

# Highly crosslinked ionic $\beta$ -cyclodextrin polymers and their interaction with heavy metals

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**Abstract** A new aqueous insoluble ionic  $\beta$ -cyclodextrin polymer (PYR) has been synthesized and a potentiometric study of the binary Cu(II)-PYR system is performed to calculate the complexation constants (as  $\log\beta$  in heterogeneous medium). The mathematical processing of the pH-metric data gave the formation constants of Cu(II) complexes and the related species distributions. The model is compatible with the presence of five complex species in the range of pH 2.5–7. Stoichiometry indicates the probable involvement of the alcoholate functionalities of the ligand in the complexation. The capacity of the polymer with respect to metal ions retention is evaluated for both Cu(II) and Cd(II) (chosen as target probes). The possibility to recover the sorbed Cd(II) is also tested by using acidic pH solutions. A complete recovery is obtained and the stability of the polymer is verified over ten steps of retention and desorption. To understand the complexation mechanism involved, two other cyclodextrin-based polymers are synthesized which are

characterized by the presence of naphthalic dicarboxylic and carbonate groups as spacers. Their interactions with Cu(II) or Cd(II) are studied. Since the  $\beta$ -cyclodextrin polycarbonate polymer does not have acidic groups on the spacer, it is interesting to compare metal ions retention between this material, which does not present a real cation exchange site, and PYR.

**Keywords**  $\beta$ -Cyclodextrin polymer · Carboxylic derivatives · Complexation constant · Metal ions · Potentiometric titrations

## Introduction

Cyclodextrins, cyclic oligosaccharides formed by  $\alpha$ -(1–4) bond of glucopyranose units, and their derivatives have received attention for the great number of applications [1].

The host–guest interaction of cyclodextrin is determinant to explain the ability to complex a wide range of compounds. The mechanism of complexation does not involve covalent bonds and the main driving force of complex formation is the release of enthalpy-rich water molecules from the cavity [2]. This type of interaction takes place with more hydrophobic guest molecules than water. For this property, cyclodextrins and derivatives are used as carriers for a wide number of poorly water soluble drugs increasing their solubility and their speed of release [3]. On the other hand, the secondary and primary hydroxyl groups can form a hydrogen bond and are responsible for the host–guest surface fit and for the solubility in water of cyclodextrin and their complexes [2, 4]. These hydrophilic properties can explain the interaction of native cyclodextrins

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and derivatives with ions. Stabilization of ionic drugs using complexation with ionic cyclodextrin derivatives is demonstrated. The ionic cyclodextrins form stronger complexes with counter-ionic drugs, compared with complexes of non-ionic cyclodextrin derivatives [5].

As recalled [1], the interactions of native cyclodextrins with metal ions are not deeply investigated in the literature. The main reason can be found in the different experimental conditions required for the stability of the two different species in aqueous systems. In fact, cyclodextrins in water solution have ionic characteristics only at basic pH values; on the other hand, free metal ions are present only in acidic systems.  $M(OH)_i$  species can be bound by alcoholate groups of the native cyclodextrin. Significant is the example of complexation of Cu(II) with  $\beta$ -cyclodextrin; the complex is stable for  $pH > 12$  [4, 6]. Moreover, cyclodextrins are defined as second-sphere ligands for Cu(II) and Mn(II) complexes [7], this explanation can open a wide perspective in the development of materials that increase the retention of metal ions. A symmetrically modified  $\alpha$ -cyclodextrin tripod, having three ureido-bipyridyl tethers, shows selective interaction with metal ions. It has been proved that complexation with lanthanides also enhances fluorescence properties [8]. In this type of complex it is difficult to differentiate the action of the first ligand sphere from the second one. Cu(II) is complexed by D-cysteine derivatives of cyclodextrin; this complex can be used as a chiral additive in ligand exchange chromatography to separate L- and D-TrpO<sup>-</sup> (tryptophan) [9]. Derivatives of cyclodextrins with metal ions increase the chiral receptor properties of native cyclodextrin, furthermore they act as a catalytic centre and mimic a metallo-enzyme model [10]. These types of complexes are used for the controlled release of chemotherapeutic agents containing toxic metal ions such as Rh(II) [11] or for the synthesis of pharmacological active complexes of Au(I) [12].

To our knowledge, where application of native cyclodextrins or their derivatives are studied, there is no evidence of formation constants. The characterization of a new cyclodextrin polymer cross-linked with pyromellitate biacid (PYR) has been shown, as well as PYR complexation properties towards eleven metal ions [1]. Based on these results, we investigated in depth the retention behaviour of metal ions on PYR. PYR capacity towards Cu(II) and Cd(II) is studied. To evaluate the performance of this material in environmental applications, reproducibility in flow condition and in consecutive steps of retention and release of Cd(II) are studied. Based on this data, the complex formation constants between PYR and Cu(II) by pH-

metric titrations are optimized. The interaction capabilities of two other cyclodextrin polymers are tested using Cd(II) or Cu(II) as target probe to better understand the mechanism of retention involved. For this reason, we synthesized two polymers containing naphthalene tetracarboxylate biacid (NAF) or carbonate (PCD) as crosslinkers. Interesting comparisons for the different cation exchange property of the crosslinker group are discussed.

