

Metal ion complexes with native cyclodextrins. An overview

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Received: 27 January 2009 / Accepted: 16 April 2009 / Published online: 30 April 2009
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Abstract The review presents a survey of the metal complexing properties of native cyclodextrins (including deprotonation in alkaline medium) and a report on some recent results on composition and stability of metal–cyclodextrin complexes.

Keywords Cyclodextrins · Metal ions · Complex formation · Review

Introduction

Cyclodextrins (CD's) present seductive molecules, appealing to scientists in both academic research and applied technologies. Cyclodextrins are cyclic oligosaccharides composed from α -D-glucopyranose units connected through α -(1 \rightarrow 4) linkages. The most common (so called “native”) forms of cyclodextrins are α -, β - and γ -cyclodextrins, which contain, respectively, six, seven and eight α -D-glucopyranose units (Fig. 1). The structure of these molecules is toroidal containing an apolar cavity with primary hydroxyl groups lying on the outside and the secondary hydroxyl groups inside [1–5].

The unique ability of cyclodextrins to form inclusion complexes is widely exploited in many areas, for example in drug carrier systems, food industry and cosmetics [6]. The principal factors involved in guest–host complex formation with organic molecules are van der Waals, hydrophobic interactions, size effects, and hydrogen bonding [1–8]. Other factors prevail upon complex formation with

small hydrophilic metal ions, when a covalent bond forms between metal ion and deprotonated $^-$ O-group. Most of the thousands papers published each year on cyclodextrins concern cyclodextrin inclusion complexes and only a few deal with cyclodextrin metal complex chemistry.

Metal ions complexes with cyclodextrins have potential as metallo-enzyme models [9]. On the other hand, the complexes mentioned could have a wide range of applications in catalysis and molecular recognition. Regrettably, the data about interaction of unmodified cyclodextrins with heavy metal ions are not numerous.

The present review will be a survey of the metal complexing properties of native cyclodextrins (including deprotonation in alkaline medium) and a report on some recent results on composition and stability of metal–cyclodextrin complexes.

Deprotonation of cyclodextrins

Interaction of aliphatic polyalcohols with metal ions is generally weak and usually not significant in acidic and neutral solutions [10]. However deprotonated polyalcohols represent rather strong and efficient metal ions binding agents [11–19]. Therefore, the acidity of terminal OH-groups plays a key role in metal–cyclodextrin complex formation.

Deprotonation of cyclodextrins in alkaline medium was previously investigated in several works using different techniques. On the basis pH dependent kinetic study on reaction of acylation of α -cyclodextrin with *m*-tolyl acetate and reaction of deacylation, the authors obtained the following pK_{a1} values: 11.8 ± 3.5 (for the acylation rate data) and 12.3 ± 1.2 (for the deacylation rate data) at 25 °C and $I = 0.2$ [20]. Acidic dissociation constants of α -cyclodextrin

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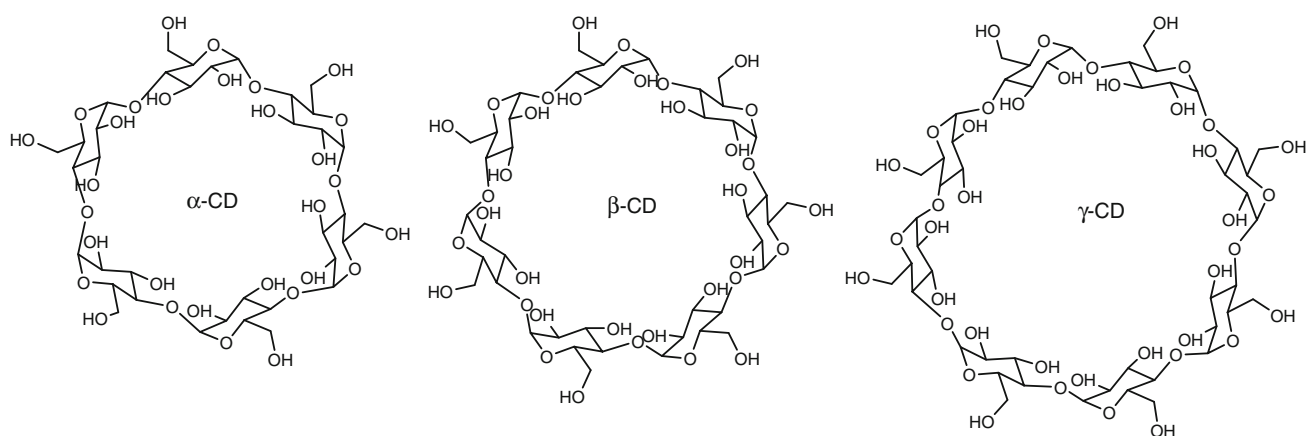


Fig. 1 Structure of α -, β - and γ -cyclodextrin

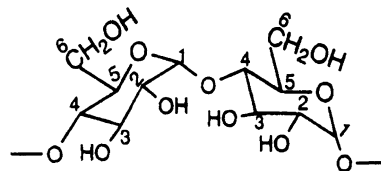
and β -cyclodextrin have been determined at 10–47 and 25–55 °C, respectively, by pH potentiometry combined with ^{13}C NMR titration [21]. The data from Ref. 21 are presented in Table 1, showing decrease of $\text{p}K_{\text{a}1}$ values with the rise of temperature for both cyclodextrins. It is worth to note, that at the same temperature the $\text{p}K_{\text{a}1}$ values of α -cyclodextrin are higher than that of β -cyclodextrin, the difference reaching of 0.13–0.17 $\text{p}K_{\text{a}}$ units (Table 1). The trend of decrease in $\text{p}K_{\text{a}}$ values with increase in number of α -D-glucopyranose units in cyclodextrins was also documented in Ref. 7, the $\text{p}K_{\text{a}}$ values for α -cyclodextrin, β -cyclodextrin and γ -cyclodextrin being 12.33, 12.20 and 12.08, respectively.

