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Complexes of natural carbohydrates with metal cations

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Abstract. Data on the interaction of natural carbohydrates (mono-, oligo-, and polysaccharides, amino sugars, and natural organic acids of carbohydrate origin) with metal cations are surveyed and described systematically. The structural diversity of carbohydrate metal complexes, caused by some specific features of carbohydrates as ligands, is demonstrated. The influence of complex formation on the chemical properties of carbohydrates is discussed. It is shown that the formation of metal complexes plays an important role in the configurational and conformational analysis of carbohydrates. The practical significance of the coordination interaction in the series of carbohydrate ligands is demonstrated. The bibliography includes 571 references.

I. Introduction

Metal complexes of natural carbohydrates have been attracting interest for many years because these compounds participate in vitally important processes; they are used for configurational and conformational analysis, determination, and separation of sugars. According to our estimates, at least 1000 studies discussing various aspects of complex formation between metal ions and natural carbohydrates (mono-, oligo-, and polysaccharides, amino sugars, their polymers, carbohydrate carboxylic acids, natural organic acids of the carbohydrate origin, and cyclic and acyclic polysaccharides) have been published. However, even the most comprehensive monographs dealing with the chemistry of coordination compounds of carbohydrates3–16 do not consider carbohydrates to be ligands. Several reviews published to date3–16 cover only some aspects of this topic.

The purpose of this review is to survey as fully as possible the published data on the known complexes of natural carbohydrates with metal cations; therefore it includes both recent studies and the most important of early studies. The formation of complexes by nucleosides and nucleotides is beyond the scope of the review, because the carbohydrate fragments of these molecules normally do not participate in the coordination of metals. Moreover, this aspect has been the subject of numerous reviews and monographs (see, for example, Refs 17, 18). The few known examples in which the carbohydrate fragments of nucleotides and nucleosides are involved in the formation of complexes with metals are presented in Section IV.

Data on the formation of metal complexes in the series of natural carbohydrates are mainly discussed in relation to reliably established structures. The information is classified according to the type of carbohydrates. Within each type, metal cations are arranged in accordance with their electronic configuration (s-, p-, d-, and f-metals) and their position in the Mendeleev Periodic Table.

II. Complexes of mono-, oligo-, and polysaccharides and their derivatives

1. Ionic complexes with s-metal cations

The first review6 on the complexation of carbohydrates with s-metal compounds was published in 1966, and now it is only of historical interest. X-Ray diffraction data for metal complexes of this type can be found in a number of reviews (see, for example, Refs 19–23) including a review devoted to saccharose.24 The data on the structures of solid ionic metal complexes obtained up to the middle of 1978 are surveyed most fully in the review by Poonia and Bajai.11

A systematic study of the structures of complexes of monosaccharides with s-metal cations in aqueous solutions carried out by Angyal7,8,12 has demonstrated that complexes of 1:1 composition predominate. In the case of cyclic forms of ligands, the most stable complexes are those with the axial–equatorial–axial orientation of three consecutively located hydroxyl groups in the ligand (complex 1a, the first Angyal rule) or those with the energetically unfavourable triaxial orientation of these groups (complex 1b, the second Angyal rule). Acyclic derivatives obey the first Angyal rule (complex 2), while furanoses obey the second rule (complex 3 with a quasiaxial orientation of the hydroxyl groups). These rules were derived using 1H NMR spectroscopy, i.e. they were first formulated for relatively con-
centrated solutions. Their validity for dilute solutions was confirmed later by calorimetry.25

Complex formation can shift the position of a tautomeric or conformational equilibrium for a ligand in an aqueous solution.7,8,12 The stability constants of the complexes are relatively low (0.1 – 6.0).7,8,12,16,26–30 The ability of s-metals to form complexes with disaccharides is less pronounced than that for monosaccharides.31,32 Evidently, this is due to the higher conformation rigidity of the former. The stability constants of s-metal complexes of monosaccharide carboxylic acids are only an order of magnitude larger.53–55 Thus, this complexation is very weak although fairly stereospecific. In solvents that are less polar than water (methanol, acetone, dioxane), these complexes are more stable because there are no water molecules to compete with the ligands for coordination to metal cations.36

The formation of these ionic metal complexes is usually regarded5–11 as consecutive substitution of water molecules in the hydration shell of a metal ion by hydroxyl groups of the ligand, the optimum number of these groups (three) being determined by the Angyal rules. During the formation of solid complexes, this process is continued with participation of other ligand molecules, but does not go to completion. The data for a number of solid complexes of sugars with s-metal salts obtained by X-ray diffraction analysis10,15,37–45 and by IR spectroscopy46–53 permit the following general conclusions.

1. Carbohydrates act most often as bidentate ligands coordinated through vicinal diol fragments, which can be different in identical ligands. In some cases, the formation of a complex ends with incorporation of a monodentate ligand.38,54 Complexes of acyclic aldonic acids can contain only monodentate ligands.55,56

2. Since there are only three known examples57–59 of tridentate coordination of cyclic ligands conforming to the first Angyal rule, one can conclude that this rule is not necessary for solid ionic metal complexes of sugars. At the same time, sugars containing no vicinal hydroxyl groups characterised by an axial–equatorial–axial arrangement (x-D-glucopyranose 4a) do not form complexes of this type.11

3. As a rule, these complexes are crystal hydrates in which all water molecules are coordinated to metal ions.

4. The complexes normally contain two or three ligands, although in some cases they contain only one ligand.60,61 In the case of acyclic carbohydrate derivatives, the number of ligands increases to four62,63 or even to six.55,56 The number of ligands in less studied disaccharide complexes is two.44,64–67 or one.68

5. After complexation, the coordination number of the metal remains approximately the same as that in the first coordination sphere of the initial hydration shell of the metal cation; most frequently it is equal to eight (square antiprism), six (octahedron), seven (pentagonal bipyramid), or nine (three-cap trigonal prism).11 The coordination polyhedra formed by calcium(II) ions are especially diverse.39

6. In the majority of complexes of carbohydrate carboxylic acids, a metal ion is coordinated to an oxygen atom of the carboxyl group and to the hydroxyl group in the z-position (z-type coordination 69). Only in complexes with these ligands, can the ring oxygen atom be involved in coordination.70

7. Conformational changes in the ligand following the complex formation are typical of neutral carbohydrates and normally reduce to the change in the conformation of the coordinated primary hydroxyl group44 or in the dihedral angle between the coordinated vicinal hydroxyl groups.11 In anionic ligands, coordination mostly involves the carboxyl group; this substantially decreases electrostatic interactions between the hydroxyl groups responsible for the conformational changes.11,64

8. The cation and the anion of the metal salt are coordinated separately and, thus, they are relatively far removed from each other. There is only one known example45 of formation of a complex in which a salt occurs as a contact ion pair.

9. The majority of the complexes studied are calcium compounds, while the smallest number is represented by magnesium compounds. The particular affinity for calcium is apparently a fundamental property of carbohydrates.11,39

As regards polysaccharides, complexes of neutral polysaccharides with s-metal cations have been relatively little studied to date. Judging by X-ray diffraction data, the K⁺ and Br⁻ ions in the complex of potassium bromide with amylose (a polymer of x-1,4-linked x-D-glucopyranose 4a) are coordinated alternately in the cavity of the helix-like polymer chain.71 It has been noted72 that cellulose (a polymer of β-1,4-linked β-D-glucopyranose 4b) only weakly binds Ca²⁺ ions. It was established unambiguously73 that reaction of cellulose with alkali metal hydroxides gives inclusion compounds containing metal ions between the planes of the cellulose crystal lattice rather than the corresponding alkoxydes.74 The formation of alkoxydes was denied even for monosaccharides75 and disaccharides;76,77 in these cases, the formation of adducts of the type RO⁻H(M)OH⁻ stabilised by hydrogen bonds between the neighbouring hydroxyl groups was postulated.

A more detailed study77 has been devoted to the formation of complexes of s-metal cations with a number of anionic polysaccharides, first of all, with pectate 5 (x-1,4-linked poly-x-D-galactopyranuronorate), alginate 6 (a polymer consisting of z-1,4-linked disaccharides formed by the z-L-gulopyranosuronic and β-D-mannopyranosonic acid residues), and with carrageenans (polysaccharides containing 3-substituted residues of β-D-galactose and 4-substituted residues of D-D-galactose or 3,6-anhydro-D-D-galactose sulfated at different OH groups). Studies on this type of compounds have been stimulated by the fact that they form stable gels in the presence of s-metal salts.77

![Diagram](image_url)
This model was proposed to interpret the gel formation by poly-L-guluronate in the presence of Ca\(^{2+}\) ions.\(^{81, 82}\) Later it was confirmed for systems comprising Ca\(^{2+}\) and polygalacturonate or Na\(^{+}\) and alginate.\(^{83, 84}\) Intramolecular complexation occurs upon the formation of a hydrophilic cavity between monomeric units of neighbouring chains (Fig. 1a).\(^{86, 87}\) The formation of these cavities can account for the more efficient binding of Ca\(^{2+}\) cations by poly-L-guluronate\(^{87, 88}\) and also for the preferred binding of K\(^{+}\) and Rb\(^{+}\) cations by carrageenans.\(^{89, 90}\)

2. Complexes with p-metal cations

Borate complexes of carbohydrates are the most studied compounds in this series. They constituted the subject of early classical studies of Böseken\(^{1}\) carried out by measuring the electrical conductivity of solutions. Later, the results of this study were supplemented by the data of\(^{1}\)H (Ref. 91),\(^{13}\)C (Ref. 92), and\(^{11}\)B (Refs 93–95) NMR spectroscopy. This resulted in the detection of neutral complexes 7 (which predominate in acidic media),\(^{92, 94}\) anionic monomeric complexes with five-\(^{(8)}\) and six-membered\(^{(9)}\) rings, and anionic dimeric complexes\(^{(10)}\) of boric acid with polyhydroxyl compounds.

