 201–207.
[18] N.S. Hush and R.J.M. Hobbs, *Prog. Inorg. Chem.*, 10 (1968) 259–359.
[19] R.E. Norman, S. Yan, L. Que, Jr., G. Bakes, J. Ling, J. Sanders Loehr, J.H. Zhang, and C.J. O'Connor., *J. Am. Chem Soc.*, 112 (1990) 1554–1562.
[20] (a) V.N. Gritsan, V.P. Panov, and V.G. Kachur, *Carbohydr. Res.*, 112 (1983) 11–21; (b) H.A. Tajmir-Riahi, *Carbohydr. Res.*, 183 (1988) 35–46; (c) H.A. Tajmir-Riahi, *Carbohydr. Res.*, 190 (1989) 29–37.
[21] H.A. Tajmir-Riahi, *J. Inorg. Biochem.*, 39 (1990) 33, and references cited therein.
[22] M. Tonkovic, O. Hadzija, and I. Nagy-Czako, *Inorg. Chim. Acta.*, 80 (1983) 251–254.
[23] L. Nagy, K. Burger, J. Kurti, M.A. Mostafa, L. Koresz, and I. Kiricsi, *Inorg. Chim. Acta.*, 124 (1986) 55–59.
[24] K.S. Murray, *Coord. Chem. Rev.*, 12 (1974) 1–85.
[25] N.N. Greenwood and G.T. Gibbs, *Mossbauer Spectroscopy*, Chapman and Hall, London, 1971, p 148.
[26] D.M. Kurtz, J., *Chem. Rev.*, 90 (1990) 585–606.
[27] J.D. Walker and R. Poli, *Inorg. Chem.*, 29 (1990) 756–761.
[28] W.H. Armstrong and S.J. Lippard, *J. Am. Chem. Soc.*, 106 (1984) 4632–4633.
[29] J.C. Jacobs and N.M. Alexander, *Clin. Chem.*, 36 (1990) 1803–1807.
[30] S.P. Kaiwar, M.S.S. Raghavan, and C.P. Rao, *Carbohydr. Res.*, 256 (1994) 29–40.