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REVIEW

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Cyclodextrins as electrode modifiers

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Abstract Complexation abilities and analytical applications of working electrodes with attached cyclodextrins (CDs) are reviewed. For the immobilization of CDs, their adsorption and formation of self-assembled monolayers, preparation of polymer films, as well as incorporation within plasticized membranes and composites such as carbon paste and gels are considered. Some electrochemical investigations of the CD interactions in solution are also reported with respect to their use at CD modified electrodes.

1 Introduction

Synthetic and natural polymeric materials have found wide application in the chemical modification of the electrode surface. Among biopolymers, deoxyribonucleic acid (DNA), cyclodextrins (CDs) and some others have been intensively studied [1]. Cyclodextrins are cyclic 1,4-linked D(+)-glucopyranose oligomers and those with 6, 7, and 8 glucose units are called α-, β-, and γ-cyclodextrins, respectively. Due to the presence of asymmetric carbons the CDs exhibit chiral properties. D-glucose units form a conical structure (Fig. 1) with a relatively hydrophobic cavity, while the exterior is relatively hydrophilic due to the presence of hydroxyl groups. Chemical modification of hydroxyl groups in 2-, 3- and 6- positions gives CDs different properties and permits preparation of CDs suitable for special uses.

Chemical structure, physical properties in solution and solid state, chemical reactivity and biological effects of the CDs were reviewed by Szejtli and Osa [2]. The most important property of CDs is an ability to form inclusion complexes with many appropriately sized organic and inorganic ions and molecules (with a diameter of 0.5 to 0.8 nm) in aqueous, non-aqueous and mixed media. The host-guest interaction leads to encapsulation of small particles into the cavity of the oligosaccharides without the formation of chemical bonds and without changing their structure. The driving forces for the complexation are non-covalent: van der Waals forces, hydrogen binding, hydrophobic interactions and energetic stabilization based on the transformation from a strained high-energy conformation to an unstrained low-energy form by the displacement of water molecules. A typical stoichiometry of 1 : 1 and 1 : 2 and the formation constants of 10 to 10^4 M^{-1} were found [3].

The formation of inclusion complexes is of interest, particularly with respect to:

– intermolecular interactions between molecules
– molecular recognition (chiral discrimination)
– solubilization of lipophilic substrates in aqueous media and stabilization of sensitive substances, including electrogenerated radicals
– modeling the catalytic (hydrolytic) enzymes
– drug delivery systems.

Complexation by CDs is widely used in the pharmaceutical industry, food technology and agriculture. Recognition and inclusion reactions of CDs were reviewed by Easton and Lincoln [4]. Analytical aspects of CDs were covered by Zhu [5] as well as by Li and Purdy [6], chromatographic separations by Snopek et al. [7] and non-separation uses by Szente and Szejtli [8]. In electrochemistry especially, CDs either added to solution or bound to the electrode surface can cause beneficial changes for stereoselective organic electrosynthesis and electrocatalytic reactions. Electroanalytical applications of CDs are based on formation of an inclusion complex, molecular recognition and selective preconcentration of analyte at the electrode.

The electrochemical behavior of CDs and CD-inclusion complexes was reviewed by Bersier et al. in the early 90 s [3] and recently by Liu et al. [9]. Selective complexation and sensitive analysis of charge-diffuse cationic species using lipophilic CDs were reviewed by Parker and

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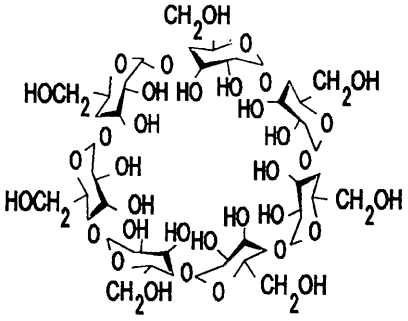

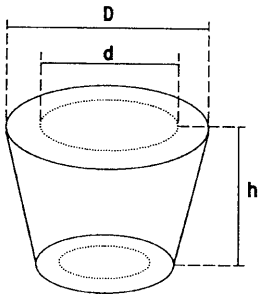

Fig. 1 Chemical structure of β-cyclodextrin

Kataky [10]. Application of chemically modified electrodes (CMEs) with ion-channel receptors for chemical sensing was reviewed by Bühlmann et al. [11]. Numerous special reports have been dedicated to highly selective sensors and indicators based on CDs. It is the aim of this paper to review investigations regarding CDs in the 90 s and to assess progress, particularly on electroanalytical applications of the CD modified electrodes.

2 Adsorption of CDs and self-assembled monolayers

Physical adsorption represents a simple way in which to modify electrodes. The CDs adsorb on a mercury drop electrode forming compact layers [12, 13]. For instance, the complexation of phenylglyoxalic acid and stereoselectivity of its reduction were investigated using the CD-modified mercury electrode [12]. A hanging mercury drop electrode was also modified by monolayers of per-methylated per-6-thiolated α, β- and γ-CDs and the inclusion of inorganic ions as well as uncharged hydrophobic guests such as adamantanol was studied [14].