## Experimental

### Instrumentation and material

The potentiometric measurements are performed at  $T = 25.0 \pm 0.1^\circ\text{C}$  and  $I = 1.0 \text{ mol l}^{-1}$  (NaCl) by a Metrohm 713 potentiometer (resolution  $\pm 0.1 \text{ mV}$ ) equipped with a combined glass electrode (91-02 sc Orion Research Inc., Beverly, MA, USA). The titrant, a standardized solution of NaOH, is dispensed with a 765 Dosimat Metrohm burette, whose minimum deliverable volume is 0.001 ml. Temperature control is achieved by water circulation in the outer chamber of the titration cell, delivered by a thermo cryostat, D1-G model Haake.

The solutions containing metal ions and polymers are filtered by a mixed cellulose ester filter, pore size  $0.2 \mu\text{m}$  from MFS (Pleasanton, CA, USA). Free metal ion concentrations are evaluated using an ICP mass spectrometer X5 ThermoElemental (Winsford, UK). A Polarograph Model 433 system (Amel Instruments, Milan, Italy) is used to evaluate the uncomplexed Cd(II) and Cu(II) in the determination of PYR capacity and to compare the interactions of these ions on PYR with NAF and PCD. Poly-Prep Chromatography Columns  $0.8 \times 4 \text{ cm}$  (10 ml), from Bio-Rad Laboratories (Hercules, CA, USA) and a peristaltic pump Minipuls 3 (Gilson, Middleton, WI, USA) are used to evaluate the reproducibility of material under sequential steps of adsorption and release of Cd(II).

### Reagents and solutions

All the solutions are prepared using ultrapure water produced by Milli-Q system (Millipore, Bedford, MA, USA). Grade A glassware is used throughout this work.

The polymer is obtained using as reagent  $\beta$ -cyclodextrin by WeckerChemie (Germany). The  $\beta$ -cyclodextrin is dried at  $120^\circ\text{C}$  to constant weight before use. Pyromellitic anhydride, 1,8,4,5-naphthalic dianhydride and diphenyl carbonate are purchased from Aldrich (Germany) and used without further purification.

Sodium hydroxide from J.T. Baker (Deventor, Holland) is used for the pH-metric titration. Standardization of sodium hydroxide solutions is obtained using potassium hydrogenphthalate from Merck (Darmstadt, Germany). The electrode is calibrated using hydrochloric acid 37% p.a. from Acros Organic (New Jersey, USA). A 0.102 mol l<sup>-1</sup> copper(II) nitrate stock solution, used for pH-metric titrations, is standardized by complexometric titration with EDTA. For retention measurements, Cu(II) and Cd(II) are prepared by dilution of standard solution at 1000 mg l<sup>-1</sup> from Merck. Sodium chloride and nitric acid 65% (max. 5 µg l<sup>-1</sup> Hg) are from J.T. Baker. All other chemical compounds and solvents are from Merck.

### Synthesis

The PYR crosslinked polymer is obtained as previously discussed [1].

### pH-Metric measurements

Before measurement, the electrode couple is calibrated in  $-\log[H^+]$  units employing alkalimetric titrations of hydrochloric acid with standardized solution of sodium hydroxide, at 25.0°C and  $I = 1.0$  mol l<sup>-1</sup> (NaCl). The non-linear least squares computer program ESAB2M is used to refine all the parameters related to  $K$  (the formal potential) evaluation of the glass electrode system [13]. This program allows the refinement of the analytical concentration of reagents and of the electrode formal potential. The interaction of  $\beta$ -cyclodextrin polymer with Cu(II) is studied with a series of alkalimetric titrations on aqueous solutions containing the washed polymer (particle dimension <90 µm, mass of suspended polymer from 0.25 to 0.40 g,  $V = 50$  ml, 1.0 mol l<sup>-1</sup> NaCl, and 2–5 mmol l<sup>-1</sup> Cu(II)). The data have been processed according to the BSTAC software [14]. Each titration is repeated at least twice and all the alkalimetric titrations are carried out in a stream of purified nitrogen gently bubbled in the titration cell to avoid O<sub>2</sub> and CO<sub>2</sub> contamination.