\[
\begin{align*}
\text{7} & \quad \text{8} & \quad \text{9} & \quad \text{10}
\end{align*}
\]

All these products are complexes formed by vicinal hydroxyl groups; nevertheless, complexes of the type 1b are the most stable in conformity with the second Angyal rule.\(^{91, 92, 95, 96}\) High stability constants \(10^{7}–10^{8}\) litre mol\(^{-1}\) imply a covalent character of these complexes; however, they have not been isolated in the crystalline state. Calorimetric,\(^{100}\) titrimetric,\(^{101}\) and polarimetric\(^{102}\) studies have not provided evidence for the existence of the complexes of type 10. However, they were detected in\(^{11}\)B NMR studies.\(^{94, 95}\)

Borate complexes of acyclic polyols of type 11a can be additionally stabilised owing to the formation of intramolecular hydrogen bonds. This accounts for the higher stability of these complexes compared to the complexes formed by cyclic forms of sugars.

\[
\begin{align*}
\text{11a} & \quad \text{11b} & \quad \text{12}
\end{align*}
\]

In aqueous solutions in the presence of borate ions, aldonic and aldaric acids\(^{8}\) tend to form complexes with Ca\(^{2+}\) ions of the composition CaBL\(_{2}\) (L is the ligand). This synergism, which is relatively uncommon in the coordination chemistry of carbohydrates, has been explained\(^{104}\) by assuming that the preliminary binding of borate ions makes carboxyl groups approach each other, which facilitates the formation of complexes 11b.

The complexation of sugars with other Group IIIA cations has not received much study. Neutral non-hydrolysable complexes of Ga\(^{III}\) with monosaccharide carboxylic acids such as D-glucaric acid (LH\(_{6}\), 12) of variable composition have been synthesised.\(^{107}\) Complexes of In\(^{III}\) with D-glucaric acid 12 of the type [InLH\(_{4}\)]\(^{2-}\), [InLH\(_{3}\)]\(^{3-}\), and [InLH\(_{2}\)]\(^{4-}\) were detected (the negative numerals in the subscripts denote the number of substituted hydrogen atoms).\(^{108}\) The results of a study of complexation of the acid 12 with Al\(^{III}\) and Ga\(^{III}\) ions carried out by spectroscopy have been interpreted\(^{107}\) in terms of an equilibrium between monomer 13a and dimer 13b, only carboxyl groups of the ligands being involved in the coordination.

\[
\begin{align*}
\text{13a} & \quad \text{13b}
\end{align*}
\]

M = Al, Ga.

The complex formation of sugars with Group IVA cations is also little studied. It has been noted\(^{108, 109}\) that germanic acid forms complexes of the composition \([\text{Ge(LH}_{3}\text{)]OH}^{-}\) and \([\text{Ge(LH}_{2}\text{)]OH}]^{2-}\) with acyclic polyols and with \(\alpha,\beta\)-D-glucopyranose 4a,b and also 1:1 complexes with pentoses.\(^{98}\) Note that in the latter case, the first Angyal rule holds. One publication\(^{110}\) describes the formation of 1:1 complexes of aldoses and ketoses with hexahydrostannate at high pH values.

The complexation of sugars with Pb\(^{II}\) has been studied somewhat more comprehensively. It has been shown\(^{111}\) that pentoses and their glycosides form complexes of the composition PbL and PbL\(_{2}\). However, other researchers\(^{112}\) claim that only the former type of complexes exists.

D-Xylaric acid reacts with Pb\(^{II}\) in an acidic medium to give the complex PbL\(_{2}\) as a result of deprotonation of the carboxyl groups.\(^{113}\) In alkaline media, this complex is hydrolysed giving a hydroxo complex,\(^{113}\) D-Gluconic acid 14a in an acidic medium binds Pb\(^{II}\) only as a monodentate ligand by the carboxyl group; this gives the complexes \([\text{PbLH}_{2}]^{2-}\) and \([\text{PbLH}]^{-}\).\(^{114}\) In an alkaline medium, \([\text{Pb(OH)}_{3}]^{-}\) reacts with D-gluconic acid 14a to afford complexes 15–17.\(^{115}\) In solid lead D-gluconate, the metal coordinates two monodentate gluconate residues through the carboxyl groups and two bidentate gluconate residues through the carboxyl group and the hydroxyl group at C(2) (α-type coordination).\(^{116}\) Thus, the Pb\(^{2+}\) cation is surrounded by six oxygen atoms. Evidently, aldaric acids bind Pb\(^{II}\) more strongly than aldonic acids.\(^{117}\)
It has been noted \(^{118,119}\) that Pb\(^{II}\) complexes with oligomeric fragments of the pectate \(^5\) are covalent compounds. In all probability, they contain two carboxyl groups per one Pb\(^{II}\) cation; apparently, this accounts for the high selectivity of formation of Pb\(^{II}\) complexes with pectin.\(^{120}\) The formation of Pb\(^{II}\) complexes with pectin can also occur with incorporation between polymer chains.\(^{121}\)

The complexation of sugars with Group VA elements is little studied. The formation of complexes of monosaccharides and polyols with As\(^{III}\) and As\(^{V}\) of the composition [As\(^{III}\)(LH\(_2\))\(_3\)]\(^-\), [As\(^{V}\)(LH\(_2\))\(_2\)(OH)]\(^-\), and [HAs\(^{III}\)(LH\(_2\))(OH)]\(^+\) has been reported.\(^{109,122}\) Recently the Bi\(^{III}\) complex with L-tartaric acid \(^\text{18}\) has been studied by X-ray diffraction analysis.\(^{123}\) The composition of this complex was found to be Bi(O\(_2\)C(CH\(_2\))\(_2\))\(_2\). CO\(_2\)\(_3\)O\(_2\)(C\(_2\)HO\(_2\))\(_2\).CO\(_2\)H\(_2\).3H\(_2\)O. In this complex, two dicarboxylate ligands are coordinated by the carboxyl and \(\alpha\)-hydroxyl groups (\(\alpha\)-type coordination)\(^{18}\) and one monocarboxylate ligand is coordinated by the two \(\alpha\)-hydroxyl groups of the carboxylate ion. The coordination number of Bi\(^{III}\) is equal to nine due to the additional coordination of three water molecules.

Complexes of monosaccharides with telluric acid (Te\(^{VI}\)) provide an example of complexes obtained for Group VIA elements. For these compounds, structure \(^\text{19}\) was proposed\(^{124,125}\). It was found\(^{126}\) that in addition to the 1:1 complex, saccharose forms the complex L(TeO\(_2\))\(_4\).

Complex formation with Group VIIIA elements has been studied only for iodine. Apparently, this is due to the fact that periodate oxidation is an important process in the chemistry of carbohydrates.\(^2\) It was suggested\(^2\) that this process starts with the formation of an unstable complex of the IO\(_2\) anion with a vicinal diol group; the structure of this complex is similar to that of the tellurate complex \(^\text{19}\), because the sizes of the corresponding ions are close. However, monosaccharides conforming to the first Angyal rule should form\(^{127}\) stable complexes with periodate, for example, a complex of type \(^\text{20}\).

Later, both the fact of formation of the intermediate complexes and the observance of the first Angyal rule have been confirmed by NMR spectroscopy\(^{127}\) and paper electrophoresis.\(^{128}\)

### 3. Complexes with d- and f-metal cations

This field of coordination chemistry of carbohydrates has been studied in the greatest detail, although quite irregularly. The vast majority of the data refer to complexes of carbohydrates with Cu, Fe, Co, Ni, Mo, and W.

Among complexes with Group IB metal cations, those with Cu\(^{II}\) have received most study. The dissolution of freshly prepared copper hydroxide in ammonia-containing or alkaline aqueous solutions of polyhydroxyl compounds, including carboxylic carbohydrates, which has long been used in analytical chemistry, was interpreted\(^{129}\) as the formation of five-membered diolate complexes \(^\text{21}\). The stability constants of these complexes for L = NH\(_3\) are of the order of 10\(^{-2}\)–10\(^{4}\) litre mol\(^{-1}\). In this case, complexes of the 1:1 composition are always formed.\(^{130–131}\) The assumption\(^{132–134}\) that cuprammonium complexes of vicinal diols are formed as structure \(^\text{22}\) (which apparently involves hydrogen bonds) is hardly consistent with both the stability of these complexes and the maintenance of fixed dihedral angles between the coordinated oxygen atoms.\(^5\)

The structure \(^\text{22}\) also does not agree with the observed induction of optical activity in the central atom (the appearance of optical activity in its electronic transitions).\(^{135}\) In fact, in the complex \(^\text{22}\), this would be less likely than in the complexes \(^\text{21}\), because in the former case, the chiral centres (inducers) are further removed from the central atom.

Mannitol was found to form the complex [Cu(LH\(_2\))] when the ligand is present in a large excess\(^{136}\) or Cu\(_2\)L when the reactants are present in equimolar amounts.\(^{136}\) The latter complex is apparently anionic. This was confirmed\(^{137}\) by isolation of a series of analogous anionic copper complexes of carbohydrates. An isomer of mannitol, sorbitol, forms the complex [Cu\(_2\)(LH\(_2\))] in strongly alkaline media\(^{138}\) and a polymeric complex in less alkaline media. An NMR study with the use of a shift reagent has confirmed\(^{139}\) that Cu\(^{II}\) is mostly coordinated to vicinal diol groups of the ligand, although the first Angyal rule can also be observed.\(^{140}\) In neutral and acidic media, polyols do not coordinate Cu\(^{II}\) ions.\(^{141}\) This would require\(^{140}\) deprotonation of at least one hydroxyl group. Structure \(^\text{23}\) similar to \(^\text{21}\) was ascribed\(^{142}\) to complexes containing ethylenediamine in place of ammonia.