Remarkable voltammetric and electrocatalytic properties of films of the C_{60}:γ-CD (1:1) and C_{60}:substituted β-CD (1:1 and 1:2) inclusion complexes are continuously investigated [15 and references therein]. The complexes were adsorbed at the droplet evaporation on the surface of glassy carbon electrode (GCE) and prevented from desorption by a Nafion layer. Behavior of hemoglobin [16], cytochrome c [17] and DNA [18] on the modified electrodes has been reported. The C_{60}:CD complex is capable of mediating the electron transfer. A very sensitive quartz crystal sensor with β-CD for the determination of blood cholesterol has been described [19]. Self-organization of α-CD on a gold(III)-covered surface was achieved by potential controlled adsorption and investigated using scanning tunneling microscopy [20].

The possibility of designing the molecular architecture of the electrode/solution interface is very attractive for electrochemistry and electrochemical sensors. Thiolate self-assembled monolayers (SAM) on a gold surface containing receptor subunits have been reviewed by Kaifer [21]. Derivatives of CDs with organo-sulfur groups have been shown to be able to chemisorb on a gold surface and form highly organized monolayers. These monolayers are suitable for the investigation of relations between the molecular structure and molecular-recognition properties of CDs. The chemical structure of CD derivatives has a great effect on the molecular organization of the monolayers.

Conversion of all seven primary -OH groups of β-CD into -SH groups led to monolayers with substantially defect densities due to the lack of favorable lateral interactions between the CD molecules [22]. In order to „patch the holes“, a mixed monolayer of the thiolated β-CD and pentanethiol was suggested. The binding constant of ferrocene of 3.9×10^4 M^{-1} was about an order of magnitude higher than in homogeneous solution.

Nelles et al. [23] examined the influence of the spacer length between the thiol group and the CD cavity as well as the number of thiol groups on molecular architecture in the resulting films. The CD derivatives were chemisorbed on freshly evaporated gold films supported by glass substrates. Among other techniques, cyclic voltammetry was used as a qualitative tool to probe the density or permeability of CD films for the oxidation and the reduction of ferricyanide in solution. The authors showed that the film of monothiolated CDs is less permeable than multithiolated films, which is in agreement with the previous observation [22]. The spacers in the monothiolated derivatives give more mobility to the CD tori to align themself in the top layer, optimizing intermolecular hydrogen bonding, in contrast to the multithiolated derivatives, in which the CD tori C_n axis are held perpendicular to the surface. The packing density of the titled CD tori increases with spacer length.

Adsorption kinetics are also influenced by the structure of CD mercapto-derivatives and can be described by a three-step process: a physisorption process, a binding and orientation step, and an adlayer formation [24]. Maeda et al. [25] investigated the regio- and stereoselective complexation of chiral phenylazobenzoate compounds with the thiolated α-CD/SAM on the gold electrode. Significant differences in association constants of ortho- and para-isomers and R- and S-enantiomers of the ortho-isomer were observed using p-hydroquinone as marker (Fig. 2). Later, the inclusion of phtalic acid esters by an SAM of thiolated α-CD on a gold electrode using hydroquinone as a probe has been reported [26]. The association constants of the esters with the immobilized CD were estimated. Thermodynamic parameters indicated that the inclusion in the SAM system was entropy-driven in difference to the free CD system. Beulen et al. [27] reported the preparation and characterization of the SAM of dialkyl sulfide

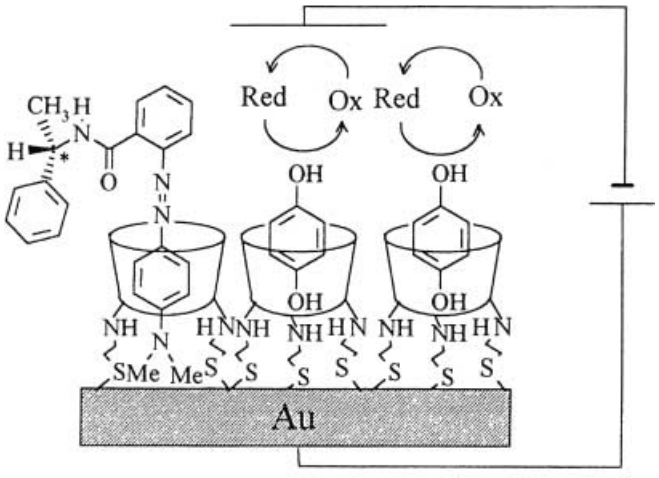

Fig. 2 Schematic drawing of inclusion complexes of hydroquinone and o-methyl red–1-phenylethylamine conjugate with 6-(2-mercaptoethylamino)-6-deoxy-α-CD adsorbed onto a gold surface. Asterisk denotes asymetric carbon atom (with permission from [25])

and alkanethiol ester and amide derivatives of the CD on the gold surface. The sulfide adsorbates use their multiple attachment points in a more efficient way than those of the thiol monolayer.

Voltammetric responsive sensors were studied for the detection of electroinactive organic species [28]. The sensor was prepared by modification of a gold electrode with the SAM of lipoyl-β-CD derivative. Ferrocene carboxylic acid was used as an electroactive marker and the formation constants of seven organic compounds with the CD derivative were obtained. Slopes of the calibration curves and the detection limits are proportional to their formation constant values. Bile acids were detected electrochemically after capillary electrophoresis separation. The inclusion of 11-(ferrocenylcarbonyloxy)undecanethiol in an SAM on the gold electrode surface by β-CD in solution was also investigated [29]. It was found that the included form is electroinactive and the stability constants for ferrocene and ferricinium derivatives were evaluated.

