Carbohydrate Research, 215 (1991) 357–360
Elsevier Science Publishers B.V., Amsterdam

Note

Complexing of sugars and sugar alcohols with metal ions: a comparative study by ion-exchange chromatography

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(Received October 19th, 1990; accepted for publication, November 30th, 1990)

Monosaccharides, glycosides, and polyols form reasonably stable complexes with metal ions in aqueous solution[1]. The most favourable sites for co-ordination are 1,3,5-triaxial or contiguous *ax–eq–ax* hydroxyl groups on six-membered rings[2], vicinal *cis,cis*-triol groupings on five-membered rings[2–4], and vicinal *threo,threo*-triol sequences in alditols[5]. Of the metal ions, Ca^{2+} and La^{3+} ions bind most efficiently[5–7], the upper limit for the stability constants of their 1:1 complexes being 10 M^{-1}. Data on the abilities of other metal ions to form complexes with sugar-type ligands are scanty[6,8,9]. Moreover, it is difficult to compare the results of various experimental methods since the observed variables, such as electrophoretic mobilities, R_F values on metal ion-loaded resins, and changes in n.m.r. chemical shifts, cannot be transformed into stability constants without extra-thermodynamic assumptions. Some conclusions, based on different experimental approaches, are contradictory[10], and results obtained by a particular technique have been unduly generalised. For example, the strong affinity of copper(II) acetate for sugar alcohols[8] has probably led to an overestimation of the role of dietary polyols in copper metabolism[11,12].

The present report provides more extensive data on the relative strengths of binding of metal ions to sugar-type ligands based on the mobilities of ligands in t.l.c. with the absorbent loaded with various metal ions. These data may be useful, for example, in the evaluation of the role of sugars and polyols in the absorption of metal ions during the digestion of food.

Tables I and II record the R_F values and the percentages of complexed ligands, calculated by the method of Briggs *et al.*[8]. The data lend additional support to the order of binding established for various sugar-type ligands. (*a*) Alditols form more stable complexes than those mono- or di-saccharides that cannot adopt an *ax–eq–ax* arrangement of three vicinal hydroxyl groups in their pyranose form[8,13]. (*b*) Of the alditols,

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0008-6215/91/$ 03.50

TABLE I

R_F values of alditols on t.l.c. in the presence of various cations, and percentages of complexed ligands

Cation	*Anion*	*Xylitol*		D-*Glucitol*		D-*Mannitol*		*Galactitol*	
		R_f	(%)[a]	R_f	(%)	R_f	(%)	R_f	(%)
H^{+}[b]	Cl	0.89		0.90		0.93		0.93	
Na^{+}	Cl	0.80	13	0.81	12	0.82	11	0.87	5
Mg^{2+}	Cl	0.89	3	0.89	3	0.89	3	0.92	0
Ca^{2+}	Cl	0.71	22	0.69	25	0.74	19	0.72	21
Sr^{2+}	Cl	0.71	22	0.70	24	0.76	17	0.76	17
Al^{3+}	Cl	0.88	4	0.87	5	0.88	4	0.91	1
Cr^{3+}	Cl	0.86	6	0.84	8	0.85	7	0.83	9
Fe^{2+}	SO_4^{2-}	0.90	2	0.90	2	0.89	3	0.91	1
Fe^{3+}	Cl	0.78	15	0.78	15	0.88	4	0.84	8
Co^{2+}	Cl	0.90	2	0.90	2	0.90	2	0.92	0
Ni^{2+}	Cl	0.87	5	0.88	4	0.90	2	0.96	0
Cu^{2+}[c]	AcO	0.10	90	0.06	93	0.17	81	0.17	81
Cu^{2+}	SO_4^{2-}	0.85	8	0.87	6	0.88	5	0.90	2
Zn^{2+}	SO_4^{2-}	0.88	4	0.89	3	0.87	5	0.91	1
Cd^{2+}	NO_3^{-}	0.86	6	0.87	5	0.88	4	0.91	1
La^{3+}	NO_3^{-}	0.57	38	0.56	39	0.72	21	0.61	33
Y^{3+}	NO_3^{-}	0.68	26	0.69	25	0.78	16	0.76	17
Pb^{2+}	NO_3^{-}	0.62	33	0.57	38	0.69	25	0.58	36

[a] Calculated by the method of Briggs *et al.*[7]. [b] The mean value of all the ligands studied (R_f 0.915) was used in calculations. [c] Strong tailing.