The complexation of Cu\(^{II}\) with carbohydrate carboxylic acids has also been studied fairly comprehensively, although, as in the previous cases, these complexes have not been isolated in the solid state. D-Galacturonic acid forms\(^{143}\) the complexes [Cu\(_2\)\(_2\)]\(^-\), [Cu\(_2\)\(_2\)(H\(_2\)O)]\(^-\), [Cu\(_2\)(LH\(_2\))]\(_3\), and [Cu\(_2\)(LH\(_2\))\(_2\)(H\(_2\)O)]\(^-\), whereas D-glucuronic acid forms only the second type of complex.\(^{143}\) In this case, coordination involves the ring oxygen atom,\(^{144}\) as has also been observed for s-metallations (Section II.1). D-Glucionic acid \(^\text{14a}\) or its dimethylglycine ester \(^\text{14b}\), pangamic acid, vitamin B\(_1\)) form mixed-ligand copper complexes in the presence of glycine.\(^{145}\) The structure of these complexes is unknown.

Glucaric acids form complexes with Cu\(^{II}\) according to the \(\alpha\)-type of coordination (Section II.1). The tartaric acids \(^\text{18}\) give hydroxo complexes \(^\text{24}\)\(^{146,147}\) containing a water, ammonia, or amine molecule as a ligand. In the case of D-glucaric acid \(^\text{12}\), formation of the complexes [Cu\(_2\)(LH\(_2\))]\(^-\) (at pH 3.65) and [Cu\(_2\)(LH\(_2\))\(_2\)]\(^-\) (at pH 5–9, coordination only through the carboxyl groups) and formation of the polymer [Cu\(_2\)(LH\(_2\))]\(^n\) (coordination through the carboxyl group of one ligand and the \(\alpha\)-type coordination in another ligand) have been reported.\(^{148}\)
Binuclear copper complexes of sugars are less frequently encountered. For example, D-gluconic acid 14a can form complexes of type 25a or 25b. In addition, one of the bridging hydroxyl groups in the complex 25b can be deprotonated. At a favourable arrangement of four vicinal hydroxyl groups (which occurs, for example, in mucoinositol), sugars in cyclic and acyclic forms can react with CuII at pH 5 yielding binuclear complexes of type 26 in which the hydroxyl groups of the tetradeinate ligand occupy bridging positions.150

Considerable attention has been devoted to the study of complexation of CuII with polysaccharides. Thus dissolution of cellulose in a cuprammonium solution is an important technological process, which has been studied most vigorously.151 The formation of chelates of the type 21 with coordination through the hydroxyl groups at the C(2) and C(3) atoms of β-D-glucopyranose 4b is considered to be the most likely. Polymers having a similar structure, dextrans, are also capable of binding CuII cations in alkaline media.152, 153 This process might be accompanied by untwisting of the helical chains of the ligand.152 The formation of complexes of the type 23 is apparently responsible for the adsorption of the complex [Cu(en)]2+ (where en is ethylenediamine) on cellulose fibres.154

Study of complexation of CuII with anionic polysaccharides has shown155 that D-galacturonate itself binds CuII more strongly than its polymer, polygalacturonate 5. The affinity for CuII decreases in the following sequence: pectate (polygalacturionate) 5 > alginate 6 > polymannuronate. A similar situation was observed for CaII ions.156 The complex formation is a cooperative process.156, 157 The ligand unit in the copper complexes of pectic acids has an octahedral configuration, the CuII cation being coordinated to four oxygen atoms in the symmetry plane. The formation of CuII complexes with anionic polysaccharides changes substantially the conformation of the polymer chains of the ligands. As in the case of CaII, the complex formation is a cooperative process.156, 157 As this takes place, a sulfated polysaccharide, -carrageanane, passes into a helical conformation.159

The formation of complexes of carbohydrates with AgI has been studied only for the silver nitrate –D-glucurono-2,6-lactone 160 and silver nitrate –D-glucuronono-3,6-lactone 161 systems. It was concluded that in both cases, this affords two types of complexes: ‘lactone’ complex 27 and ‘carboxyl’ complex 28.

Among complexes with cations of Group II B δ-metals, compounds of ZnII and CdII have been studied most thoroughly. β-D-Fructopyranose 29 and L-arabinopyranose 30 react with these cations, as with HgII cations, to give solid complexes of the composition [MLX2·4H2O], where X = Cl, Br. In the complex of fructose, the coordination involves two ligand molecules; one of them binds the central ion through the O(2) and O(3) atoms and the other one binds this ion through O(4) and O(5).162 In the case of L-arabinopyranose 30, the two ligands are also coordinated through different sites: the O(3) and O(4) atoms of one molecule and the O(1) and O(5) atoms of the other molecule.163

In the ZnII and CdII complexes with both ligands (29 and 30), the metal ion coordinates additionally two water molecules, and thus its coordination number is equal to six. For the HgII cation, there is no coordination with water (the coordination number is four). The counter-ion of the initial salt is bound to the metal cation by electrostatic forces.

 Sugars and their O-glycosides react with cadoxen (a solution of cadmium hydroxide in ethylenediamine) to give complexes incorporating two deprotonated equatorial hydroxyl groups of the pyranose ring. Presumably, they have the structure 31.164

This structure is additionally stabilised by hydrogen bonds. However, as in the copper complexes 22, in this case, too, it is difficult to explain the observed induction of optical activity in the electronic transitions of CdII.165

D-Glucuronic acid 14a and CdII form complexes with a Cd : L ratio of 1 : 2 (pH 5.8), 2 : 3, and 2 : 1 (pH 13 – 14).166 D-Glucuronic acid forms two types of solid complexes with ZnII, CdII, and HgII: complexes produced via coordination through the carboxyl group and the ring oxygen atom of the first ligand molecule and the carboxyl group and the O(4) atom of the second molecule and those 32 in which coordination involves only the carboxyl groups.167 In the O-methylglycoside of D-glucuronic acid, ZnII is bound to the carboxyl group and to the ring oxygen atom.16 It has been noted168 that D-glucaric acid 12 forms a complex with CdII, but its structure has not been described.

© is a cellulose fragment.

Complex formation of O-methylglucosides in aqueous solutions of zinc chloride has been reported.169 Presumably, the metal ion is coordinated to the O(2) and O(3) atoms. The complex formation accounts168 for swelling of cellulose in these solutions.151 Cellulose is known151 to dissolve in cadoxen. Apparently, this yields polymeric complexes like 31. The reaction of rhodanine with cellulose in the presence of a cadmium salt gives rise to complex 33 with different ligands.169 Substituted rhodanines afford similar complexes.170

It was found that cadmium(II) 171 and zinc(II) 172 ions are bound to pectate 5 through the carbohydrate groups, although the α-type coordination also cannot be ruled out. A similar situation is observed in the case of oligosaccharide fragments of pectic acids.172

\[ \text{Zn}^{2+} + 2 \text{O-methylglucoside} \rightarrow \text{Zn(O-methylglucoside)}_2^{2+} \]
Complexes of carbohydrates with Group IIIIB d-metals are represented by Y\textsuperscript{III} complexes of tartaric acid, the composition of which varies from 1 : 1 to 1 : 5 depending on the pH.\textsuperscript{173} and by Y\textsuperscript{III} complexes of D-glucic acid 14a, the composition of which is 1 : 1 and the charge varies depending on the pH.\textsuperscript{174, 175} Complexes of La\textsuperscript{III} with tartaric, D-glucaric 12, and D-galactaric acids have been obtained, their composition (1 : 1 or 1 : 2) being also dependent on the pH value.\textsuperscript{176} No data on the structures of these complexes have been reported.

Several complexes formed by Group IVB elements are known. These are Ti\textsuperscript{IV} complexes\textsuperscript{177} with tartaric (18) and D-glucic (14a) acids and with mannitol (their composition is 1 : 1 or 1 : 2 depending on the pH), the Zr\textsuperscript{IV} complex with trihydroxyglutaric acid [Zr(OH)\textsubscript{3}(LH\textsubscript{2})\textsuperscript{2–}].\textsuperscript{178} and Zr\textsuperscript{IV} and Hf\textsuperscript{IV} complexes with tartaric, trihydroxyglutaric, and D-galactaric acids, which have similar structures.\textsuperscript{179}

The known complexes of Group VB d-metals are mostly formed by vanadium. For example, metavanadate in aqueous solutions reacts with aldoses to give complexes incorporating the [VO\textsubscript{2}L\textsubscript{2}]\textsuperscript{–} and [VO\textsubscript{3}L\textsubscript{5}]\textsuperscript{3–} anions.\textsuperscript{180} In the latter case, complex formation is observed only for D-glucitol (sorbitol) and maltose (which is a disaccharide), L-Tartaric acid 18, its D-enantiomer, and the corresponding racemate form binuclear complexes with the vanadyl ion VO\textsuperscript{2+}; the composition of the complexes is [VO\textsubscript{2}L\textsubscript{2}H\textsubscript{2}O\textsubscript{n–}](n = 5, 6, or 8 depending on the pH).\textsuperscript{181} Mesotartaric acid forms a trinuclear complex, [VO\textsubscript{3}L\textsubscript{5}H\textsubscript{2}]\textsuperscript{2–}.