Godinez et al. [30] demonstrated the aggregation of amphiphilic α-, β-, and γ-CD receptors with positively charged amino groups on the surface of bare and modified gold electrodes. While a highly disorganized multilayer with the liquid-like orientation of the CD molecules is formed on the bare electrode, the chemical modification of a gold surface with the mercaptocarboxylic acids exerts a template effect on the aggregation of CDs by modifying not only the degree of packing and thickness of the multilayer assembly but also the orientation of the adsorbed amphiphiles (Fig. 3). This templating effect is important in the context of a simple preparation of modified electrodes with molecular recognition properties.

Lahav et al. [31] prepared the SAM of β-amino-CD on a functionalized gold surface which was used as an active interface for the amperometric and microgravimetric transductions of optical signals recorded by a photoisomerizable electroactive bipyridinium-azobenzene diad. The photoisomers exhibit a different affinity to the CD receptor sites.

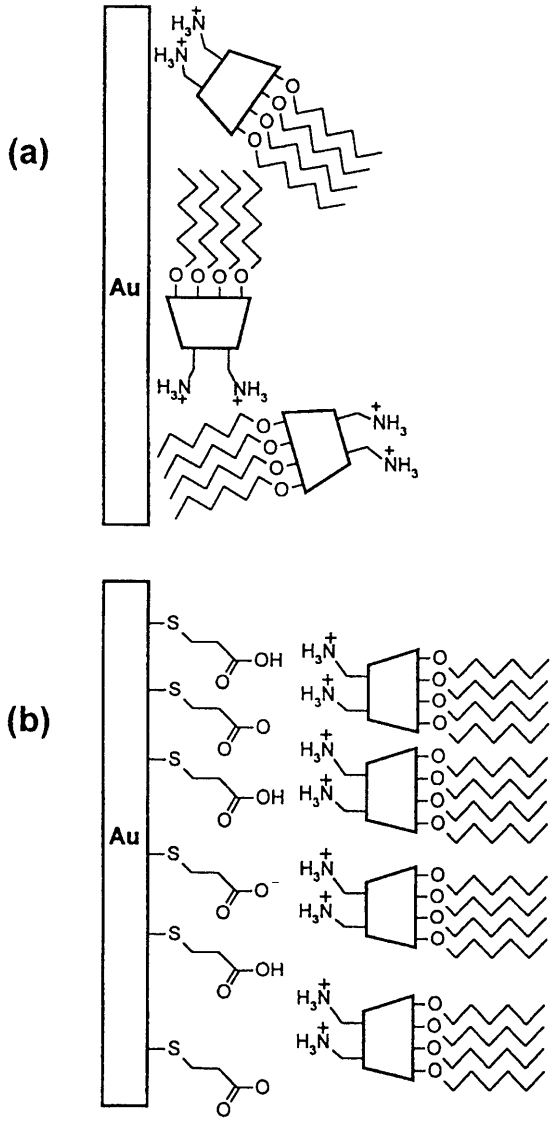

Fig. 3 Schematic model for the interfacial aggregation of 2,3-*O*-hexyl-6-deoxy-6-amino-α, β- and γ-CDs on (*a*) bare gold and (*b*) gold-mercaptopropionic acid surfaces (with permission from [30])

Wang and Kaiser [32] immobilized positively charged β-amino-CDs electrostatically as an adlayer on an SAM of thioctic acid on gold. The CDs do not form a compact monolayer due to repulsive Coulombic interactions between neighboring CD receptors. In CD free solution, a slow redissolution of the hosts from the electrode surface was observed. Similarly to [22], binding constants for the complexation of ferrocenecarboxylate guest are presented as larger than the value obtained in homogeneous solution. However, these binding constants describe equilibria for the distribution of guest between two phases, i.e. SAM and solution, and, therefore, they cannot be compared directly with the respective stability constant of the supramolecular complex formation in solution.

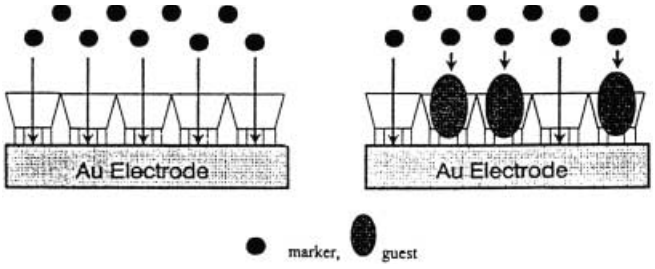

Fig. 4 Working mechanism of the self-assembled monolayer electrode as channel sensor (with permission from [34])

CDs can act as intramolecular channels in a channel sensor where the access of a redox marker through these channels is blocked by the formation of inclusion complexes with the nonelectroactive analytes. The first report [33] concerned monolayers of a long alkyl β-CD-derivative at the air-water interface and an *in situ*-placed pyrolytic graphite working electrode. In order to measure the pure marker-analyte channel competition, several factors have to be controlled such as possible marker-analyte association in solution, structural defects of the monolayer and diffusion/adsorption contributions to the marker response. Advantages of a hanging mercury drop electrode for the study of intramolecular channels have been described [11].

A channel sensor was prepared by the modification of a gold electrode with the SAM of per-6-thio-β-CD derivative simply by dipping the bare electrode overnight in a millimolar solution of the modifier [34]. SAM defects were repaired by the electropolymerization of 5-hydroxy-3-indoleacetic acid which covered only pinholes maintaining free the CD cavities. Ferrocene carboxylic acid and hydroquinone were used as electroactive markers and cetyltrimethylamonium acetate and ursodeoxycholic acid as guest molecules (Fig. 4). Higher values of the formation constants for both guests were obtained at the electrode without pinholes.