Results obtained in our laboratory on Cu(II)– β -CD [22] and Cu(II)–saccharose [15, 16] complex formation suggested that deprotonation of β -CD takes place in more

basic solutions than was previously reported. Published $\text{p}K_{\text{a}1}$ values for cyclodextrins (see above and Table 1) and saccharose ($\text{p}K_{\text{a}1} = 12.43$ [23]) are rather similar, suggesting that complex formation in Cu(II)– β -CD and Cu(II)–saccharose systems should be similar, since only deprotonated O^- -groups can serve as donors for Cu(II) ion in highly basic media. This conclusion is supported by complexation results obtained in Cu(II)–tartrate [24], Cu(II)–glycerol [14, 16], Cu(II)–dextran [25], Cu(II)–D-mannitol [17] and Cu(II)–D-sorbitol [18] systems, where soluble complex formation is detected polarographically at pH's ca. 1–3 units lower than $\text{p}K_{\text{a}}$ value of the corresponding polyhydroxylic ligand. Soluble Cu(II)–saccharose complexes begin to form at pH above 11 [15, 16] (i.e. at $\text{pH} \approx \text{p}K_{\text{a}} - 1$), whereas Cu(II)– β -CD complexes begin to form only at pH above 12.5 [22] (i.e. at pH higher than reported $\text{p}K_{\text{a}}$ values of cyclodextrins). Furthermore, metal ion– β -CD complexation data [22, 26–30] indicate that at least doubly deprotonated anion of β -cyclodextrin ($\beta\text{-CD}^{2-}$) is involved in complex formation. Dissociation of two OH-groups adjacent to C-2 and C-3 was already discussed [21], although no $\text{p}K_{\text{a}2}$ value were reported. Another ^{13}C NMR study has also shown that C-2 and C-3 resonances of α -cyclodextrin and β -cyclodextrin are particularly sensitive to pH [31], which suggests that the acidic dissociation involves both OH-groups from C-2 and C-3 carbon atoms of α -D-glucopyranose unit (Scheme 1).

Table 1 $\text{p}K_{\text{a}}$ values of α -cyclodextrin and β -cyclodextrin at different temperatures [21]

t (°C)	$\text{p}K_{\text{a}}$
α -Cyclodextrin	
10	12.649 ± 0.011
15	12.565 ± 0.014
25	12.332 ± 0.011
30	12.263 ± 0.012
40	12.083 ± 0.014
47	11.882 ± 0.014
β -Cyclodextrin	
25	12.203 ± 0.006
25	12.201 ± 0.004
30	12.091 ± 0.008
30	12.088 ± 0.009
40	11.911 ± 0.004
50	11.675 ± 0.005
55	11.295 ± 0.010



Scheme 1 Numbering of C-atoms in α -D-glucopyranose units of cyclodextrins

Accurate pK_{a2} value however is required in order to study any metal ion–cyclodextrin equilibrium. Reinvestigation of β -cyclodextrin deprotonation by means of ^{13}C and ^1H NMR titrations was carried recently [32]. Variable pH ^{13}C NMR and ^1H NMR spectroscopic studies of the β -cyclodextrin in alkaline aqueous solutions revealed that β -cyclodextrin does not deprotonate at $\text{pH} < 12.0$. Further increase in solution pH results in the deprotonation of OH-groups adjacent to C-2 and C-3 carbon atoms of β -cyclodextrin α -D-glucopyranose unit, whereas the deprotonation of OH-groups adjacent to C-6 carbon atoms is expressed less markedly. The pK_a values for β -cyclodextrin OH-groups adjacent to C-2 and C-3 carbon atoms are rather close, $pK_{a1,2}$ being 13.5 ± 0.2 at $22.5\text{ }^\circ\text{C}$ [32].

Interaction of cyclodextrins with metal ions

Complexes with pentavalent metal ions (V(V))

The interaction between vanadium(V) and β -cyclodextrin (β -CD) has been studied in aqueous solutions (pH approximate to 7.5, 298.15 K) using multinuclear NMR spectroscopy, coupled with measurements of diffusion coefficients and electrical conductivity [33]. The transport properties of vanadate ion solutions were markedly influenced by the presence of β -cyclodextrin. Data from V-51, H-1 and C-13 NMR spectroscopy showed that these effects are due to strong interactions between β -cyclodextrin and vanadate due to formation of 2:1 (β -CD:vanadate) complexes. The formation of such 2:1 complexes was also supported by molecular mechanics calculations. Complexation was seen by conductometric and diffusion techniques to lead to a significant decrease in the molar conductivity and diffusion coefficient of vanadate solutions in the presence of β -cyclodextrin. Using the above stoichiometry, it has been possible to calculate the association constant, leading to the value $K = 4.3 \times 10^4$ from the analysis of the conductivity data [33].

Complexes with tetravalent ions [Sn(IV), Pb(IV), Mn(IV), Ge(IV), V(IV), Si(IV)]

P. Klüfers and co-workers have synthesized and crystallized (layered with ethanol or methanol) mononuclear β -cyclodextrin complexes with tin(IV), lead(IV), manganese(IV), germanium(IV) [34]. It can be noted, that all compounds were prepared from aqueous alkaline solutions and characterized after crystallization by means of X-ray diffraction analysis. The data on synthesized complexes are summarized in Table 2. When investigating aqueous solutions, the ^{119}Sn NMR spectrum of a threefold molar amount of β -cyclodextrin with hexahydroxystannate(IV)

showed a single signal, whose chemical shift indicated a new, hexacoordinate, tin-containing species in solution. Lowering the pH value to about 8 did not change the signal, but the solution started to become cloudy (e.g., pH 8.8 clear solution, pH 7.8 slightly cloudy solution, pH 7 SnO_2 precipitate). The tentative coordination compound was obviously destroyed at pH 7. According to the authors, this behavior indicated that deprotonated β -cyclodextrin species were the actual tin-binding entities. The results from the structural analysis were consistent with the spectroscopic results. The most conspicuous building unit of the crystals is a bucket-wheel-shaped assembly with threefold rotational symmetry that consists of three components: three β -cyclodextrin dianions, three tetrahedral tetraaqualithium cations, and a tetravalent metal center. The coordination of Sn(IV) occurs via deprotonated OH-groups from C-2 to C-3 carbon atoms of α -D-glucopyranose unit of each β -cyclodextrin molecule. An ethanol guest molecule inside each β -cyclodextrin ring may be regarded as a fourth kind of building unit whose presence is responsible for the necessary decrease of the solubility of the assembly at the onset of crystallization. The absence of mixed cyclodextrin–hydroxidostannate species was understandable for authors, because only the complete trimer benefits from the stabilization by the hydrogen bonds between β -cyclodextrin units and with the hydrated counterions. Accordingly, the overall stability of the bucket-wheel shaped stannate is higher than the stability of stannates of related glycosides [34]. Both the high tendency for formation of the bucket-wheel motif and its robustness were shown when investigating complex formation between β -cyclodextrin and other central ions: lead(IV), germanium(IV) and manganese(IV)—the structure determination again revealed the bucket-wheel shape [34].