For polynuclear complexes of acyclic polyols and aldonic acids in aqueous solutions,\textsuperscript{184} at pH 3 – 7, Nb\textsuperscript{V} ions and D-glucic acid form the complexes [Nb(OH)\textsubscript{3}(LH\textsubscript{2})\textsuperscript{2–}] – \textsuperscript{–}, while at pH 7 – 9, the complexes [Nb(OH)\textsubscript{4}(LH\textsubscript{2})\textsuperscript{3–}] – \textsuperscript{–} are produced.\textsuperscript{185}

The complexation of sugars with cations of Group IIIIB d-metals has been studied fairly intensively. Primary attention has been devoted to complexes of molybdenuim and tungsten. Chromium(III) cations do not form stable complexes with sugars in aqueous solutions,\textsuperscript{186} whereas in dry methanol, aldoses form complexes with Cr\textsubscript{Cl\textsubscript{3}}:Py (Py is pyridine); the composition of these complexes is 1 : 3 (aldose : CrCl\textsubscript{3} : Py)\textsuperscript{186} Conversely, D-glucaric acid 12 (and, perhaps, all the aldric acids) and Cr\textsuperscript{III} in aqueous solutions form an equilibrium system, similar to the 13a = 13b system.\textsuperscript{187} It has also been reported\textsuperscript{187} that a stable complex of Cr\textsuperscript{III} of an unknown structure is formed during oxidation of D-galacturonic acid with Cr\textsuperscript{III} cations.

The complex formation of sugars and Mo\textsuperscript{VI} and W\textsuperscript{VI} oxo cations has been studied most comprehensively. Since the structures of carbohydrate complexes formed by these metals are similar,\textsuperscript{188 – 190} they will be discussed together. In most cases, binuclear complexes ML\textsubscript{2} with bidentate (complex 37) and tridentate (complex 38) types of ligand coordination are produced in aqueous solutions. The structure of 37 was unambiguously established only for the molybdenuim complex of D-glucuronic acid β-methylglycoside. According to X-ray diffraction analysis,\textsuperscript{153} this complex is characterised by the 3- and 4-coordination. For carbohydrates existing in acyclic forms (alditols, aldonic acids), this type of coordination is accomplished in one tetradeinate ligand in which the neighbouring hydroxyl groups occupy cis-positions.\textsuperscript{191 – 194} The complexes like 38 are formed in conformity with the first Angyal rule\textsuperscript{193, 194} even if the initial chair-like conformation of the pyranose ligand is distorted.\textsuperscript{195, 196}

Since, due to their conformational mobility, acyclic forms of sugars are more prone to form complexes, it has been assumed and, to some extent, confirmed\textsuperscript{197} that the hydrate of the aldehydo form 39 participates in the complex formation. It has been reported\textsuperscript{198} that D-lyxose, D-mannose, and L-rhamnose are coordinated as tetradeinate ligands in the cyclic pyranose form, although D-lyxose in the furanose form can be also coordinated in this way (see structures 40 and 41). However, other researchers\textsuperscript{199} claim that these ligands are coordinated in a tridentate fashion. Upon the interaction of WVI ions with an acyclic polyol (sorbitol), in addition to the tetradeinate coordination (1 : 1 complexes as tetradeinomers), a complex of the type 37 in which the ligand is coordinated bidentately has been detected.\textsuperscript{200} The carbohydrate complexes of WVI are three orders of magnitude more stable than complexes of Mo\textsuperscript{VI}. This is due\textsuperscript{198} to the fact that WVI forms polyoxo anions more readily than Mo\textsuperscript{VI}.

Attempts to determine the structure of the carbohydrate complexes of Mo\textsuperscript{VI} and WVI by X-ray diffraction analysis are not always successful. Thus, according to X-ray diffraction data,\textsuperscript{201} the crystalline compound isolated upon the interaction of D-xyloluranose with ammonium molybdate proved unexpectedly to be a complex of D-lyxose 40. The transformation of D-lyxose into D-lyxose, which is the C(2) epimer of the initial ligand, was explained by the Lory de Bruyn – Alberda van Ekenstein rearrangement occurring during the synthesis of the complex (Section VI.2). It was shown that the new ligand is coordinated in the furanose form 41. Later, using X-ray diffraction analysis, a similar structure has been found for the molybdenum complex of an acyclic tetraol (erythritol).\textsuperscript{202} Based on 13\textsuperscript{C} and 95Mo NMR spectra, it was shown that in solutions, molybdenum complexes of other acyclic polyols (mannitol, etc.) have similar structures.\textsuperscript{203} After these publications, there are grounds for believing that the other Mo\textsuperscript{VI} and WVI oxo complexes discussed above also have binuclear structures of the type 40.
can be stabilised by acyclic polyhydroxyl ligands in aqueous solutions.\textsuperscript{231, 232} The greater the number of hydroxyl groups in the ligand, the more pronounced this stabilisation, because, according to the principle of hard and soft acids and bases,\textsuperscript{205} the Mn cations ligand, the more pronounced this stabilisation, because, according to the principle of hard and soft acids and bases,\textsuperscript{205} the Mn cations form complexes with Mn\textsuperscript{II} ions.\textsuperscript{206} However, it was stated\textsuperscript{207} that the complexes of sorbitol with Mn\textsuperscript{II} ions are also stable. The composition of complexes of acyclic polyols with Mn\textsuperscript{II} was found\textsuperscript{204, 207} to be 1:2 or 1:3. In aqueous solutions, D-glucic acid 14a forms complexes \([\text{Mn}(\text{LH}_2)\text{O}]^2–, [\text{Mn}(\text{LH}_2)\text{O}]^2–, \) and \([\text{Mn}^\text{IV}(\text{LH}_2)\text{OH}]^2–\) (from data on electrochemical oxidation with variation of the electrode potential).\textsuperscript{208} The former complex is able to dimerise with successive deprotonation yielding a series of binuclear compounds. The complex of D-glucic acid of the composition \([\text{Mn}(\text{LH}_2)\text{O}]^2–\) is the first example of a stable carbohydrate derivative of Mn\textsuperscript{IV}. In the solid Mn\textsuperscript{II} gluconate, which is the only carbohydrate complex of manganese studied by X-ray diffraction analysis,\textsuperscript{209} the central ion was found to have an octahedral environment formed by two ligands and containing the carboxyl and hydroxyl oxygen atoms. These ligands exist in two conformations: a zigzag-like (similar to that of alkanes) and a bent conformation. The same conformation of the carbohydrate ligand was found in an aqueous solution of Mn\textsuperscript{II} gluconate.\textsuperscript{210} Tartaric acid 18 forms a neutral Mn\textsuperscript{II} tartrate,\textsuperscript{211} which is deprotonated upon an increase in the pH, and in alkaline solution, it is oxidised by atmospheric oxygen to give hydroxyltartrate complexes of Mn\textsuperscript{III}.\textsuperscript{212} Manganese(II) does not form complexes with D-gluconic acid by atmospheric oxygen to give hydroxytartrate complexes of Mn\textsuperscript{III}.\textsuperscript{212} Manganese(II) does not form complexes with D-gluconic acid\textsuperscript{148} but with different colours and different chiroptical properties, \textsuperscript{151} which have a structure like 43.\textsuperscript{227} In addition to these chelates, Co\textsuperscript{III} ions form a binuclear complex \([\text{Co}_{(N\text{H}_3)\text{OH}}(\text{H}_2\text{O})\text{L}]^3+\) with D-arabinose.\textsuperscript{218}

In the series of carbohydrate carboxylic acids, complex formation of Co\textsuperscript{II} and Ni\textsuperscript{II} with D-glucic acid 14a has been studied most extensively. It has been noted\textsuperscript{4} that this is not accompanied by substantial changes in the ligand conformation and that Ni\textsuperscript{II} chelates are more stable than Co\textsuperscript{II} chelates.\textsuperscript{229} It was found that in an acidic medium, unstable complexes \([\text{Ni}(\text{LH}_2)\text{O}]^2–\) are formed.\textsuperscript{230, 232} Polymeric complexes \([\text{Co}(\text{OH})\text{L}(\text{LH}_2)\text{HO}_2]\) and \([\text{Co}_2(\text{OH})_2(\text{LH}_2)\text{HO}_2]^2\) were detected in the pH range of 7.5 – 9.5.\textsuperscript{231} The latter is a polymer of structure 44. The complexes \([\text{Ni}(\text{OH})(\text{LH}_2)]^2–\) and \([\text{Ni}(\text{OH})_2(\text{LH}_2)]^–\), which might have a similar structure, have been obtained.\textsuperscript{230} Tetraaminecobalt(II) reacts with D-glucic acid (14a) and D-glucic acids to give the complexes \([\text{Co}(\text{NH}_3)_3\text{L}]^2+ (n = 4, 5)\) in which the ligands behave as monodentate ones.\textsuperscript{235} Study of solid nickel gluconates \([\text{Ni}(\text{LH}_2)\text{HO}_2] 2\) and \([\text{Ni}(\text{OH})(\text{LH}_2)\text{HO}_2]^2\) by spectroscopic and magnetic methods has shown that the chelate units in both complexes have a distorted octahedral configuration.\textsuperscript{234} The second complex has a polymeric structure with hydroxyl bridges, apparently, similar to the structure 44.