Almirall et al. [35] utilized a silver electrode chemisorbed with a polythiocarbamate derivative of β-CD. The electrode was used for the discrimination of positional isomers of the nitrobenzoate anion and nitrophenol. While the ortho-isomers did not exhibit any reduction peak, meta- and para-isomers were recognized as the nitro-group of the included compounds was susceptible to interact with the silver surface. An enhancement of the molecular-recognition properties against the thiolated derivatives was observed.

3 Polymeric films with CDs

The ability of CDs to form inclusion complexes is usually the same or even enhanced when their are in the form of polymers. CD polymers (CDP) as modifiers of metal and carbon electrodes have been investigated by Kutner et al. [36–46] also in cooperation with our laboratory. A chemically modified β-CDP-25-PTFE-carbon (10 : 60 : 30% w/w) composite electrode was prepared and investigated by cyclic voltammetry using ferrocene and regioisomeric nitrobenzene derivatives as guest compounds [37]. It was shown that the β-CDP-25 polymer is suitable for membrane-type applications because of its selectivity, chemical inertness, and insolubility in both protic and aprotic solvents. The diffusion mechanism was postulated for the guest molecules in the β-CDP-25 polymer matrix, which invoked hopping of the molecules between inclusion sites. Different diffusion coefficients were found for different regioisomers as well as the stabilization of free nitro anion radicals in the β-CDP-25 environment.

Cyclodextrin polymeric films have been deposited by polycondensation of soluble α-, β- and γ-CD prepolymers with glutaric dialdehyde (GD) [38]. The optimum mass ratio of GD to the CD-prepolymer was found to be 1:10. These films are stable, insoluble and nonreducting. Scanning electron microscopy and electrochemical quartz crystal microbalance (EQCM) measurements were widely used for the study of these films on glassy carbon and gold/quartz electrode surfaces.

A glassy carbon electrode coated with α-CDP film was used for the study of the α-CDP/(4-nitrophenol/4-nitrophenolate) inclusion system [39]. The positive end of the guest dipole, i.e. nitro group, points out from the polymer into the solution phase and cation-exchange properties of the film are induced by included deprotonated 4-nitrophenolate.

A molecular inclusion of ferrocene and ferrocene carboxylic probes in the β-CDP and anionic carboxymethylated β-CDPA deposited on a gold/quartz electrode has been investigated [40]. Carboxylic group sites of the β-CDPA film are available for cation exchange. It was shown that the inclusion as well as the release of redox and acid-base type guests by the polymeric film can be controlled by switching the potential of working electrode and/or the solution pH. Practical implications may be found in a selective drug release, design of electrochromic display devices, and high performance capillary liquid chromatography columns.

Accumulating properties of the condensation polymer films of β–CDP and carboxymethylated β-CDPA on a metal surface were compared with respect to azepine and phenothiazine antidepressant drugs by using simultaneous cyclic voltammetry and piezoelectric microgravimetry [41]. The accumulation of protonated, i.e. positively charged, drug molecules is much higher in the anionic, i.e. cation-exchange, form of the β-CDPA film than in the non-ionic β-CDP film. Most likely, this difference in the accumulation level is due to a combined effect of the supramolecular complex formation between the β-CD inclusion sites and drug molecules as well as ion exchange for the former. Therefore, the β-CDPA film is recommended, preferably, for fabrication of sensors for the trace determination of these drugs. The values of sorption equilibrium constants, β_{pol}, and changes of the free energy of sorption, ΔG°_{pol}, have been determined from the Langmuir-type sorption isotherms for all drugs and for both polymers. For the β–CDP film, mutual differences in the determined