TABLE II

R_F values of sugars on t.l.c. in the presence of various cations, and percentages of complexed ligands

Cation[a]	*Anion*	D-*Glucose*		D-*Fructose*		D-*Galactose*		D-*Xylose*		*Lactose*	
		R_f	(%)[b]	R_f	(%)	R_f	(%)	R_f	(%)	R_f	(%)
H^{+}[c]	Cl	0.92		0.92		0.90		0.91		0.94	
Na^{+}	Cl	0.90	2	0.88	4	0.90	2	0.91	1	0.92	0
Ca^{2+}	Cl	0.91	1	0.81	12	0.80	13	0.89	3	0.92	0
Sr^{2+}	Cl	0.89	3	0.86	7	0.90	2	0.96	0	0.95	0
Cr^{3+}	Cl	0.90	2	0.93	0	0.92	0	0.88	4	0.91	1
Co^{2+}	Cl	0.92	0	0.88	4	0.89	3	0.91	1	0.92	0
Cu^{2+}[d]	AcO	0.94	0	0.88	4	0.89	3	0.91	1	0.92	0
Cu^{2+}	SO_4^{2-}	0.85	8	0.85	8	0.86	7	0.90	2	0.90	2
Zn^{2+}	SO_4^{2-}	0.91	1	0.87	5	0.86	6	0.87	5	0.90	2
Cd^{2+}	NO_3^{-}	0.88	4	0.89	3	0.88	4	0.88	4	0.93	0
La^{3+}	NO_3^{-}	0.85	8	0.80	13	0.79	14	0.83	9	0.85	8
Y^{3+}	NO_3^{-}	0.88	4	0.91	1	0.91	1	0.92	0	0.92	0
Pb^{2+}	NO_3^{-}	0.88	4	0.76	17	0.76	17	0.88	4	0.90	2

[a] No interaction with Mg^{2+} (Cl^{-}), Al^{3+} (Cl^{-}), Fe^{3+} (SO_4^{2-}) or Ni^{2+} (Cl^{-}). [b] Calculated by the method of Briggs *et al.*[7]. [c] The mean value of all the ligands studied (R_f 0.915) was used in calculations. [d] Strong tailing.

D-glucitol and xylitol, each of which contains a vicinal *threo,threo*-triol arrangement, form complexes more strongly than D-mannitol or galactitol, which have an all *erythro,threo/erythro,erythro* configuration[5,14]. (*c*) Of the monosaccharides, the ability to form complexes decreases in the order D-fructose > D-galactose > D-xylose ≈ D-glucose[8,13]. (*d*) The ability of lactose to form complexes is negligible[8] except with La^{3+}.

All of the alditols studied formed reasonably stable complexes with lanthanide (La^{3+}, Y^{3+}) and alkaline earth metal ions (Ca^{2+}, Sr^{2+}), consistent with previous findings[1]. Of the other metal ions, only Pb^{2+} exhibited a comparable ability to bind. The alditol complexes of Pb^{2+} appear to be as stable as those of La^{3+} and, hence, more stable than those of Ca^{2+}, Sr^{2+}, or Y^{3+}. The formation of complexes by Pb^{2+} with sugar-type ligands has received little attention, although this ion binds to the α-pyranose forms of D-ribose[15] and D-allose[6] approximately as firmly as does Ca^{2+} (ref. 13), and exhibits markedly negative enthalpies of interaction on mixing with methyl α-D-ribo- and α-D-lyxo-furanoside[9]. The differences in stability of the various alditol complexes are small, the complexes of D-mannitol and galactitol being slightly less stable than those of D-glucitol and xylitol. The higher ability of the latter alditols to form complexes is expected on the basis of preferential binding to a *threo,threo*-sequence. In contrast, it is surprising that galactitol, which contains no such binding site, interacts with Pb^{2+} and La^{3+} almost as well as D-glucitol.