The diastereomeric A- and Δ-complexes \([\text{Co}(\text{LH}_2)\text{L}(\text{en})]^2+\) and \([\text{Co}(\text{LH}_2)\text{L}(\text{en})]^2+\) have been obtained by the reaction of racemic \([\text{Co}(\text{CO})_3(\text{en})]^2+\) with aldones and separated.\textsuperscript{17} Aldaric acids form\textsuperscript{148} chelates of the type \([\text{M}(\text{LH}_2))\text{OH}]^2–\) and \([\text{M}(\text{LH}_2)\text{OH}]^2–\) with different colours and different chiroptical properties, \textsuperscript{151} which have a structure like 43.\textsuperscript{227} In addition to these chelates, Co\textsuperscript{III} ions form a binuclear complex \([\text{Co}(\text{N\text{H}_3})\text{OH}(\text{H}_2\text{O})\text{L}]^3+\) with D-arabinose.\textsuperscript{218}

Preparation of polymeric Fe\textsuperscript{III} complexes of the type 42 with sorbitol or D-glucic acid has been reported.\textsuperscript{226}

Cobalt(II) and nickel(II) cations form 1:1 coordination complexes with mannitol.\textsuperscript{136} Ammonia complexes of Co\textsuperscript{II} react with D-ribose and L-sorbos to give chelates \([\text{Co}(\text{NH}_3)\text{L}(\text{LH}_2)]^2+\) chiroptical properties of which point to a structure like 43.\textsuperscript{227} In addition to these chelates, Co\textsuperscript{III} ions form a binuclear complex \([\text{Co}(\text{N\text{H}_3})\text{OH}(\text{H}_2\text{O})\text{L}]^3+\) with D-arabinose.\textsuperscript{218}

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The complexation of carbohydrates with cations of platinum group metals has been studied mostly in connection with their therapeutic effect (Section VI.1). When cisplatin 45 was made to react with D-mannitol, two complexes with identical structures (46) but with different colours and different chiroptical properties were isolated.\textsuperscript{236} The reasons for this result are unknown.
The reactions of acyclic polyols with the 1,3-bis(diphenylphosphino)propane platinum complex result in the formation of stable diolate chelate-type complexes 47, which are additionally stabilised by intramolecular hydrogen bonds. The complexes have been structurally characterised. The reaction is regioselective and occurs most efficiently with vicinal diol groups. Peculiar anionic complexes, so called osmarines, are formed upon the reaction of osmium salt 48 with aldoses.238, 239

These complexes are polymers the backbone of which consists of linked (possibly, via oxygen) Os atoms with ‘grafted’ monosaccharide residues. The molecular masses of these compounds are between 10^3 and 10^5 dalton. Some of the aldose fragments are oxidised to aldonic acids during complex formation; therefore, the complexes can be described by the general formula KₙOsO₇₋ₙYₐZₐ(H₂O)ₓ₋ₚ, where Y is aldose, Z is aldonate (the therapeutic properties of these polymers are described in Section VI.5).

D-Glucuronic acid 14a forms two extremely stable complexes of the composition 1: 1 with PtIV cations; these products result from slow hydrolysis of the initial polymers of the composition 6: 1.7 The RuIII cation also forms a stable complex compound with D-glucuronic acid in an alkaline medium.240 Similar stable complexes of D-glucuronic acid have been obtained for OsIII, OsIV, and OxbV ions.241 Mixed-ligand chelates [PtL₁(1,3-diamine)] have been obtained with D-glucuronate and D-glucuronate in the presence of 1,3-diamines.242

Among the complexes formed from f-metals with sugars, those of lanthanides have been studied most thoroughly. The use of water-soluble lanthanide salts as shift reagents in NMR spectroscopy has demonstrated that the first Angyal rule holds for both cyclic and acyclic carbohydrate forms, while the second Angyal rule is obeyed for furanoses,245 i.e. there is a similarity between the behaviours of lanthanides and s-metals.

The complexation of lanthanide cations with carbohydrate carboxylic acids has been studied fairly comprehensively. The chiroptical properties of the complexes of lanthanides with tartaric acid 18 are discussed in a review.246 The z-type bidentate coordination and tridentate coordination through both hydroxyl groups and the carboxyl group have been assumed for the complexes resulting from the reaction of glycicic acid with CoIII.247 D-Galacturonic acid coordinates EuIII ions through the oxygen atom of the carboxyl group, the hydroxyl group at the C(4) atom, and the ring oxygen atom (1: 1 complex),248 while the O-methylglycoside of this acid binds EuIII only by the carboxyl group and the ring oxygen atom [the [Eu(LH⋯13)] complex].249

D-Glucuronic acid 14a forms the most stable chelates with CeIII ions.250 Structures with the z-type coordination and with tridentate coordination involving the carboxyl group have been proposed for 1: 1 complexes of lanthanides.250, 251 The stability constants of these complexes at low and high pH values have been determined. An increase in the glucuronic concentration leads to the formation of complexes [Mₙ(LH⋯13)]n[X–n]”, where n = 2–4.255

As regards actinides, only data on the complex formation of UVI (as the uranyl cation, UO₂²⁺) have been reported. This cation coordinates aldonopranoses and cyclic polyols at pH > 10 without observance of the first Angyal rule. Apparently, this is due to its large size.259 D-Glucuronic acid forms complexes 49 and 50 with these ions.259 Similar complexes are produced in the case of tartaric acid 18 and trihydroxyglutaric acid.257

### III. Complexes of cyclodextrins

Cyclodextrins (CD) are cyclic oligosaccharides consisting of six (α-CD), seven (β-CD), or eight (γ-CD) residues of α-D-glucopyranose 4a. They are capable of incorporating various organic molecules into inner hydrophobic cavities.258–262

Less is known of the ability of cyclodextrins to form complexes with metal ions. Thus β-CD complexes alkali metal salts, although this mostly occurs due to binding of the anion.263 Complexes of α-CD with iodine of the type (α-CD)2 LiI: I2: 8H₂O (a model of the blue iodine complex with amylose) and with cadmium ions have been described.264 In the β-CD complex with KOH, the K⁺ ion is bound by six coordinate bonds with the hydroxyl groups of the glucopyranose residues thus forming a distorted trigonal prism.265 The lutetium ion can also be bound to β-CD.266 Metal complexes of coronands (crowns ethers)267, 268 or their acyclic analogues, podands,268 can be incorporated into the cavities of cyclodextrins.

Some complex compounds of cyclodextrins with d-metal cations are also known. α-Cyclodextrin forms binuclear complexes 51 with CuII; complexes of β-CD are formed similarly but contain deprotonated oxygen bridges.269–271

![Diagram](image_url)

Other d-metals are also prone to form polynuclear complexes with β-CD. For example, the complexes [Mₙ(OH₂)(β-CD): 2H₂O] (M = MnIII, CrIII), Na₃[M₂(OH)₄(β-CD): 2H₂O] (M = CoII, NiII, CuII), and [M₄(OH)₄(β-CD): 2H₂O] (M = FeIII) have been described.272, 273

However, the primary attention is paid to the inclusion of d-metal complexes into cyclodextrin cavities (second-sphere coordination).274, 275 Thus 2-, 3-, and ρ-CD form host–guest complexes (inclusion compounds) 52a, 52b, and 52c, respectively, with ferrocene.276–278

![Diagram](image_url)

The ‘guest’ molecules in these complexes can rotate freely only at elevated temperatures.279 The axial incorporation of ferrocene in the complex 52b was confirmed in a study of complexation of cyclodextrins with a model ferrocene derivative that can be arranged in the cavity only equatorially, as in the complex 52c.280 Since the cavity of α-CD is small, it can incorporate only...
monosubstituted ferrocenes, whereas the other cyclodextrins form complexes with disubstituted ferrocenes as well.277,278 In this type of cyclodextrin complex, a chiral ‘host’ molecule induces optical activity in a ‘guest’ molecule. This facilitates investigation of these compounds.281,282 The complex \([\eta^2\text{C}_6\text{H}_5\text{FeC}_6\text{H}_5\text{PF}_3\cdot 2\alpha\text{-CD}]\) of the type 52a and its analogues containing naphthalene, indan, tetralin, or thiophene instead of benzene284 have been prepared. Complexes of \(n\)-arenetricarbonylchromium with \(\beta\)- and \(\gamma\)-CD of the composition 1 : 1 are known.285

Incorporation of organometallic \(\pi\)-complexes such as \([\eta^1\text{allyl}]{\text{Pd}}\)286 \[[\text{cod}]\text{RhCl}_2\] (cod is cyclooctadiene),287 \[[\text{cod}]\text{Rh}(\text{X})_2\] \((\text{X} = \text{Cl}, \text{Br}, \text{I})\),287 \[[\text{cod}]\text{Rh(NH}_3)_2\]288 – 290 and ordinary platinum complexes such as 45290 – 293 into cyclodextrins has been studied.

Bulkly metal complexes such as macrocyclic Ni\(^{III}\) complex 53294 or the Fe\(^{III}\) complex with protoporphyrin IX (hemin)295 can also occupy the hydrophobic cavities of cyclodextrins.

Rotaxane complexes of type 54 have been synthesised.296 – 299

Since the CD molecule is chiral, the synthesis involves asymmetric induction and yields predominantly stereoisomers with the \((\Delta,\Delta)\)-configuration of the chelate units.298,299

In the metal complexes of ribonucleosides 55a, metal ions are normally coordinated to endocyclic nitrogen atoms in a base of the pyridine type (B).300 – 303 In the case of ribonucleotides 55b, additional coordination to the phosphate group is possible; this gives cyclic complexes of the type 56, in conformity with the principle of hard and soft acids and bases.205

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{Cl} \\
\text{N} & \quad \text{Cl} \\
\text{N} & \quad \text{Cl} \\
\end{align*}
\]

\(n = 8, 10, 12, 14.\)

![Complexes of natural carbohydrates with metal cations](image)

IV. Complexes of nitrogen-containing natural carbohydrates

In the metal complexes of ribonucleosides 55a, metal ions are normally coordinated to endocyclic nitrogen atoms in a base of the pyridine type (B).300 – 303 In the case of ribonucleotides 55b, additional coordination to the phosphate group is possible; this gives cyclic complexes of the type 56, in conformity with the principle of hard and soft acids and bases.205

However, within the scope of this review we are interested in the exceptions to this rule, namely, complexes resulting from coordination of carbohydrate fragments. Thus in disodium uridine 3'-phosphate, the Na\(^{+}\) cation is coordinated not only to the phosphate but also to the oxygen atoms at C(2') and C(3').304 Likewise, the ribose residue is one of the sites of coordination of the Li\(^+\) ion to the nucleosides 55a.305 In the sodium inosine phosphate, the Na\(^{+}\) cation is coordinated to the hydroxyl groups at the C(2') and C(3') atoms of the ribose residue.306 The interaction of borate ions with pyrimidine nucleosides involves coordination at the vicinal diol group at C(2') and C(3') and results in a complex of the type 8.307 Vanadate ions are coordinated in a similar way.183,308 The same hydroxyl groups and Cu\(^{II}\) ions give binuclear complexes Cu2L2 of the type 51.309,310 It has been suggested that Cu\(^{II}\) acetate forms three-dimensional binuclear complexes like 57,311 however, other results312,313 attest to the formation of ordinary coordination units of the type 21. The uranyl complex of adenosine has the binuclear bridged structure 58.314,315 Desoxyribonucleosides and -nucleotides do not contain a vicinal diol group; therefore, their carbohydrate fragments do not participate in coordination.