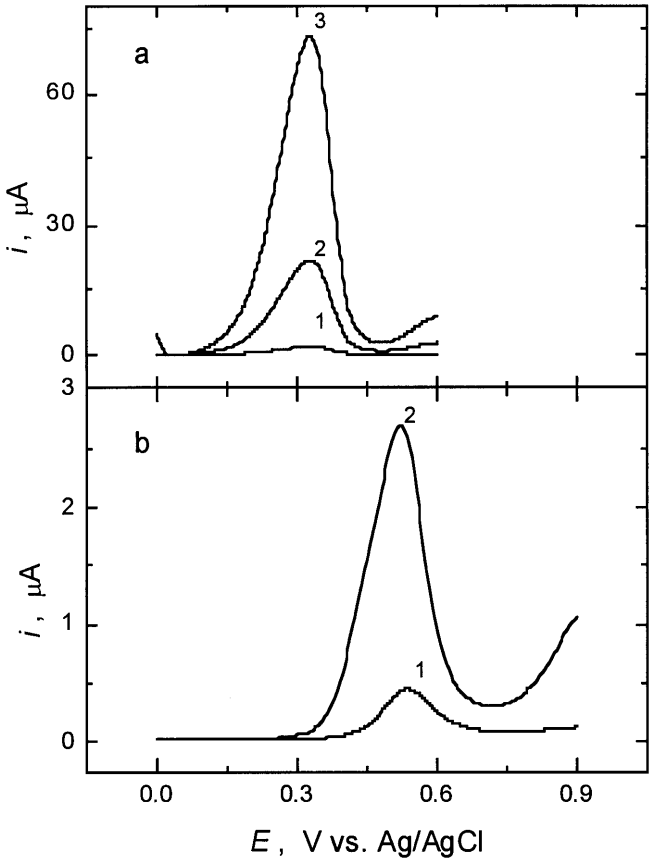

Fig. 5 Preconcentration effect of immobilized CDs: (**a**) bare screen-printed electrode (curve *1*), β–CDP film (curve *2*), β-CDPA film (curve *3*), (**b**) bare carbon paste electrode (curve *1*), β-CD modified CPE (curve *2*). DP voltammograms after 120 s accumulation at –0.15 V vs Ag/AgCl, recorded in (a) 2.7×10^{-6} M thioridazine, 0.1 M phosphate buffer pH 7.4, (b) 1×10^{-5} M thioridazine, 0.07 M phosphate buffer pH 6.6, pulse amplitude 100 mV, potential scan rate 10 mV/s

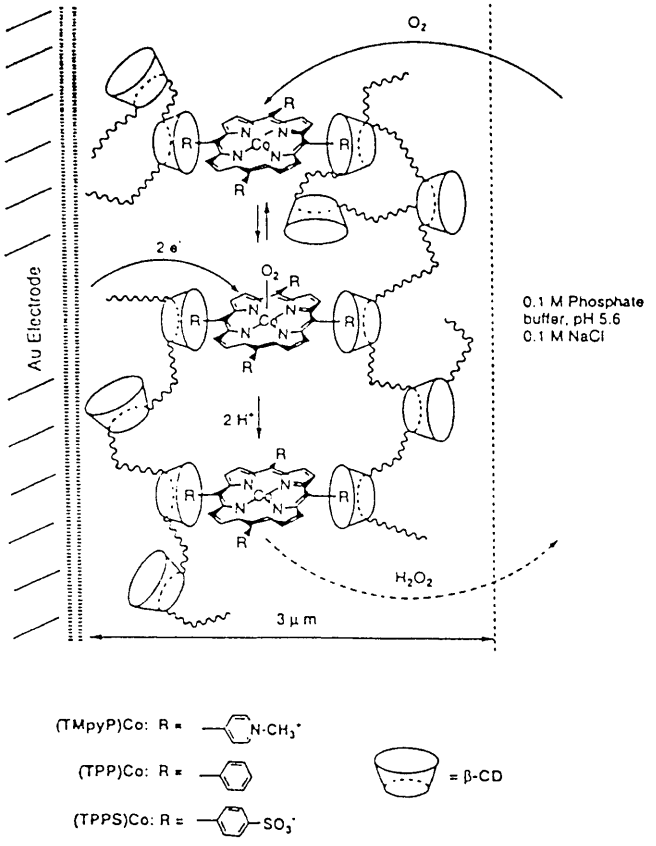

Fig. 6 Scheme of electrocatalytic dioxygen sensing at the gold electrode coated with the β-CDP and β-CDPA film containing cobalt porphyrin (with permission from [44])

for all drugs β_{pol}, and $\Delta G°_{pol}$ parameters are consistent with the differences in the stability constants of respective supramolecular complexes in solution.

The β-CDP and β-CDPA films were also deposited on carbon-based screen-printed electrodes and applied to the determination of antidepressant drugs [42]. Figure 5a shows a comparison of the preconcentration effect of the CD films with respect to thioridazine. In a model solution, linear calibration curves within the range of 1.96×10^{-7}–2.75×10^{-6} M and the detection limits of 4×10^{-8}–5×10^{-7} M and 7×10^{-9}–1×10^{-7} M for individual drugs with 120 s accumulation were obtained for β-CDP and β-CDPA modifiers, respectively. The modified electrode was applied to the determination of drugs in serum.

Electrocatalytic sensors for dioxygen dissolved in both aqueous and mixed solvent solutions have been suggested [43, 44]. They are based on neutral β-CDP and cation-exchange β-CDPA polymer film modified gold electrodes hosting cobalt porphyrins. These compounds are able to form supramolecular complexes with cyclodextrins. The films were cast from aqueous solution of the respective prepolymer, redox mediator and glutaric dialdehyde, GD, which results in an open structure, readily permeable to dioxygen (Fig. 6). The catalyst was molecularly dispersed in the polymer matrix and at an irreversible immobilization it revealed well-defined solution electrochemical behavior. This is an advantageous difference from other types of immobilization. The sensor had a response time of nearly 0.5 s and was stable for days if stored in air of high humidity.

Cyclodextrin polymer films can form a unique environment for the immobilization of redox mediators and enzymes. This approach was used for the preparation of an amperometric glucose biosensor of the second generation [45]. Glucose oxidase (GOD) was covalently linked to the α-CD polymer backbone, while the mediators 1,4-benzoquinone (BQ) and tetrathiafulvalene (TTF) were immobilized in the α-CDP cavities (Fig. 7). A high mediator concentration can be attained due to the high, ca. 1 M, concentration of the inclusion sites in the α-CDP/GD film. It enables the mediator to transfer the charge to and from the enzyme most likely by diffusion. It was shown that the inclusion and ion-exchange sites have to be present in the polymer to retain both the oxidized and reduced forms of the mediator. The detectability of glucose with the (α-CDP)-GOD-BQ electrode was 10 mM and the stability of the (α-CDP)-GOD-TTF electrode was over 2