Ca^{2+}, Pb^{2+}, and La^{3+} also form relatively stable complexes with D-fructose and D-galactose, whereas complexation with D-glucose and D-xylose is negligible. It has been suggested[13] that HO-1,2,3 in D-fructose may assume a relationship similar to the *ax–eq–ax* arrangement. In α-D-galactopyranose, HO-3,4,5 form a potential binding site[16].

As seen from Table I, Fe^{3+} is the only 3*d* transition metal ion that interacts markedly with alditols. No complexing with monosaccharides was detected. The data in Table I also support the previous findings that alditols are markedly retained on ion-exchange plates loaded with copper(II) acetate[8] but not on plates loaded with copper(II) sulfate[10]. Studies of the electrophoretic mobility of sugar-type ligands in solutions in copper(II) acetate and sulfate gave similar results[10]. Moreover, the enthalpy of interaction of copper(II) nitrate with methyl glycofuranosides was small[9]. These apparently contradictory results have been accounted for by assuming that, whereas alditols complex efficiently with the dimeric $[Cu_2(OH)_2]^{2+}$ ion present in copper(II) acetate solutions, their interaction with a monomeric aquo-ion of Cu^{2+} is weak[10]. Cr^{3+} has been reported[8] to complex with D-mannitol more strongly than Ca^{2+} and Sr^{2+}, but the present data do not agree with this finding. Similarly, the complexing ability of Ni^{2+} is weaker than previously suggested[8].

Of the other metal ions studied (Na^+, Al^{3+}, Zn^{2+}, Cd^{2+}), only Na^+ exhibits a significant ability to form complexes. It has been suggested[8] that Al^{3+} would interact with D-glucitol and D-mannitol more strongly than Na^+, but the data in Table I do not corroborate this view.

EXPERIMENTAL

The R_F values of sugars and sugar alcohols were determined on POLYGRAM IONEX-25 SA sheets converted into various metal ion forms as described[8]. Aliquots (5μL) as aqueous 5% solutions (galactitol as a 3.5% solution) were used and, after development for 2 h with distilled water, detection was effected by treatment of the dried sheets with acetone saturated with potassium permanganate.

REFERENCES

1 S. J. Angyal, *Adv. Carbohydr. Chem. Biochem.*, 47 (1989) 1–43.
2 S. J. Angyal, *Tetrahedron*, 30 (1974) 1695–1702.
3 H. Lönnberg and A. Vesala, *Carbohydr. Res.*, 78 (1980) 53–59.
4 A. Vesala and H. Lönnberg, *Acta Chem. Scand., Ser. A*, 35 (1981) 123–126.
5 S. J. Angyal, D. Greeves, and J. A. Mills, *Aust. J. Chem.*, 27 (1974) 1447–1456.
6 S. J. Angyal, *Aust. J. Chem.*, 25 (1972) 1957–1966.
7 R. E. Lenkinski and J. Reuben, *J. Am. Chem. Soc.*, 98 (1976) 3089–3094.
8 J. Briggs, P. Finch, M. C. Matulewicz, and H. Weigel, *Carbohydr. Res.*, 97 (1981) 181–188.
9 A. Vesala, H. Lönnberg, R. Käppi, and J. Arpalahti, *Carbohydr. Res.*, 102 (1982) 312–315.
10 S. J. Angyal, *Carbohydr. Res.*, 200 (1990) 181–188.
11 M. Fields, C. G. Lewis, and T. Beal, Metabolism, 38 (1989) 371–375.
12 M. M. Hämäläinen and K. K. Mäkinen, *Miner. Electrolyte Metab.*, 15 (1989) 346–352.
13 S. J. Angyal and J. A. Mills, *Aust. J. Chem.*, 32 (1979) 1993–2001.
14 A. P. G. Kieboom, T. Spoormaker, A. Sinnema, J. M. van der Toorn, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 94 (1975) 53–59.
15 L.-G. Ekström and Å. Olin, *Acta Chem. Scand., Ser. A*, 31 (1977) 838–844.
16 M. E. Daman and K. Dill, *Carbohydr. Res.*, 132 (1984) 335–338.