Among natural aminosaccharides, D-glucosamine (2-amino-2-deoxy-D-glucopyranose, 59a) has received most attention. Metal complexes of D-glucosamine have been studied by electron spectroscopy, potentiometric titration, calorimetry, and EPR spectroscopy. No X-ray diffraction data for these complexes are available.

The complex formation of D-glucosamine 59a with Cu\(^{II}\) has received the most study.141,316 – 324 This interaction involves coordination not only to the amino group but also to the hydroxyl groups at the C(1) and C(3) atoms adjacent to the amino group.316,321 In the complexes CuL and CuL2,317,320 the hydroxyl groups of the ligands can be either free321 or deprotonated.323 Other researchers141 deny participation of free hydroxyl groups in the coordination and assume that deprotonation is typical first of all of the hydroxyl group at C(1), because it is the most acidic.323 In the case of the Cu\(^{II}\) complex of N-acetylglucosamine 59b, the N-acetyl group is not coordinated to the Cu\(^{II}\) ion but stabilises the complex (Cu(LH\(_2\))\((\text{OH})_2\))\(^-\).141

The cationic complexes [FeL(OH)\(_2\)]\(^+\) and [FeL(OH)]\(^2+\) are formed from Fe\(^{III}\) and D-glucosamine in a physiological salt solution.326 The crystalline complexes \([\text{NiL}_2\text{X}] (\text{X} = 2\text{Cl}, \text{SO}_4^{2-})\) have been obtained.327 Synthesis of cis-dichlorobis(D-glucoseamine)platinum(II) has been reported.328

The interaction of D-glucosamine 59a with tris(ethylenediamine)cobalt has led to contradictory results. First, it was reported329 that this gives an outer-sphere complex with a structure of the type 31. Subsequently, it was shown330 that this affords four isomers with a \(\Delta: \Lambda\) ratio of 7 : 3, which differ in the
anomeric configuration of the ligand and configuration of the chelate unit (complexes like 43 with an amino group instead of a hydroxyl group). Finally, recently it was shown that the composition of the product mixture is even more complicated; eight(!) isomers were isolated from the mixture and characterised by X-ray diffraction analysis. In all of these compounds, the ligand had been converted preliminarily into a substituted N-glucoside, and after that, the reaction gave complexes of the type 43 [with an amino group instead of the hydroxyl group at the C(1) atom of the sugar]. The ligand in this complex was either transformed into the aldehyde form of the type 39 or into the furanose (keto) form as a result of the Amadori rearrangement, or remained in the native pyranose form.

In order to model the chemical behaviour of natural polysaccharides containing residues of D-glucosamine 59a, which might be able to form multi-ligand complexes, a ternary complex consisting of CuIII, D-glucosamine, and prometon [2-methoxy-4,6-bis(iso-propylamino)-s-triazine, PR] of the composition [CuPR(LH2)] was synthesised.332

The complex formation of other natural 2-amino sugars has been much less studied. It has only been reported that CuIII forms complexes with D-mannosamine 333, D-galactosamine, and D-talosamine.334 The latter complex is the most stable among copper complexes of natural 2-amino sugars. This was explained334 by the formation of a very strong hydrogen bond between the hydroxyl group at C(4) and the amino group at C(2), owing to their diaxial orientation.

An important constituent of natural glycolipids and glycoproteins is N-acetylgalactosaminic acid. The β-anomer of this acid 60a forms 335–337 a fairly stable complex with CaII of the composition 1:1 (Kc = 121 litre mol⁻¹).335 The calcium complex with N-glycolylnemuramic acid 60b is even more stable (Kc = 193 litre mol⁻¹).336

The complex formation of CaII with the ligand 60a has been reported335 to involve the ring oxygen atom and the hydroxyl groups at the C(7), C(8), and C(9) atoms; however, according to another publication,337 coordination occurs through the ring oxygen atom and the hydroxyl groups at C(2) and C(8). The natural β-anomer of the N-acetylgalactosaminic acid 60c weakly binds CaII,337 binding of metal cations by the ligand 60c becomes markedly stronger when CaII is replaced by GdIII or MnII,338 which coordinate 60c in the region of the glycerol ‘tail’ and the carboxyl group. Natural gangliosides (oligosaccharides containing the acid 60c and long hydrocarbon chains attached to them) coordinate metal cations by the glycerol fragment of the natural β-anomer 60c. In this case, CaII ions are bound much more strongly than MgII. However, since the O-methylglycoside of the β-anomer 60c scarcely binds CaII, the coordination involves neighbouring monosaccharide fragments, in addition to the N-acetylgalactosaminic fragment. A similar enhancement of complexation is also observed341 in the binding of CdII by glycopha- rīn A—a transmembrane glycoprotein with a high content of N-acetylgalactosaminic acid 60c. In aqueous solutions, N-acetylgalactosaminic acids 60a,c do not coordinate Na⁺ and K⁺ cations.342

Glycosaminoglycans are polymers containing 2-amino sugars and occurring in connective tissues (mucopolysaccharides); therefore, study of their complexation presents considerable interest from biochemical and medical viewpoints. A typical representative of mucopolysaccharides is an anticoagulant hepa-
The presence of doubly charged s-metal cations ensures a helical conformation of hyaluronic acid. In accordance with polarographic data, CuII forms complexes of the type CuL, CuL2, and CuL3 (L is deprotonated hyaluronic acid). In the former case (an inner-chain complex), CuII is chelated by the carboxyl group and by the bridging oxygen atom, while at high pH values, the deprotonated N-acetyl group also participates in the coordination.

Chondroitin-6-sulfate binds Na+ and Ca2+ ions non-specifically. In terms of the strength of their binding to chondroitin-4-sulfate, s-metal cations can be arranged in the same sequence as in the case of heparin (see above). In the case of chondroitin-6-sulfate, there is no difference between the strengths of binding of doubly charged s-metal cations. For a mixture of chondroitin-6-sulfates, it has been shown that the efficiency of binding increases in the sequence CuII < YbIII < LaIII. In addition, chondroitin-4-sulfate binds YbIII cations by the carboxyl group and the sulfo group of one chain and by two carboxyl groups of a parallel chain.

V. Complexes of natural acids of the carbohydrate origin

In this Section, we describe a number of complexes such as ascorbic (64), shikimic (65), kojic (66), and phytic (phytin, myo-inositol hexaphosphate, 67) acids. These particular subjects were chosen due to their biosynthetic origin from carbohydrates.

Numerous studies and a comprehensive review covering publications up to 1977 have been devoted to metal complexes with ascorbic acid (vitamin C) 64. Being a dibasic acid [owing to the proic activity of the hydroxyl groups at C(2) and C(3)], ascorbic acid can be converted into two anions, (LH−) and (LH−)2−. It forms complexes [MLxLz], [MLn(LH−)y], [ML(LH−)z], and [ML(LH−)z]OH− with virtually all metal cations including oxo cations. Salts of ascorbic acid are formed upon coordination of a metal cation by the deprotonated hydroxyl group at C(3) (the strongest acidic site). The subsequent coordination involves the hydroxyl group at C(2) (either free or deprotonated) and the lactone carbonyl group at C(1). The vicinal hydroxyl groups in the tail at the C(5) and C(6) atoms do not participate in the coordination in solutions, although in the condensed phase, this coordination is possible. Thus in solid Ti3 ascorbate, the metal ion is additionally bound not only to the hydroxyl groups at C(5) and C(6) but also to the lactone carbonyl group. In solid ascorbates of divalent s-metals, a cation is coordinated to three anions, and only MgII binds two anions. In aqueous solutions, cations of univalent s-metals are bound by an ionic bond, except for Li+, which is bound by a covalent bond.

In the case of InIII and GaIII, polynuclear complexes predominate in acidic media, while lanthanides form complexes [ML(LH−)z]. The following stability series has been elucidated for the complexes of divalent metals: Be > Pb > Mn > Fe > Co > Ni. These metals form complexes of the composition 1:1 and only BeII forms stable 1:2 complexes.

Complex formation of VIV, V, III, and V1, IV has been studied in detail. Upon the reaction with VIV, dehydroascorbic acid undergoes the lactone ring opening being thus converted into diketogulonic acid. Catechol 68 is formed apparently from the enol form of this acid and the vanadyl ion.

Complex formation of ascorbic acid with d- and f-metal cations has been studied. This ligand forms solid three-dimen-sional polymeric complexes with ZnII, CoII, and HgII. Solutions, monodentate [through the O(3) atom] or bidentate [through the O(2) and O(3) atoms] coordination is possible. The complexes of the acid with CoII have been studied in most detail. A study of spin–lattice relaxation in the 13C NMR spectra has confirmed the predominant chelation of CoIII, FeIII, and MnII by the O(2) and O(3) atoms, while the lactone and ring oxygen atoms and the hydroxyl groups at C(5) and C(6) are weaker coordination sites.