Two dinuclear tin(IV) compounds containing deprotonated β -cyclodextrins have been constructed by using different organotin and inorganotin precursors under solvothermal conditions [35]. A novel dinuclear tin(IV) compound with the deprotonated β -cyclodextrins, $[\text{Sn}_2(\beta\text{-CD})_3]\text{H}_{8.8} \cdot \text{H}_2\text{O}$, has been obtained from the reaction of $\text{BuSnO}(\text{OH})$ and β -cyclodextrins. The result showed that the organotin precursor has translated into an inorganotin through Sn–C bond cleavage under the solvothermal condition. The use of $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ as a raw material instead of an organotin precursor under the same reaction conditions gave rather similar compound, namely $[\text{Sn}_2(\beta\text{-CD})_3]\text{H}_{8.8}$ [35]. The single-crystal X-ray structural analysis revealed that the structure of compounds contains one kind of crystallographically unique cyclodextrin ion and two kinds of crystallographically unique Sn atoms that have the similar coordination environments. It was found, that each Sn(IV) ion is located on the genuine 3-fold rotation axis and coordinated by six hydroxyl O^- atoms from three

Table 2 Data on β -cyclodextrin complexes with Sn(IV), Pb(IV), Ge(IV) and Mn(IV), taken from Ref. 34

Complex compound	Colour	Precursor
$[\{\text{Na}(\text{H}_2\text{O})_4\}\{\text{Li}(\text{H}_2\text{O})_4\}_2\{\Lambda\text{-Sn}(\beta\text{-CDH}_2)_3\}]\text{H}_{.1} \cdot 27\text{H}_2\text{O} \cdot 3\text{C}_2\text{H}_5\text{OH}$	Colorless	$\text{Na}_2\text{Sn}(\text{OH})_6$
$[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-Pb}(\beta\text{-CDH}_2)_3\}]\text{H}_{.1} \cdot 34\text{H}_2\text{O} \cdot 5\text{C}_2\text{H}_5\text{OH}$	Yellowish	$\text{Na}_2\text{Pb}(\text{OH})_6$
$[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-Ge}(\beta\text{-CDH}_2)_3\}]\text{H}_{.1} \cdot 24\text{H}_2\text{O} \cdot 3\text{C}_2\text{H}_5\text{OH}$	Colorless	$\text{Ge}(\text{OCH}_3)_4$
$\text{K}_2[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-Mn}(\beta\text{-CDH}_2)_3\}]\text{H}_{.3} \cdot 23\text{H}_2\text{O} \cdot \text{CH}_3\text{OH}$	Dark red	$\text{Mn}(\text{NO}_3)_2^a$

^a $\text{K}_3\text{Fe}(\text{CN})_6$ was used as oxidizing agent in the course of synthesis of Mn(IV) compound

fourfold deprotonated β -cyclodextrin anions (deprotonated are OH-groups adjacent to C-2 and C-3 carbon atoms of neighboring α -D-glucopyranose units of β -cyclodextrin molecule—Scheme 1), showing a distorted octahedral geometry. Each β -cyclodextrin anion coordinates to two Sn(IV) ions through four hydroxyl O^- atoms. Three β -cyclodextrin ions are bridged by two Sn ions forming an airscrew-like structure [35].

A polynuclear complex of multideprotonated α -cyclodextrin with oxo-vanadium(IV) ions (VO^{2+}) was prepared from alkaline solution on reaction of α -cyclodextrin, an oxovanadium salt and sodium hydroxide [36]. The composition of blue crystals formed was found on the ground of X-ray analysis: $\text{Na}_6[\text{Na}_6(\text{H}_2\text{O})_6(\text{VO})_6(\alpha\text{-CDH}_{12})_2] \cdot 59\text{H}_2\text{O}$. The authors proposed the structure of this complex containing double-toroidal anions [36].

Solid-state complexes of undeprotonated cyclodextrins with salts can be considered as models for organic-mineral composites. Klüfers et al. Reported on the structure of a molecular inorganic-organic composite constructed from a double six ring silicate and α -cyclodextrin [37]. The structure of the assembly may be regarded as a model of an extended hydrogen-bonded silicate-polyol interface at an atomic level. Triclinic crystals of dicyclohexasilicate- α -cyclodextrin adduct of the formula $\text{K}_{12}\text{Si}_{12}\text{O}_{30} \cdot 2\alpha\text{-CD} \cdot 36\text{H}_2\text{O}$ were formed from the reaction of α -cyclodextrin with tetramethoxysilane in aqueous KOH solution. According to the authors, the X-ray crystal structure analysis reveals a prismatic dicyclohexasilicate ion intercalated in a pair of α -cyclodextrin tori as the most salient feature of the crystal structure, and in this molecular assembly a cyclodextrin acts as a multidentate hydrogen-donor. As a result, all of secondary hydroxo-groups of both α -cyclodextrin molecules act as donors, and all of the 12 formally O^- functionalities of the silicate act as acceptors [37].

Complexes with trivalent metal ions [Mn(III), Bi(III), Ln(III), Tb(III), Pr(III), Ce(III), Co(III)]

Dinuclear neutral manganese(III) hydroxycomplex—bis(μ -hydroxo)(β -cyclodextrin)dimanganese-(III,III) ($\text{Mn}_2(\text{OH})_2(\beta\text{-CD})$) was synthesized according to following procedures

[38]: β -CD (0.56 g, 0.5 mM) was dissolved in 30 mL of Ar-flushed DMF, Mn(II) acetate (0.26 g, 1.0 mM) was added, and the reaction mixture was stirred under Ar for 1 h. An alcoholic solution of NaOH (10 mL, 0.2 M) was added, and the resulting solution was exposed to bubbling air. After the solvent was stripped under vacuum, an excess of ethanol was added to precipitate the compound. It was filtered, washed with ethanol, and air-dried. The compound was recrystallized from 3:1 DMF–ethanol. An alternate procedure starting with Mn(III) acetate and the absence of oxygen also yielded the same compound. The compound was found to be soluble only in water, DMF, and Me_2SO . DMF and Me_2SO solutions of the compound were stable for days, whereas an aqueous solution of the compound was quite unstable and decomposed to hydrated oxides of Mn. The trivalent state of manganese ions to be 3+ was confirmed by treating the compound with aqueous acid to remove the metal ion from the coordination sphere of cyclodextrin and reacting with Fe(II). The electronic spectrum of the compound in DMF had an absorption maximum at 482 nm. On the basis of magnetic moment measurement, the authors concluded, that the complex has a bis(μ -hydroxo)-bridged structure. In order to establish which side of the β -cyclodextrin ligand the Mn coordinates to, the complex was treated with terephthaloyl chloride, which selectively esterifies the primary hydroxy-groups: a “capped”- β -cyclodextrin product that retained the original manganese. Conclusively, the experiment showed that it is the secondary hydroxyls of β -cyclodextrin that coordinate both Mn ions [38].