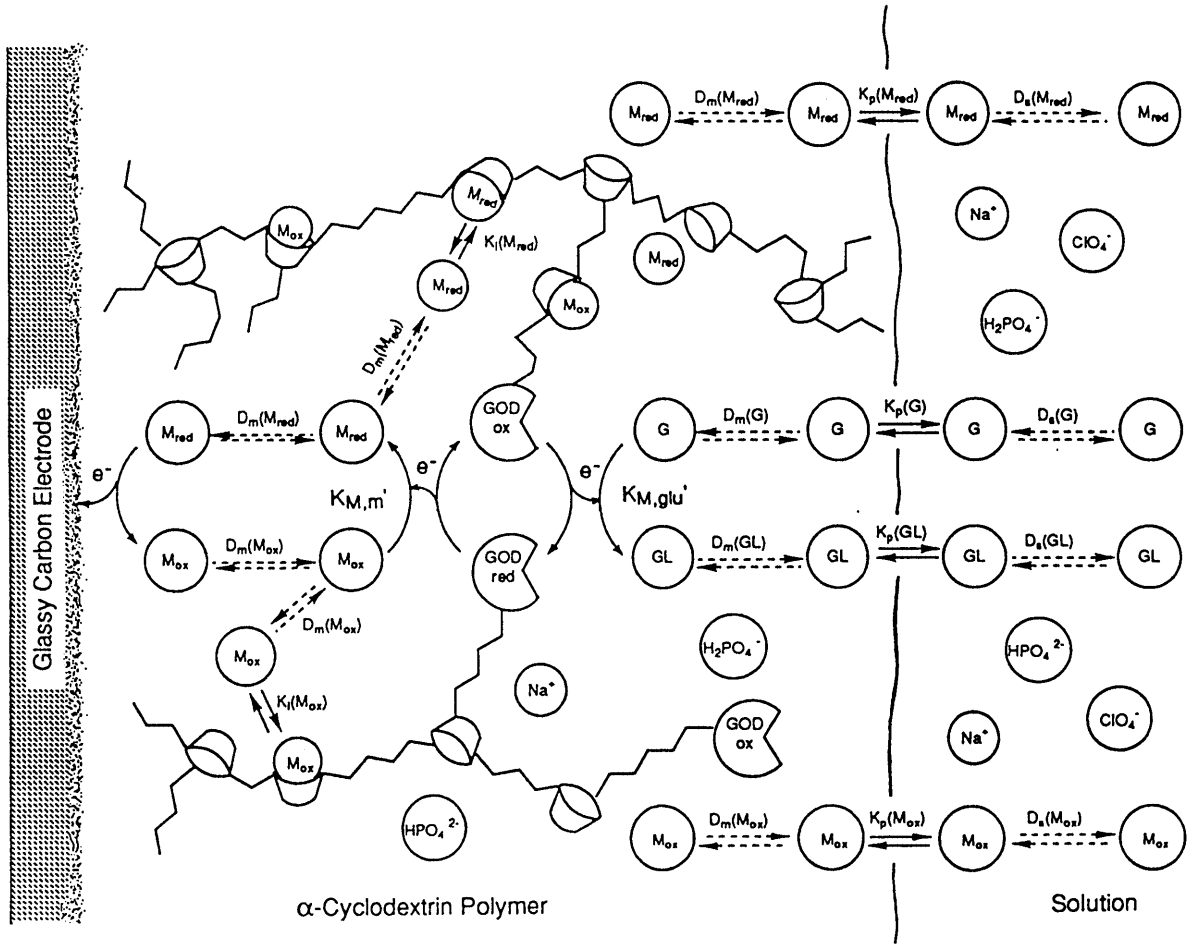

Fig. 7 Scheme of biocatalytic glucose (G) electrooxidation to gluconolactone (GL) at a glassy carbon electrode coated with α-CDP membrane containing covalently immobilized glucose oxidase (GOD) and included mediator (M) (with permission from [45])

weeks. A 10 μm diameter platinum microelectrode was utilized for the fabrication of a glucose microsensor.

Using biosensors with the β-CD polymeric membranes, the retention of the tetrathiafulvalenium/tetrathiafulvalene mediator was greatly improved in carboxymethylated polymer (β-CDPA), which allows both inclusion and ion exchange binding of the mediating couple [46]. The 0.2 mM detectability and 25.5 s response time towards glucose were achieved. Due to rejecting properties of the membrane, the sensor is selective towards glucose in the presence of commonly interfering substances. A disposable biosensor based on a screen-printed two-electrode transducer was also fabricated.

An amperometric glucose and lactose sensitive biosensor was prepared by immobilizing GOD, β-galactooxidase, mutarotase and ferrocene in the β-CD polymer on the surface of a glassy carbon electrode [47]. Recently, a hydrogen peroxide sensor was fabricated based on a β-CD polymer as immobilization matrix for peroxidase and a redox mediator [48].

Nagase [49] described voltammetric sensors for anionic guests, such as phtalate derivatives, consisting of a glassy carbon electrode modified with CD-polyaniline and ferrocyanide as marker. A poly(cyclodextrin-pyrrole) modified glassy carbon and platinum electrodes capable of molecular recognition of phenothiazine and napthalenedisulfonate were obtained on the electropolymerization of a monomer derivative of heptakis-2,6-di-O-methyl-β-CD with 3-(pyrrol-1-yl)propionic acid [50]. Another way to immobilize CD is its electrostatic incorporation in a polymeric film. For instance, sulfonated β-CD was fixed as a dopand into polypyrrole (Ppy) [51].