The reaction of the acid with [Co(NH3)4]2+ gives two complexes: a monodentate complex [with coordination through O(3)] and a bidentate one (with coordination to the lactone and ring oxygen atoms). A stable ternary complex 69 formed by ascorbic acid and bis(2,2-bipyridyl)nickel(II) has been described. Binuclear complexes of CuII 70 are readily reduced by ascorbic acid if the sizes of the reactants are fitted in the intermediate complex.

An unusual organometallic complex of platinum with ascorbic acid (71) containing a C–Pt σ-bond has been synthesised within the framework of studies dealing with the development of new anticancer preparations. Complexes of the acid with dicyclopentadienyltitanium [η-C5H5]2TiL2 and with dialkyltin [R2SnL·H2O] (R = Me, Et) have also been obtained. In the latter complex, the ligand L can be coordinated both in monodentate [by O(3)] and bidentate [by O(2) and O(3)] fashions.

Shikimic acid 65 forms a 1,2-diaminocyclohexanetriplatinum complex similar to the compound 71 prepared from ascorbic acid [the metal is coordinated to the carboxyl oxygen atom and to the alkene carbon atom C(2)].

Kojic acid 66a containing an oxo-enol fragment forms numerous complexes with various cations, including s-metal ions. The compounds of kojic acid with metal ions can be built either as complex salts with coordination to the oxygen atom at C(6) or as chelates with an additional coordination to the oxo group. Synthetic 5-phenacylkojic acid 66b also acts as a complexone. In its complexes, a metal ion is linked to...
the carbonyl fragment of the phenacyl group, to the carbonyl group at C(4), and to the oxygen atom at C(6).

The formation of metal complexes with phytin has been intensely studied due to the dietary significance of this compound (Section VI.1). The thermodynamics of phytin complexation with $\text{Ca}^{2+}, \text{Zn}^{2+}, \text{Cu}^{2+}$, $\text{Mn}^{2+}, \text{Ni}^{2+}, \text{Fe}^{3+}$, and $\text{Cr}^{3+}$ have been studied by calorimetry. Complex formation of incompletely substituted ester, myo-inositol 1,2,6-triphosphate, with alkali $^{407}$ and transition $^{408}$ metal cations has been investigated. For none of the complexes obtained, has the structure been determined.

VI. The significance and applications of metal coordination to carbohydrates

1. The influence of complex formation on the chemical properties of carbohydrates

The catalytic role of metal cations in a key transformation of carbohydrates, namely, in the Lobry de Bruyn – Alberda van Ekenstein rearrangement $^{2,409}$ (epimerisation of aldoses at the C(2) atom and their conversion into ketoses), has been explained by assuming the intermediate formation of complex $^{72,409}$ In a discussion of the dehydration of carbohydrates, the special case of alkaline dehydration of D-mannose was interpreted using the suggestion $^{410}$ of formation of an enediol complex of type 73. The formation of similar enediol metal complexes has been assumed $^{411}$ to rationalise the mechanism of oxidation of monosaccharides by hydrogen peroxide. These complexes have been identified by electronic and NMR spectroscopy. $^{412}$ The enediol complex 74 has been isolated and characterised. $^{413}$

![Diagram 72](image)

Thus, the hypothesis of the formation of enediol forms of carbohydrates stable as metal complexes, put forward $^{2,370}$ to account for the above transformations, can be considered to be experimentally proven. However, in view of the most recent results, participation of these species in epimerisation seems doubtful (see below).

Angyal $^{414} - 417$ have shown that O-glycosylation according to Fischer (treatment of sugars with a methanolic solution of HCl) $^{2}$ carried out in the presence of calcium or strontium salts results in increased yields of O-methylfuranosides. This discovery made this type of compound readily accessible. Acyclic forms, aldose dimethyl acetal, can also be formed under these conditions. $^{418}$

The promotory effects of Ca$^{2+}$ and Ba$^{2+}$ ions on the alkaline oxidation of aldoses by 2-anthraquinonesulfate to aldonic acids of the type 14a has been explained $^{419}$ by the fact that the stability of the intermediate aldose-2-uloses 75 increases when these metal ions are coordinated to the hydroxyl group at the C(3) atom and to the o xo group. The angle between the two coordinate bonds must be $0 - 30^\circ$; otherwise, the influence of these cations is not manifested.

![Diagram 75](image)

Complexation with boric and phenylboronic acid has been used $^{420}$ to perform selective acetonation of monosaccharides; a similar approach used in the series of nucleosides and nucleotides is employed for their selective methylation at the base. $^{421}$

The use of a complexing polymer, polystrylylboronate, made it possible to prepare partially acylated derivatives of O-methylglycosides, valuable from the synthetic viewpoint. $^{422}$ The addition of a borate during the aldol condensation of 2-acetamido-2-deoxy-D-glucose $^{59b}$ with oxaloacetate giving N-acetylenuraminic acid (a mixture of anomers $^{60a,b}$) increases the yield of the product. Apparently, complexation suppresses side reactions. $^{423}$

The presence of a borate shifts the aldose $\rightarrow$ ketose equilibrium (the Lobry de Bruyn – Alberda van Ekenstein rearrangement $^{2,409}$) towards the latter. $^{424,425}$

Cations of $\text{d}$-metals also catalyse this rearrangement. $^{426}$ It was shown $^{427,428}$ that the main event in the catalytic action of sodium alumnate on the isomerisation of D-glucose to D-fructose is stabilisation of the intermediate enediol $\text{via}$ coordination giving a structure like 73. The presence of an anion exchanger in the paramolybdate form also facilitates this transformation by suppressing side reactions. $^{429}$

Complex formation has been successfully used to protect particular functional groups during selective N-acylation of aminoglycoside and aminocyclitol antibiotics in the presence of heavy metal salts. $^{430} - 432$ The direction of acetylation can be changed simply by changing the metal cation used. $^{430}$

The numerous reactions of oxidation of aldoses in the presence of metal salts often yield initially intermediate metal complexes the stability of which varies over wide limits. Complex formation can occur in a transition state, or it can give highly unstable complexes. $^{433, 434}$ The intermediates can decompose either in a single-electron process giving free radicals, which act as the reactive species, $^{435} - 438$ or by a two-electron transfer mechanism giving reaction products. $^{439} - 441$

In a number of studies, $^{442} - 458$ a preparative method has been developed, based on the ability of molybdate ions Mo$^{VI}$O$_4^2-$ to catalyse epimerisation of aldoses and ketoses and their derivatives in relation to the carbon atom nearest to the carbonyl group. The most prominent example of this epimerisation, $^{452}$ the transformation of D-xylofuranose into D-lyxose, was discussed in Section II.3. When molybdate is replaced by tungstate, the complexation is not accompanied by epimerisation. $^{453}$ because the carbohydrate complexes of tungstate are much more stable than the molybdate complexes. $^{454}$ (see Section II.3). However, in the presence of a borate, D-arabinose incorporated in the tungstate complex readily epimerises to D-ribose, since the borate complex of the latter is more stable. $^{460}$

Previously, the mechanism of epimerisation has been interpreted by assuming $^{3,441}$ the intermediate formation of planar complex 76, deprotonated at the C(2) atom, in which the metal is coordinated to the O(1) and O(3) atoms of the cyclic form of the substrate. The subsequent diastereofacial protonation of the complex 76 was assumed to give both the complex of the substrate and that of the product. However, later, using NMR spectroscopy of aldoses enriched in the $^{13}$C and $^2$H isotopes at the C(1) atom, it was shown $^{461}$ that in reality, this epimerisation includes a rearrangement of the substrate carbon skeleton. The C(1) and C(2) atoms exchange their positions in the hypothetical binuclear transition complex 77 containing the initial aldose in the acyclic aldehydo form. A similar complexation has been proposed $^{462}$ to explain epimerisation of D-glucose to D-mannose catalysed by Mo$^6$O$_{16}^4-$ ions.
It has been suggested that in the presence of Ni^{II} and \( \text{Ni}^{II} \text{,} \text{N} \text{,} \text{N} \text{,} \text{N} \text{,} \text{N} \text{-tetramethylthelylenediamine, aldoses are wholly epimerised at the C(2) atom with a similar rearrangement of the carbon skeleton via transition complex 78 with the aldehyde form of the substrate. An analogous reaction occurs when Cu^{II} is used instead of Ni^{II}. Finally, it has been found that a rearrangement of the carbon skeleton of carbohydrate complexes accompanied by epimerisation occurs even in such a simple system as methanol–calcium hydroxide. It is obvious that in view of these findings, the generally accepted mechanisms of the Lobry de Bruyn–Alberda van Ekenstein rearrangement should be revised. In the methanol–Ni^{II}–N,N-diethylenediamine system, D-fructose undergoes a more extensive rearrangement of the carbon skeleton resulting in a branched aldehyde, 2-C-hydroxymethyl-D-ribose. It is noteworthy that the side formation of ketoses in these processes is not accompanied by a rearrangement of the carbon skeleton of the initial aldoses. Apparently, ketoses are formed via the generally accepted mechanism of the Lobry de Bruyn–Alberda van Ekenstein rearrangement. The discovery of the change of the carbohydrate carbon skeleton upon the formation of metal complexes is undoubtedly an outstanding achievement in the coordination chemistry of carbohydrates.

2. Reactions involving metal complexes of carbohydrates

Cyclodextrins react with RhCl₃ to give colloidal dispersions of rhodium, which efficiently catalyse hydrogenation of alkenes carried out at 30 °C under atmospheric pressure of hydrogen. Complexes of Cu^{II} with β-CD and its polyphosphate initiate vinlyc polymerisation. Sugars are often used as donors of hydrogen in the catalytic hydrogenation of carbonyl compounds with hydrogen transfer. The mechanism proposed for this process assumes participation of metal complexes of carbohydrates formed intermediately. One example of the use of cyclodextrin as phase transfer catalyst, owing to its ability to coordinate s-metal cations, was reported.