The same complex compound was synthesized according to procedure given above, and characterized by means of FT-IR and Raman spectroscopy [39].

A polynuclear complex of multideprotonated α -cyclodextrin with bismuth(III) ions was prepared from alkaline solution [36]. The composition of crystals formed was determined on the basis of X-ray analysis: $[\text{Na}_6(\text{H}_2\text{O})_6\text{Bi}_6(\alpha\text{-CDH}_{12})_2] \cdot 47\text{H}_2\text{O}$. The authors proposed the structure of this complex containing double-toroidal anions [36].

Several works were devoted to investigation of lanthanide ions interaction with cyclodextrins [40, 41]. It was established, that γ -cyclodextrin forms complexes with

lanthanide(III) ions in basic aqueous solutions. This complex formation in basic solution dramatically enhances the solubility of lanthanide(III) ions, which are otherwise insoluble due to the formation of hydroxide gels [40].

The interaction of trivalent lanthanide(III) ions with α -cyclodextrin was investigated in acidic and basic aqueous media [41]. At low pH, the association constants for 1:1 complexes were in the range $\log K = 2\text{--}4$ ($I = 0.1$ M, NaCl or TMACl), as determined by pH-potentiometric study of the hydrolysis of the lanthanide(III) ions in absence and in presence of cyclodextrin. The thermodynamic parameters of the inclusion reaction showed that the complexation of lanthanide(III) ions inside the cyclodextrin cavity is entropically driven and does not depend upon the host. ^1H and ^{13}C NMR spectra pointed to inclusion of lanthanide(III) cations in the cavity of α -cyclodextrin occurring in the narrowest part of the host molecule, close to the C-5 carbon atoms. α -Cyclodextrin acts like a crown ether, its anomeric oxygen atoms being the donor atoms. Complexation of Tb^{3+} by partially deprotonated α -cyclodextrin was investigated at pH 12.33: ^{13}C NMR measurements showed that complexation occurs at the OH-3 secondary hydroxyl groups of α -cyclodextrin while UV-Vis spectrophotometric titration leads to an apparent constant $\log K_{\text{app}}$ approximate to 4.2 (1:1 complex) [41].

In the case of cobalt, the data about mixed Co(III) complex formulated as $[\text{Co}(\text{en})_2\text{CD}]\text{ClO}_4$ for α - and β -CD were reported [42].

Complexes with divalent metal ions [Cu(II), Pb(II), Cd(II), Mn(II), Fe(II), Ca(II), Mg(II)]

Complexes with Cu(II)

When analyzing literature sources on metal ions interaction with cyclodextrins, it is seen that the main part of the publications deals with divalent ions, simultaneously copper(II) being “front-runner”.

Complexation of Cu(II) ions by β -cyclodextrin in alkaline solutions for the first time was documented by Messmer [43], and further investigations were made by Matsui and co-workers [26–30]. The latter authors first reported the preparation of the Cu(II) complexes with α -cyclodextrin and β -cyclodextrin which correspond to a Cu:cyclodextrin ratio of 2:1 in 0.1–1.0 M NaOH solutions. Molecular models led to the structures, where both metal ions are themselves linked to each other either through two μ -OH bridges (Figs. 2, 3). The light absorption spectra of $\text{Cu}_2(\text{OH})_2\beta\text{-CD}^{2-}$ and $\text{Cu}_2(\text{OH})_2\alpha\text{-CD}^{2-}$ complexes in 0.1 M NaOH solution were characterized by a maxima at 668 nm (molar extinction coefficient being 118 ± 1) and 666 nm (molar extinction coefficient being 128 ± 1), respectively [26].

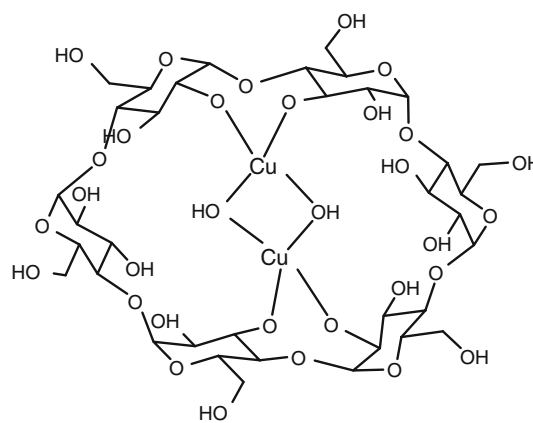


Fig. 2 Structure of $\text{Cu}_2(\text{OH})_2\alpha\text{-CD}^{2-}$ complex

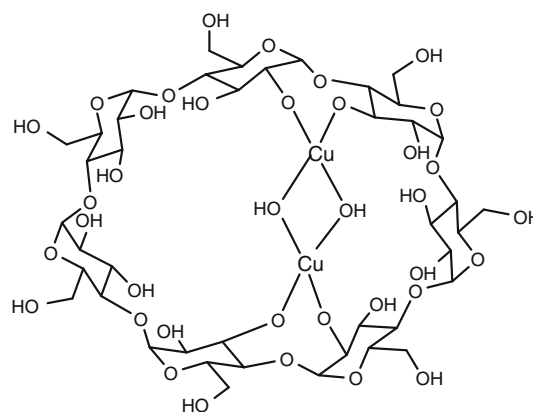


Fig. 3 Structure of $\text{Cu}_2(\text{OH})_2\beta\text{-CD}^{2-}$ complex

$\text{Cu}_2\text{-}\beta\text{-CD}$ complex was investigated by means of pH-metric and conductometric titrations and polarimetric measurements [27]. The authors found that one mole of β -cyclodextrin in the presence of two moles $\text{Cu}(\text{OH})_2$ consumes three moles of hydroxide ion, whereas one mole of α -cyclodextrin in the presence of two moles $\text{Cu}(\text{OH})_2$ consumes two moles of hydroxide ion. Based on observations they determined $\text{Cu}_2(\text{OH})(\text{O})\beta\text{-CD}^{3-}$ (Fig. 4) and $\text{Cu}_2(\text{OH})_2\alpha\text{-CD}^{2-}$ (Fig. 2) and as the formulas of the complexes with β -cyclodextrin and α -cyclodextrin, respectively (cyclodextrins being fourfold deprotonated). Using framework molecular models it was suggested, that the two pairs of deprotonated C-2 and C-3 secondary OH-groups of adjacent α -D-glucopyranose units are cross-linked by the $=\text{Cu}(\text{OH})(\text{O})\text{Cu}=\text{}$ ion bridge in the case of β -cyclodextrin [27], whereas the bridge of $=\text{Cu}(\text{OH})_2\text{Cu}=\text{}$ was shown also to be possible in the case of α -cyclodextrin [28, 29]. In the course of later study the possibility of 1:1 Cu(II)– α -CD complex formation was shown in alkaline solutions. The suggested formula of this complex $\text{Cu}\alpha\text{-CD}(\text{OH})_2^{2-}$ (i.e. α -cyclodextrin being in form of double-deprotonated anion)