### Analysis of pH-metric data

The pH-metric data obtained from titrations of polymer and polymer/metal systems have been processed with the BSTAC software [14]. This software has been extensively used to investigate complexation equilibria in homogeneous solution and employs an iterative and convergent numerical method based upon the linear combination of mass balance equations [1]. The functional groups of  $\beta$ -cyclodextrin polymer can be considered, for their acid-base and complexing properties,

as ligands in solution. Processing of pH-metric data provided the protonation constants of the functional groups [1] and they are here used to compute the related formation constants of complexes with Cu(II). The heterogeneous stability constants (included protonation constants) of the complexes are expressed by the general formula:  $\beta_{pqr} = [M_pL_qH_r]/[M]^p[L]^q[H]^r$ , being the formation of a complex species expressed by the equilibrium:  $pM + qL + rH \Delta MpLqH_r$ . Several chemical models are taken into account during software processing. To ensure coherence between the weighed masses of the polymer and the concentration of its ligand sites we adopted a constraint principle. In the processing of potentiometric data for the  $\beta$ -cyclodextrin polymer/proton/metal systems, the hydrolysis and the chloride complexes of the metal ion [15] are also taken into account.

### Capacity of PYR against Cu(II) or Cd(II)

All the solutions are prepared at pH 3, with metal ion concentrations ranging between 0.163 and 3.170 mmol g<sup>-1</sup> of polymer for Cu(II), and between 0.088 and 1.771 mmol g<sup>-1</sup> of polymer for Cd(II). The solutions are equilibrated for 48 h with 0.05 g of PYR and, after filtration, the concentration of the free metal is measured by voltammetric analysis. The analysis is performed at differential pulse potential scanning and using a 0.1% HNO<sub>3</sub> solution as electrolyte. The quantifications are obtained using at least three standard additions of an opportunely diluted standard solution of each metal ion.

### Retention and recovery of Cd(II) sorbed on PYR

A portion of 500 mg of PYR (particle dimensions <90 µm) is slurry packed in a Bio-Rad column (10 ml). The column is washed with four aliquots of 10 ml each of 0.1 M HNO<sub>3</sub>, conditioned with 10 ml 0.01 M HNO<sub>3</sub> and finally loaded with a 50 ml of solution 10 mg l<sup>-1</sup> of Cd(II) in 0.01 M HNO<sub>3</sub>. The amount of Cd(II) retained is eluted by 10 ml of 0.1 M HNO<sub>3</sub>. To ensure a complete recovery, another step of elution with 10 ml 0.1 M HNO<sub>3</sub> is performed. The whole procedure is repeated for three different columns and for one blank column (without Cd(II)). The eluates are collected and analysed by ICP-MS with the modality previously described.

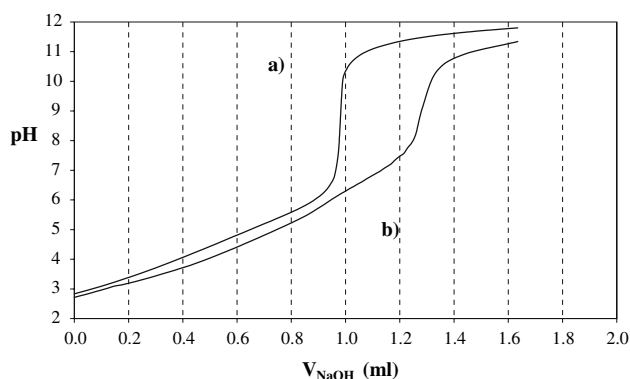
### Synthesis of new derivatives of the polymer with different type of spacers. Study of metal retention

In order to evaluate the effect of different kinds of ionic groups on metal ion complexation, other mate-

rials have been synthesized. The ionic moiety can be introduced opportunely selecting the spacers. Therefore a new polymer of cyclodextrin containing  $\gamma$ -cyclodextrins groups linked together with naphthalene tetracarboxylate biacid groups, has been synthesized (NAF). It should be remarked that it is not possible to synthesize a polymer with  $\beta$ -cyclodextrin containing the same spacer since reaction does not take place. Polycarbonate  $\beta$ -cyclodextrin (PCD), previously synthesized has been chosen for other comparisons. PCD does not have an acidic group as linker and hence it does not have ionic exchange properties. It is so possible to compare the interaction of these three different types of polymers (PCD, PYR, and NAF) with metal ions. In a first approach, Cu(II) and Cd(II) are chosen. Solutions at pH 4, containing  $10 \text{ mg l}^{-1}$  of each metal ion are equilibrated with each polymer for 48 h; the procedure is performed in triplicate. The concentrations of uncomplexed metal ions are obtained after filtration and voltammetric analysis, according to the procedure previously described.