The chirality of carbohydrates is employed in enantioselective catalysis. Well known 472–475 catalysts for hydrogenation are L-tartaric acid or its D-enantiomer adsorbed on the metal surface; in this case, chelation leading to the formation of a chiral environment on the metal surface is assumed. The optical yields in these reactions reach 55%–63%. 476–478 This is a significant achievement, because these catalysts can be used repeatedly. Similar reactions catalysed by palladium supported on cellulose 479 resulted in optical yields of only 0.10%–0.15%. Apparently, in the latter case, no metal binding on the surface of a chiral support is involved. The optical yields in the reduction of the complexes of ferrocenyl ketones with β-CD of the type 52b vary from 5% to 32%–80%. 481,482

3. Modelling of enzymes by metal complexes of carbohydrates

This field of application of carbohydrate metal complexes is still limited to cyclodextrins. Thus alkaline hydrolysis of p-nitrophényl acetate is suppressed almost entirely by the addition of the binuclear complex of Cu^{II} with α-CD 51. 483 When the corresponding complex with β-CD is used, the retardation of the reaction is less pronounced. This is due to the formation of a stable inclusion compound from the former complex and the substrate; this permits regarding this complex as an adequate model of a metal enzyme. A structurally related binuclear complex of Mn^{II} with β-CD has been proposed as a model of a photosynthesis enzyme, which catalyses water oxidation to oxygen. It has been shown that complex formation of d-metals with cyclodextrins is a general way of stabilising hydroxo complexes of d-metals for the modelling of terminal enzyme systems for photosynthesis.

One aspect of enzyme activity, namely, the decrease in the number of degrees of freedom of the substrate upon its complexation with the enzyme, has been modelled by alkaline hydrolysis of esters of ferrocenecarboxylic acids. The molecular design was accomplished in such a way that the catalytic centre (a hydroxyl group of cyclodextrin) was located in the optimum vicinity of the reaction centre of the substrate when the latter had entered the cyclodextrin cavity.

4. Analytical methods based on the formation of metal complexes with carbohydrates

An important application of complex formation with metals is the solution of analytical and structural problems in the series of carbohydrates.

A large set of qualitative and quantitative electro(iono-)phoretic and chromatographic methods for the separation of sugar mixtures based on the complexation with metals have been developed. Early 491,492 and more recent 493 reviews survey the data on paper electrophoresis of sugar mixtures in aqueous solutions in the presence of various salts such as borates, germa-nates, stannates, arsenites, molybdates, and tungstates. It is significant that these modifications of the method supplement one another. Other efficient procedures are paper electrophoresis in the presence of Cu^{II} periodate, tellurate, acetate, and basic acetate 495 and capillary electrophoretic separation of enantio-meric monocarbohydrates in the borate–dextrin (cyclodextrin) system, i.e. under conditions of double complexation. 496 Electro-dialysis through a polymeric membrane with grafted boric acid residues has been proposed as a method for separation of multicomponent product mixtures obtained upon the formose reaction.

A broad range of methods consisting in paper and column chromatography of carbohydrates based on complex formation with metals have been surveyed in a review. 493 The main column chromatography technique is ion exchange chromatography using Li⁺, K⁺, Ca²⁺, and Ba²⁺ forms of cation exchangers and cellulose or silica gel impregnated with a borate. Column chromatography of aqueous solutions of sugars on alumina is also accompanied by complex formation. 498 Closely related approaches are chromatography on anion exchangers in the aluminate form 499 and chromatography on paper (cellulose) containing carboxylate groups grafted as La³⁺, Cu²⁺, and Ba²⁺ salts. 500 Yet another efficient method is thin layer chromatography of sugars and their derivatives using the Cu²⁺ and La³⁺ forms of cation exchangers. 501 Racemic mixtures of ferrocene derivatives are readily separated on polyamyl using an aqueous solution of β-CD as the eluent.

Complex formation with metals has long been used for the determination of sugars. The most widely used procedures are the quantitative Bertrand method based on oxidation of copper complexes of aldoses to give Cu²⁺ oxide and the related qualitative Fehling 2 and quantitative Somogyi methods. There are grounds for believing that oxidation occurs in enediol Cu¹ complex. 502 Determination of sugars based on their oxidation by the Cu¹ periodate complex 503 or Cu²⁺ sulfate 504 has also been described.

The formation of complexes of carbohydrates with metals proved to be useful for electrochemical, mainly polarographic, determination of metals. In the presence of acyclic or cyclic polyols, the half-wave potential of the metal cation being analysed substantially shifts, which enables its determination in the presence of other metal cations. 508–510 The volumetric determination of Pt¹ in an alkaline solution of D-mannitol in the presence of
cations of other platinum metals is another example of this approach.\textsuperscript{511} It is difficult to overestimate the role of complex formation in the configurational and conformational analysis of carbohydrates.\textsuperscript{512, 513} Thus, determination of the stability constants of the borate complexes of pyranoses permitted Angyal to propose a method for the calculation of the conformation energies of these ligands,\textsuperscript{512, 513} while the change of the specific rotation of aldoses following their complexation with borate made it possible to determine their anomeric configuration.\textsuperscript{2, 3}

Several methods of the conformational analysis of carbohydrates are based on the correlation between the complexing and rotational (chiroptical) properties of ligands [optical rotatory dispersion (ORD) and circular dichroism (CD) spectroscopy].\textsuperscript{514– 518} Thus CD spectroscopy of molybdate complexes has revealed a correlation between the orientation of the hydroxyl groups at the C(2) and C(3) atoms in the pyranose form (see the structures 4a, b) and the signs of the Cotton effects in the CD spectrum of a colourless solution of the molybdate complex. Chiroptical methods are applied most often to solutions of coloured metal complexes containing Cotton-ginic (manifested in the visible ORD and CD spectra) groups. This line of research was initiated by the classical studies of Reeves\textsuperscript{2} dealing with the rotational properties of copper complexes of O-methyl-

5. The significance for biology and medicine

Previously the views on the biological functions of carbohydrates reduced to their food (glucose, fructose, starch) and structural (cellulose, chitin) properties. However, during the last decades, carbohydrates have been found to play a crucial role in a number of vitaly important processes such as mutual recognition of molecules and cells (cell adhesion, agglutination, reception),\textsuperscript{3, 4} tissue calcification as the initial stage of the formation of vertebrate bones and shells of molluscs and bird eggs.\textsuperscript{45} These discoveries substantially raised the biological status of carbohydrates. Since all the processes listed above are Ca\textsuperscript{2+}-dependent, this has also stimulated studies dealing with the complex formation of carbohydrates with s-metal cations (Section II.1). The studies performed have demonstrated that carbohydrates are weak complexes with these cations and that complex formation with s-metals cannot play an important role in the above biological processes. For example, \(\text{N-acetylneuraminic acid 60c, which is an indispensable component of biologically significant oligo-}

Metal complex formation with natural carboxylic acids of carbohydrate origin (see Section V) is important for medicine. Thus ascorbic acid decreases the level of mutations in workers in contact with heavy metals.\textsuperscript{555} Phytic acid is present in substantial amounts in vegetable oils, and its ability to form an insoluble complex with Ca\textsuperscript{2+} decreases the removal of calcium with urine.\textsuperscript{556} Binding with heavy metal cations can even inactivate metal-dependent enzymes, for example, \(\text{x-amylase 557 and carboxypeptidase A. 558}\)

The platinum complexes\textsuperscript{46, 236 and [PtL(1,3-diamine)]242 (L is D-glucuronate or D-glucuronate) exhibited a considerable antitumour activity. This activity was also found for the platinum complex 71, 594 Polymeric osmium carbohydrate complexes, osmarines,\textsuperscript{238, 239 (Section II.3) are used as antiarrhythm preparations owing to their capability of binding superoxide ions, which are responsible for this disease.\textsuperscript{239} Copper(II) complexes with cycloexodrin of the type 51 can be used\textsuperscript{529 for treating the mildew blight of grapes, because these compounds are not toxic in wine. Water-soluble iron complexes of glucose and fructose 42 are used to treat anemia.\textsuperscript{560 Phytin 67 prevents foodstuff from going bad under the action of atmospheric oxygen, because it binds Fe\textsuperscript{3+} and Ca\textsuperscript{2+} cations, which can act as efficient catalysts for undesirable oxidation processes.\textsuperscript{561} The complex formation of metals with polysaccharides has also found use in medicine. Pectins (polymers of the type 5 with partly esterified carboxyl groups) isolated from fruits or vegetables efficiently bind toxic metal cations and thus they can be used for detoxification of an organism.\textsuperscript{562} It has been proposed\textsuperscript{563 to use iron complexes of chondroitin sulfates 63a, b for curing iron deficiency anemia. Metal complexes of dextran and inulin can be used as paramagnetic contrasting reagents\textsuperscript{564} in medical NMR spectroscopy. Treatment of cellulose with heavy metal salts and subsequent interaction with antibodies imparts antibacterial properties to textiles.\textsuperscript{565} In nature, complex formation of metals with polysaccharides can be undesirable. Thus the formation of gels on the surface of plant roots may have negative consequences for plants, since their main components, acidic polysaccharides, bind metal cations, which come directly from soil particles and are needed for nutrition.\textsuperscript{566}

s-Metal cations\textsuperscript{567 and d-metal cations\textsuperscript{568 are used to strengthen agaroid jellies. d-Metal hydroxides treated with sugars are employed for enzyme immobilisation.\textsuperscript{569} The natural polymer of \(\text{N-acetyl-D-glucosamine — chitin — has been proposed}\textsuperscript{700 as a reagent for extraction of heavy metals from waste water; the ferrite – alginite system is employed for the preparation of ferromagnetic particles used as a contrasting reagent\textsuperscript{571 in NMR spectroscopy for medical purposes.}
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