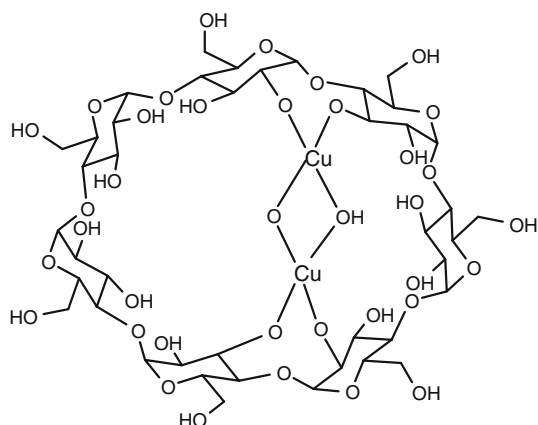


Fig. 4 Structure of $\text{Cu}_2(\text{OH})(\text{O})\beta\text{-CD}^{3-}$ complex

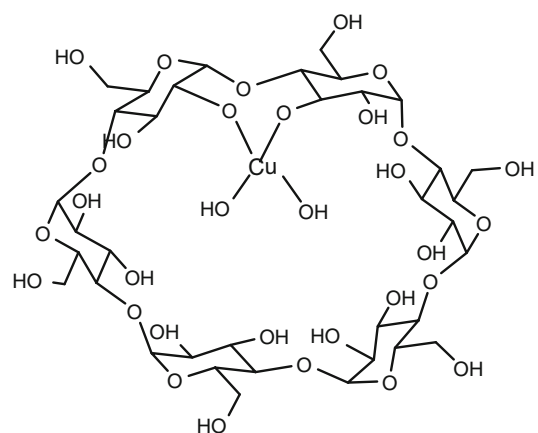
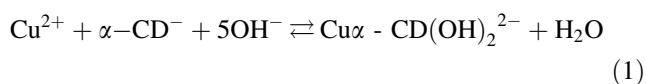
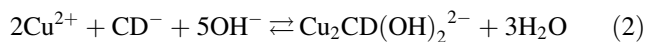


Fig. 5 Structure of $\text{Cu}\alpha\text{-CD}(\text{OH})_2^{2-}$ complex

(Fig. 5) [29]. The equilibrium constant of the reaction of dihydroxocomplex formation:

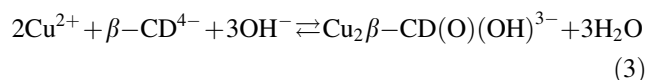


was determined in 1 M NaOH solution. The obtained logarithm value was found to be 18.09 [29]. In the same work the equilibrium constant of the reactions of copper(II) with α -cyclodextrin and β -cyclodextrin:



was determined also in 1 M NaOH solution. The obtained logarithms value were found to be 37.41 for α -cyclodextrin system and 37.66 for β -cyclodextrin system [29].

The determination of the formation constant of 2:1 Cu(II)– β -CD complex was carried out by spectrophotometric titration with EDTA using optical window factor analysis [30]. The equilibrium relationship was written as:



and the formation constant as:

$$K = \frac{[\text{Cu}_2\beta\text{-CD}(\text{O})(\text{OH})^{3-}]}{[\text{Cu}^{2+}]^2[\text{OH}^-]^3[\beta\text{-CD}^{4-}]} \quad (4)$$

The large value of the formation constant ($\log K = 35.78 \pm 0.38$) suggest, according to the authors opinion, that the complex is highly stable in alkaline solutions [30].

The $\text{Cu}_2\text{-}\beta\text{-CD}$ complex was synthesized and characterized by means of electronic spectroscopy, magnetic susceptibility, FTIR and Raman spectroscopic studies [44]. The structure of this complex was assigned as $\text{Na}_2[\text{Cu}_2\beta\text{-CD}(\text{OH})_2 \cdot 2\text{H}_2\text{O}]$. According to the authors, the data presented is consistent with the proposal of dinuclear hydroxy-bridged complex and the presence of simultaneous first and second sphere interaction [44].

Other authors obtained similar FTIR results, however, their interpretation did not involve a hydroxy-bridged structure [45]. The results supported the assumption that the $\text{Cu}_2\text{-}\beta\text{-CD}$ complex is formed by linkages between secondary OH-groups of β -cyclodextrin and Cu(II) ions. The spectral data discussed are consistent with those reported in [44] and lend support of the proposal of the existence of simultaneous first and second sphere interaction. However, evidences for the dinuclear hydroxy-bridged system were not found, rather for a structure containing two aquo-Cu(II) ions for one molecule of β -cyclodextrin. Cu(II) ions react with the secondary OH-groups of β -cyclodextrin, and water molecules, coordinated to Cu(II) ions are directed partly into and partly out of the β -cyclodextrin cavity [45].

The evidence of covalent binding between Cu(II) ions and α - and β -cyclodextrins was shown on the basis of circular dichroism study—significant changes observed in spectra of Cu(II)–CD complexes suggest that the covalent binding of Cu(II) ions to the OH-groups of cyclodextrins is involved [46].