Dermody et al. [52] reported a new "molecular-filter" based chemical sensor. This sensor was prepared by coating of the gold electrode with a hyperbranched poly(acrylic acid) film incorporating β-CD as receptor and a ultrathin chemically grafted polyamine overlayer. The latter layer is a pH-sensitive molecular filter. Positively charged benzylviologen (BV) and negatively charged anthraquinone-2-sulfonate (AQS) were used as electroactive probes to show the function of the molecular filter at different pH values within the regions of pH < 4, pH from 4 to 10, and pH > 10. The composite hyperbranched polymer films address problems of mass and charge transfer as well as time stability.

The presence of the poly(acrylic acid) film itself results in a 50 mV positive shift in a cathodic peak potential for BV and a 43 mV negative shift for AQS relative to the naked gold electrode. After grafting β-CD into the film, an additional 20 mV positive shift for BV was observed

due to the stronger β-CD binding of BV^+ radical compared to BV^{2+} cation making reduction more energetically favorable. The reverse behavior was found for AQS with a 54 mV negative potential shift at pH 6.7. These results suggest β-CDs as receptor sites [52].

Neutral N-methylphenothiazine can be entrapped in the $PPy^+/\beta\text{-CDSO}_3^-$ film and electrochemical cycling of such electrodes represents a way for electro-controlled delivery of the drug. Molecularly imprinted β-CD/polymers have been investigated as selective receptors for steroids such as cholesterol and stigmasterol [53]. Dithiophenes were electropolymerized in aqueous solution as 1:1 host-guest compounds with β-CD [54]. Polymerization is expected to occur outside the cavity.

4 Lipophilic CDs in plasticized membranes

By alkylation of the hydroxyl groups in the 2-, 3- and 6-positions, cyclodextrins become lipophilic. It enables their incorporation in plasticized PVC membranes and use as ionophores in ion-selective electrodes for the detection of a wide range of alkyl- and arylammonium ions. Typically, the Nerstian slopes, detection limits down to 10^{-6} M and low interferences from sodium, potassium, calcium and several organic cations were achieved. Structural origins of enantioselection were also defined. Much work on this topic was done by Parker and Kataky. Some examples are presented in Table 1.

These types of electrode modifiers were also utilized in voltammetric measurements. For instance, differential pulse voltammetry was used to perform the oxidation of dopamine on a screen-printed carbon electrode coated with 2,3,6-tri-*O*-ethyl-β-CD [66]. Analyte concentrations down to 10^{-11} M may be detected in this way.

Amperometric sensors for tricyclic antidepressant drugs were obtained by depositing alkylated CDs in a plasticized polymer matrix containing lipophilic anions on screen-printed electrodes [60]. The inclusion complex formation depends on the presence of background electrolyte components. A controlled potential-aided accumulation for 45 min has allowed the detection of sub-nanomolar levels of the analytes by square wave voltammetry.

Low specificity of sensors towards organic cationic species was addressed by coupling the CD-host into a biosensor. A screen-printed electrode with layers of ferrocene-based redox mediator, enzymes (horseradish peroxidase, choline oxidase and acetylcholine esterase) and alkylated-β-CD in plasticized polyurethan was prepared, which allows the measurement of acetylcholine at sub-picomolar levels with negligible interference from ascorbic acid, dopamine and atropine [10, 58, 59]. Many other species can be detected using this detection principle.

5 Immobilization of CDs within composites

Early work on a carbon-based composite electrode with β-CD polymer has been already mentioned above [38]. Later, Kim et al. [67] prepared a β-CD modified carbon paste electrode (CPE) composed of graphite powder, Nujol oil and β-CD (60% w/w) for the voltammetric determination of phenol, o-, m- and p-cresol. Phenol derivatives were chemically deposited via complex formation with β-CD. The total content of phenol derivatives in an aqueous sample can be determined with a detection limit of 5×10^{-7} M for 25 min deposition. The electrode can be regenerated by 1 M nitric acid in 5 s.

A carbon paste electrode modified with simple monomeric β-CD was also proposed for the DP voltammetric determination of tricyclic antidepressants imipramine, trimipramine and thioridazine [68]. A preconcentration effect of the electrode modifier can be seen (Fig. 5b) which is significantly lower than in the case of CD polymers [43] (Fig. 5a). Nevertheless, detection limits down to nM concentrations have been achieved with 120 s accumulation which is considerably a shorter time than that used with alkylated CDs in a plasticized polymer matrix [60]. The electrode was applied for the determination of imipramine and thioridazine in pharmaceuticals.

Recently, CD/polymethyl hydroxysiloxane gel deposited on the $Si\text{-}SiO_2$ structure was suggested as a sensitive membrane for a heavy metal ion sensor [69]. Nerstian response towards cadmium and lead ions was obtained.