Klüfers and co-workers [47] isolated from solution blue crystals, formulated as $\text{Li}_4[\text{Li}_7\text{Cu}_4(\beta\text{-CDH}_{11.5})_2] \cdot x\text{H}_2\text{O}$ (where $\beta\text{-CDH}_{21}$ is undeprotonated β -cyclodextrin, and $x \sim 40$). The stoichiometry of 2:1 for Cu(II): β -CD was obtained, and the X-ray data were interpreted in terms of a β -cyclodextrin double torus with bridges formed between four Cu(II) ions. No hydroxy-bridges were found [47]. When investigating interaction of α -cyclodextrin interaction with copper(II) ions in alkaline solutions of different alkali ions, it was observed, that α -cyclodextrin is multiply deprotonated in alkaline aqueous solution in the presence of cupric ions [48]. With lithium or sodium as the counterions, trinuclear sandwich-type cuprate ions of the formula $[\text{Cu}_3(\alpha\text{-CDH}_6)_2]^{6-}$ are formed, whereas dinuclear $[\text{Cu}_2(\alpha\text{-$

$(\text{CDH}_4)_2^{4-}$ ions are isolated in the form of the potassium and the rubidium salts. The structures of the cyclodextrinatocuprate ions resemble cylinders, since the usual conical shape of a cyclodextrin is altered due to the formation of shorter hydrogen bonds on the O2/O3 rim of the α -cyclodextrin torus [48].

An polynuclear copper(II)- β -cyclodextrin complex (molar ratio 7:4) also was found to be formed when investigating interaction of copper(II) ions with cellulosic fibers modified by β -cyclodextrin [49].

It can be noted that the most results refer are only qualitative and do not provide information about stability constants of the complexes formed in alkaline Cu(II)- β -CD solutions, but a couple of recent investigations deals with determination of stability constants of copper(II) complexes with β -cyclodextrin based on spectrophotometric [50] and polarographic and spectrophotometric methods [22].

Formation of dinuclear copper(II) complex with β -cyclodextrin was investigated in alkaline aqueous medium (pH > 12.5) under conditions of metal ion excess [50]. The authors found, that copper(II) complexation begins at pH over 12.5, and $\text{Cu}(\text{OH})_2$ precipitate is formed when Cu(II): β -CD ratio exceeds 2:1. The results obtained were accounted for by the dinuclear Cu(II)- β -CD complex formation with the deprotonated form of β -CD. Light absorption spectra of dinuclear Cu(II)- β -CD complex almost coincide in pH range from 12.5 to 13.9. According to the authors, the constancy of absorbance in rather wide range of alkalinity (from 0.05 to 1.0 M NaOH) suggest formation of one kind complex, e.g. solely—dinuclear Cu(II)- β -CD complex Cu_2CD (CD^{4-} is anion of fourfold deprotonated β -CD) (Fig. 6), and support earlier published data, that no hydroxy-bridges are formed in the complex [45, 47]. The spectrophotometric method of ligand displacement was applied for the determination of the stability constant of this complex using EDTA and OH^- ions as competitive ligands [50]. The values of the stability constant of Cu_2CD complex, expressed as:

$$\beta = [\text{Cu}_2\text{CD}] / [\text{Cu}(\text{II})]^2 \cdot [\text{CD}^{4-}] \quad (5)$$

were calculated, the logarithms of stability constant being 39.2 ± 0.2 and 38.4 ± 0.8 , using EDTA and OH^- ions as competitive ligands, respectively [50]. The authors concluded, that the near values of the $\log \beta_{\text{Cu}_2\text{CD}}$ obtained using two different systems, i.e. Cu(II)- β -CD-EDTA and Cu(II)- β -CD- OH^- , are in agreement with the model of dinuclear Cu(II)- β -CD complex formation under the conditions investigated, and with the results of other authors about composition of this dinuclear complex [45]. No evidence of formation of Cu(II)- β -CD polymeric or hydroxy-complexes was found [50]. Additionally it was

shown, that Cu_2CD complex predominate in the solutions within pH range from 12.5 to 14.3 (3 M NaOH solution) [50], transforming with further increase in alkalinity to known tetrahydroxycuprate(II) complex ($\text{Cu}(\text{OH})_4^{2-}$) [51].

Solution equilibria in the system copper(II)- β -cyclodextrin was studied under conditions of β -cyclodextrin excess [22]. Polarographic investigations of copper(II) complexation in alkaline solutions showed that the complex formation begins at pH > 11, the concentration of free (uncomplexed) Cu(II) ions being in the range from ca. 10^{-12} to ca. 10^{-19} M, depending on β -cyclodextrin concentration and pH. The formation of copper(II) 1:1 dihydroxy-complex with double deprotonated β -cyclodextrin anion (CD^{2-}) was observed at pH 11–14 (Fig. 7). The logarithm of the stability constant of $\text{CuCD}(\text{OH})_2^{2-}$ complex was found to be 19.7 ± 0.2 (20 °C, ionic strength 1.0), the determined values of the molar extinction coefficient and of the diffusion coefficient of this complex were $50 \text{ M}^{-1} \text{ cm}^{-1}$ ($\lambda_{\text{max}} = 660 \text{ nm}$) and $1.0 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$,

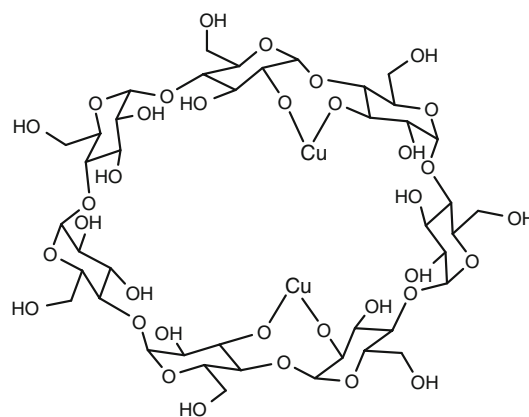


Fig. 6 Structure of $\text{Cu}_2\beta\text{-CD}$ complex

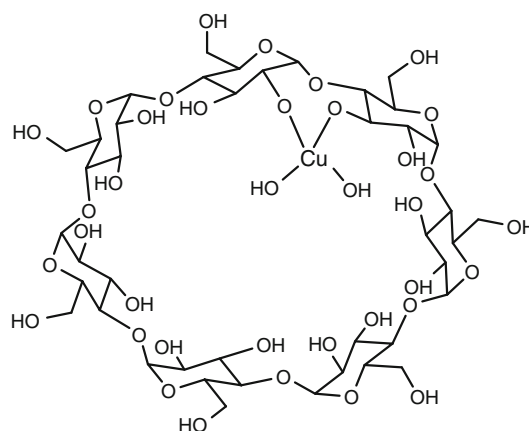


Fig. 7 Structure of $\text{Cu}\beta\text{-CD}(\text{OH})_2^{2-}$ complex

respectively. No evidence of Cu(II) ions or Cu(II) hydroxy-species encapsulation into the β -CD cavity (host–guest complex formation) was found [22]. The difference between pCu values obtained and pCu values calculated according to solubility product of Cu(OH)₂ reached ca. 0.5 unit at pH 11.0, whereas it increased up to ca. 2–3 units at pH over 13.0, showing significant complexation of Cu(II) ions in strongly alkaline solutions of β -cyclodextrin [22]. The comparison of CuCD(OH)₂²⁻ complex with other Cu(II) complexes with polyhydroxylic or hydroxypolycarboxylic and polyaminopolycarboxylic ligands shows that the stability of Cu(II) complex with β -cyclodextrin is in the same range as that of Cu(II) complexes with EDTA, DTPA, L- and DL-tartrate, and saccharose [52].

The above-reviewed interactions of cyclodextrins with copper(II) ions occur in alkaline solutions and are characterized by formation of coordination compounds, i.e. covalent binding of copper(II) to cyclodextrins via deprotonated OH-groups. However several works report on interaction of cyclodextrins with copper(II) salts in neutral aqueous solutions, i.e. formation of inclusion complexes [53–55]. According to authors of Ref. 53, the reaction of β -cyclodextrin (β -CD) with CuCl₂ in neutral aqueous solutions gave a stable molecular complex without any side-arm support. The X-ray crystallographic analysis clarified that the copper(II) ion was located at the bottom of the primary-hydroxy side as a CuCl₂(H₂O)₂ form. Hydrogen bonds were found between the Cl⁻ and H₂O ligands and β -cyclodextrin hydroxy- and ether-groups, the copper(II) ion being axially coordinated with a hydrox-group of a neighboring β -cyclodextrin molecule, giving a one-dimensional β -cyclodextrin/CuCl₂ array [53]. The interaction between copper(II) chloride and β -cyclodextrin has been studied also using measurements of diffusion coefficients and electrical conductivity [54]. Significant effects on the electrical conductivity were observed in the presence of the β -cyclodextrin, suggesting interactions between this carbohydrate and copper(II) chloride (support for this came from diffusion coefficient measurements) [54]. Formation of inclusion complex between β -cyclodextrin and copper(II) salt was also observed in the system β -cyclodextrin/copper(II) acetate [55]. It was reported on the synthesis of a supramolecular complex between β -cyclodextrin and copper(II) acetate. The studies showed that the complex is of the 2:1 (host:guest) type, in which the compounds interact weakly with each other. Further, a novel supramolecular approach to fabricate CuO nanoparticle via a green pathway has been proposed by using the β -cyclodextrin-encapsulated precursor of copper(II) acetate. It has been noticed that under the effect of β -cyclodextrin the CuO nanoparticles produced are nearly spherical in shape and showed minimal agglomeration [55].

Complexes with lead(II)

Lead(II) can form as polynuclear [56], as well as mononuclear [57] complexes with deprotonated cyclodextrins. The formation of inclusion complexes is also documented [58, 59].

A polynuclear complex of multideprotonated γ -cyclodextrin (complete deprotonation of the secondary hydroxyls) with lead(II) was prepared from alkaline solution on reaction of γ -cyclodextrin, lead(II) nitrate and sodium hydroxide. The composition of colourless crystals formed was found on the ground of X-ray analysis: [Pb₁₆(γ -CDH₁₆)₂] · 20H₂O [56]. The authors proposed the structure of this complex, where each secondary alkoxide anion is coordinated to two bridging lead(II) ions.

Solution equilibria in the system lead(II)– β -cyclodextrin was studied in alkaline solutions under conditions of β -cyclodextrin excess [57]. Polarographic and UV-spectrophotometric investigations of Pb(II) complex formation with β -cyclodextrin have showed that the complexation of Pb(II) ions begins at pH over 10. The formation of lead(II) 1:1 complex with β -cyclodextrin anion was observed at pH 10–11.5 (Fig. 8). The logarithm of the stability constant of this complex compound was found to be 15.9 ± 0.3 (20 °C, ionic strength 1.0) and the molar extinction coefficient value was ca. 5500 ($\lambda_{\text{max}} = 260$ nm). The diffusion coefficient values of Pb– β -cyclodextrin complex were in the range $(2.2–1.2) \times 10^{-6}$ cm² s⁻¹, depending on β -cyclodextrin concentration. With further increase in solution pH the Pb(II)– β -cyclodextrin complex decomposes and converts to Pb(OH)₂ or Pb(OH)₃⁻ hydroxy-complexes. This process occurs with a decrease in Pb(II) complexation degree. The latter result authors explained by a decrease in the β -cyclodextrin anion activity. Neither

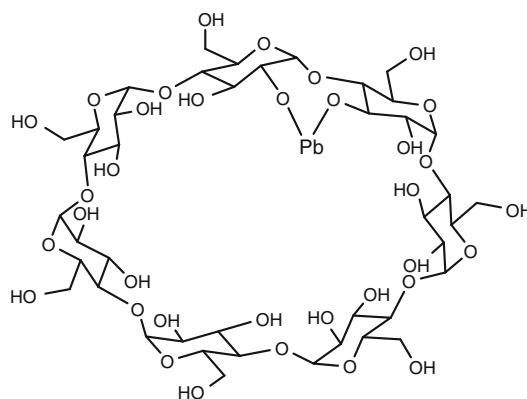


Fig. 8 Structure of Pb β -CD complex

$\text{Pb}(\text{OH})_2$ nor $\text{Pb}(\text{OH})_3^-$ encapsulation into β -cyclodextrin cavity was observed [57].

Spectrophotometric and electrochemical at pH 6.2 studies showed the evidence of the interaction among the $[\text{PbAc}]^+$ and $[\text{PbEDTA}]^{2-}$ with the β -cyclodextrin, and the equilibrium constants for 1:1 inclusion complexes were determined: for the β -CD- $[\text{PbAc}]^+$ complex a $pK_{\text{CD:Guest}} = 1.6 \times 10^3$ was obtained and for the β -CD- $[\text{PbEDTA}]^{2-}$ it was $pK_{\text{CD:Guest}} = 3.7 \times 10^2$ [58]. The interaction of between lead(II) ions and α -, β - and γ -cyclodextrins was studied using electrochemical technique [59]. The formation constants of surface inclusion complexes determined using a carbon paste electrode and cyclic voltammetry for aqueous-based media containing Pb(II) and mentioned cyclodextrins were in the range from 727.5 to 883.7 M^{-1} , whereas α -cyclodextrin displayed the greater affinity to lead(II) as compared to the β -cyclodextrin and γ -cyclodextrin [59].