Table 1 CDs immobilized in plasticized membranes of potentiometric ion-selective electrodes and their analytical use

Incorporated CD	Analyte	Reference
Poly-*O*-octyl-α-CD	ephedrinium ions (chiral sensing)	[55]
Peroctylated-α-, β- and γ-CDs	tetraalkylammonium ions, dopaminium ion, acetylcholine	[56]
2,3,6-Trioctyl-βCD, 2,6-didodecyl-β-CD	local anesthetics	[57]
2,6-Didodecyl-β-CD, 2,3,6-triethyl-β-CD	acetylcholine	[58]
2,3,6-Triethyl-α-, β-and γ- CDs, 2,6-didodecyl-α-, β-and γ- CDs, 2,3,6-trioctyl-α-, β-and γ- CDs,	tricyclic antidepressants (imipramine, desipramine, trimipramine), potentiometry and amperometry	[60]
2,6-Di-*O*-alkyl-α- and β-CDs	propranolol, ephedrine, amphetamine (enantioselectivity to (+) propanolol)	[61]
2,6-Di-*O*-dodecyl-β-CD	guanidinium ions (metformin, phenformin)	[62]
2,6-Di-*O*-dodecyl-α- and β-CDs, 2,3,6-tri-*O*-ethyl-β-CD	guanidine, creatinine, choline, acetylcholine	[63, 64]
2,6-Di-*O*-dodecyl-β-CD	lidocaine	[65]

Table 2 Inclusion complex formation for CDs in solution detected by electrochemical methods

Guest molecule	CD derivative	Remarks	Reference
Acetophenone	α-, β- and γ-CDs	dimer products formed in DMF isolated	[70]
Antraquinone	β-CD	1:1 complex formation	[71]
Aromatic sulfonate system	β- and γ-CDs	selective reduction	[72]
Ascorbic acid	β-CD	increases stability in the presence of oxidizing agents	[73, 74]
Benzothiazole derivatives	α-, β- and γ-CDs	1:1 and 1:2 association constants	[75]
Chloramine T, chlorpromazine and others	α-, β- and γ-CDs	binding constants and non-specific interactions using ion selective electrodes	[76]
Chloronitrobenzene	β-CD	influence of organic solvents on the stability of complexes	[77]
Cobaltocenium ion and its carboxyderivative	β-CD	association constants	[78]
Copper(II) complex compound	α-, β- and γ-CDs	formation of novel and regular arrays of CDs around the complex	[79]
Dicyanobenzenes anion radicals generated electrochemically	α-, β- and γ-CDs, 2,6-di-*O*-dimethyl-β-CD	stabilization by CD derivatives as 1:1 inclusion complexes	[80]
Diphenylamine derivatives	β-CD	redox change of the guest molecule outside the cavity	[81]
Dipyrrolyls	β-CD	complexation was utilized at the electropolymerization	[82]
Ferrocene and azaferrocene	α-, β- and γ-CDs	stoichiometry of 2:1, 1:1 and 1:2, resp.	[83]
Ferrocene	β-CD	electrocatalytic oxidation of NADH	[84]
Ferrocenecarboxylic acid	α-, β- and γ-CDs	formation constants	[85]
Ferrocene derivatives	β-CD	formation constants	[86]
Fullerene	γ-CD	RDE study of 1:1 C60:CD complex	[87]
Fullerene	γ-CD	1:1 and 1:2 water soluble complexes	[88]
Methylene blue	β-CD	complexation constants, interaction with DNA	[89]
Nickel(II) tetraaza macrocyclic complex	β- and γ-CDs	effect of supporting electrolyte on the inclusion constants	[90]
Phenothiazine dyes	β-CD	1:1 and 1:2 dye-CD complexes	[91]
Sodium dodecyl sulfate	γ-CD	elimination of interactions with Ru(II) and Co(III) probes	[92]
Viologen dications	α- and β-CDs	CD-induced conproportionation	[93]
Alkylviologens	α-CD	analyte adsorbed on a mercury electrode with binding of alkyl chains by the CD	[94]
Methylalkylviologens	α-, β- and γ-CDs	reversible behavior	[95, 96]
Methylviologen	β-CD and its derivatives	enantioselectivity at the electrocatalytic reduction of benzylformic acid	[97]
Viologens	β-CD	electrochromic optical filter	[98]
Vitamin K-3	β-CD	1:1 inclusion complex, dissociation constants	[99]

6 Conclusions and outlook

Cyclodextrins on the electrode surface have been shown to be effective and sometimes also selective binding agents for various compounds fulfilling structural requirements of the CD cavity for inclusion complex formation. This is of great electrochemical, particularly electroanalytical, interest. CDs can be immobilized on the working electrodes in ways which are typically used for the preparation of chemically modified electrodes. The inclusion complexes are of moderate stability and can be utilized for the preconcentration of trace analytes prior to their measurement, as well as for the immobilization and stabilization of other reagents, such as redox mediators, etc. For further research on this topic, numerous interactions of CDs in solution studied by electrochemical techniques are of interest. Some examples are summarized in Table 2.

As for other similar types of complexants, the selectivity of host-guest interactions at CDs is rather limited, mostly to families of compounds. Up to now, the selectivity of separation techniques using CDs has not been reached with CD-modified electrodes. Nevertheless, CDs play an important and undisputed role among the electrode modifiers, and electrodes with attached CDs have been successfully utilized for the solution of many specific electrochemical and electroanalytical tasks.

Taking into account a success in molecular recognition of chiral analytes with CDs in the solution phase, more examples of regio- and stereoselective complexation and/or stereoselective redox reaction on CD modified electrodes can be awaited in future. Preparation of molecularly imprinted CD polymers represents one of promising ways on this topic. Multicomponent electrode coatings and microstructured modified electrodes will be able to fulfil analytical requirements on robust conventional as well as special micro type sensors. Some CD-based sensors can be expected to come also on the market soon.

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