Modification of carbon paste electrodes with cyclodextrins was applied for analytical purposes. Carbon paste electrodes modified with α -cyclodextrin or β -cyclodextrin were used to determine lead(II) ions in solutions within the range from 1×10^{-5} to 1×10^{-3} M [60]. α -Cyclodextrin and β -cyclodextrin modified carbon paste electrodes also were used to determine Pb(II) by means of anodic stripping voltammetry [61]. Both modified electrodes displayed good resolution of the oxidation peak of lead. Statistic analysis of the results strongly suggested that the carbon paste electrodes modified with β -cyclodextrin exhibited a better analytical response than the carbon paste electrodes modified with α -cyclodextrin, while the detection limits obtained for lead(II) were 6.3×10^{-7} and 7.14×10^{-7} M, respectively [61].

Membrane gels obtained by chemically grafting cyclodextrin molecules on polymethylhydrosiloxane or incorporated into plasticized polyvinylchloride (PVC) membranes were used as heavy metal ion sensors—the Nernstian response of an β -cyclodextrin membrane towards lead(II) ions was observed [62]. Similar results were obtained when cyclodextrin-polysiloxane gel matrices were used—the membranes containing β -cyclodextrin were sensitive to lead(II) ions [63, 64].

Complexes with cadmium(II)

Polarographic study of alkaline solutions of cadmium(II) and β -cyclodextrin was carried out recently [65]. It was shown, that β -cyclodextrin in alkaline solutions dramatically enhances the solubility of cadmium(II) ions, which are otherwise practically insoluble due to the formation of hydroxide gels. No Cd(II)- β -CD complex formation was observed at pH < 11, even if solutions an excess of β -cyclodextrin contained. The polarographic waves of

Cd(II) reduction in alkaline β -cyclodextrin solutions shifted to more negative potentials in the pH range from 12.0 to ca. 14.0 (this fact was attributed to deprotonation of β -cyclodextrin in alkaline solutions and herewith to strengthening of β -CD complexing ability and complex formation). On the ground of data on the slope of the half-wave potential shift, which depended on solution pH and on concentration of β -cyclodextrin, authors concluded, that cadmium(II) forms complex with two ligands—double deprotonated anion of β -cyclodextrin and OH^- groups—with a general formula $\text{Cd}\beta\text{-CD}(\text{OH})_2^{2-}$ (Fig. 9). The results of the $\text{Cd}\beta\text{-CD}(\text{OH})_2^{2-}$ complex stability constant calculations correlated well the mean value of the logarithm of stability constant being 10.4 ± 0.1 . The diffusion coefficient of mentioned complex was calculated from limiting current values. The value obtained ($D = 1.0 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$) shows a large size Cd(II) complex species formation in alkaline solutions containing β -cyclodextrin [65]. It can be noted, that $\text{Cd}\beta\text{-CD}(\text{OH})_2^{2-}$ diffusion coefficient value coincide with that calculated for Cu(II)- β -CD complex [22].

The complexation of cadmium(II) ions by cyclodextrins was employed for removal of mentioned metal ions from contaminated soil [66].

Earlier described carbon paste electrodes modified with α -cyclodextrin or β -cyclodextrin were employed to determine also cadmium(II) ions in solutions [61]. Accordingly authors, the carbon paste electrodes modified with β -cyclodextrin had a better analytical response than the carbon paste electrodes modified with α -cyclodextrin, while the detection limits obtained for cadmium(II) were 2.03×10^{-6} and 2.15×10^{-6} M, respectively [61].

Above mentioned membrane gels obtained by chemically grafting cyclodextrin molecules on polymethylhydrosiloxane or incorporated into plasticized polyvinylchloride membranes were used also as cadmium(II) ions sensors—the Nernstian response of an α -cyclodextrin membrane

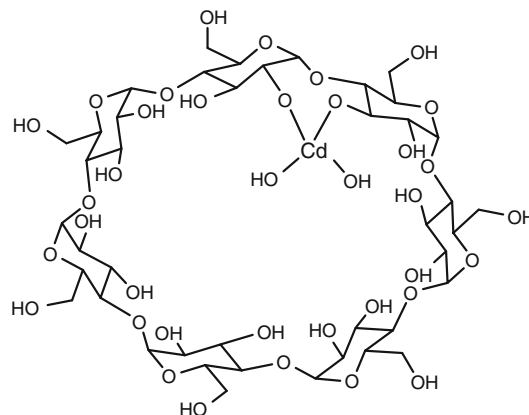


Fig. 9 Structure of $\text{Cd}\beta\text{-CD}(\text{OH})_2^{2-}$ complex

towards cadmium(II) ions was observed [62]. Similar results were obtained when cyclodextrin–polysiloxane gel matrices were used. The membranes containing α -cyclodextrin were sensitive to cadmium(II) ions, a Nernstian response as well as good detection limit were obtained, and the membranes showed good affinity to cadmium ions [28 mV/pCd(II)] [63, 64].

Complexes with other divalent metal ions

A polynuclear complex of multideprotonated α -cyclodextrin with iron(II) ions was prepared from alkaline solution [36]. Clear solutions formed instead of hydroxide precipitate when lithium salts were added to $\text{Fe}(\text{OH})_2/\alpha\text{-CD}/\text{NaOH}$ slurries—or more directly, when lithium hydroxide was used instead of sodium hydroxide. The composition of crystals formed after crystallization was determined on the basis of X-ray analysis: $\text{Li}_5[\text{Li}_6(\text{H}_2\text{O})_6\text{Fe}_3(\alpha\text{-CDH}_{7.5})_2\text{H}_2] \cdot 56\text{H}_2\text{O}$; a very similar molecular structure was observed for with manganese [36].

Molecular composites containing cyclodextrins and hydrated chlorides of alkali earth metals magnesium(II) [67] and calcium(II) [68, 69] are documented. Suitable crystals for X-ray analysis were grown by slow evaporation of a saturated MgCl_2/β -cyclodextrin solution, the composition of compound being: $\beta\text{-CD}$, $2[\text{Mg}(\text{H}_2\text{O})]\text{Cl}_2$, $3.5\text{H}_2\text{O}$ [67]. The same authors group reported on molecular composites of calcium(II) chloride with β -cyclodextrin [68] and α -cyclodextrin [69], the composition of complexes being $\beta\text{-CD} \cdot 2\text{CaCl}_2 \cdot 11.25\text{H}_2\text{O}$, $\alpha\text{-CD} \cdot 3\text{CaCl}_2 \cdot 19\text{H}_2\text{O}$ and $[0.5(\alpha\text{-CD}) \cdot 1.5\text{CaCl}_2 \cdot 8.5\text{H}_2\text{O}]$, respectively.

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