## Results and discussion

The comparison between the alkalimetric titration curves of  $\beta$ -cyclodextrin polymer with and without Cu(II) shows a remarkable acidifying effect due to the metal cation (see Fig. 1). The trend of the experimental data obtained with Cu(II) can be explained with the speciation model reported in Table 1, where  $L'$  and  $L''$  are a diprotic and triprotic ligand sites, respectively (see [1]). This speciation model assumes the presence of species with stoichiometry  $\text{CuHL}''$ ,  $\text{CuL}''$  and  $\text{CuL}'_2$ , where the metal replaces



**Fig. 1** Alkalimetric titration curves of PYR with and without Cu(II). Curve (a): titration curves of 0.250 g PYR; Curve (b): titration curves of 0.250 g PYR and  $4.45 \times 10^{-3} \text{ mol l}^{-1}$  Cu(II). Titrant:  $1.187 \text{ mol l}^{-1}$  NaOH,  $T = 25^\circ\text{C}$ ,  $I = 1.0 \text{ mol l}^{-1}$ , ionic medium NaCl

subsequently the acidic protons of the polymer, and a species with stoichiometry  $\text{CuL}'\text{H}_{-2}$  (the symbol  $\text{H}_{-2}$  indicates that the polymer releases two protons more than those released during titration of the polymer without the addition of the metal cation). Coherently with the polymer structure, the stoichiometry found ( $\text{CuL}'\text{H}_{-2}$ ) and the co-ordinating ability of Cu(II) ion, it is reasonable to suppose that the metal ion is bonded to alcoholate groups ( $\text{R-O}^-$ ) of  $\beta$ -cyclodextrin fraction. Intermediate complexes such as  $\text{CuLH}_{-1}$  are rejected by the refinement process as dimeric species. The model excludes co-operation between  $L'$  and  $L''$  sites with respect to the co-ordinating ability (species such as  $\text{CuL}'\text{L}''$  are rejected by the calculation program). Figure 2 shows the species distribution, as a function of pH, of a solution (50 ml) containing  $4.45 \times 10^{-3} \text{ mol l}^{-1}$  of Cu(II) and 0.250 g of polymer. We can observe that 64% Cu(II) is bound to the  $\beta$ -cyclodextrin polymer as the maximum value at pH 5.2. As result of this modelling information it is interesting to compare the data obtained with the total amount of Cu(II) retained on PYR at different pH values.

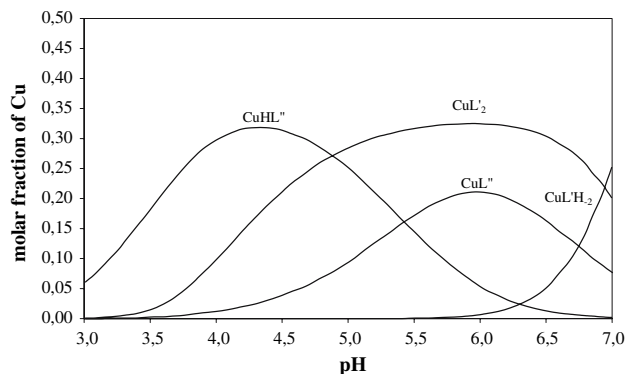
Using a Debye–Hückel type equation [16] it is possible to calculate  $\log\beta$  values at an ionic strength value different from that obtained during the mea-

**Table 1** Formation constants of PYR/Cu(II) complexes

| Equilibrium <sup>(a)</sup>  | $\log\beta$ <sup>(b)</sup> | std. dev. ( $\pm 3s$ ) |
|---|----------------------------|------------------------|
| $\text{Cu} + \text{H} + \text{L}'' \Delta \text{CuHL}''$            | 7.90                       | 0.18                   |
| $\text{Cu} + \text{L}'' \Delta \text{CuL}''$                        | 2.49                       | 0.17                   |
| $\text{Cu} + 2\text{L}' \Delta \text{CuL}'_2$                       | 8.38                       | 0.15                   |
| $\text{Cu} + \text{L}' \Delta \text{CuL}'\text{H}_{-2} + 2\text{H}$ | -9.38                      | 0.12                   |

(a) The charges of the species are omitted for clarity

(b) The  $\log\beta$  values are referred to  $25^\circ\text{C}$  and to ionic medium  $1.0 \text{ mol l}^{-1}$  NaCl



**Fig. 2** Molar fraction of Cu(II) vs. pH. Conditions: 50 ml solution containing  $4.45 \times 10^{-3} \text{ mol l}^{-1}$  Cu(II) and 0.250 g PYR.  $T = 25^\circ\text{C}$ ,  $I = 1.0 \text{ mol l}^{-1}$ , ionic medium NaCl

surements ( $I = 1$  M). Retention experiments are performed at very low ionic strength, around  $I = 0.01$  M. The constants at  $I = 0.01$  M allow us to calculate the species distribution and to obtain the Cu(II) retained by PYR from the potentiometric data and to compare it with the total retained Cu(II) at different pH values obtained by batch experiments ( $I = 0.01$  M). Table 2 shows the results obtained with the two methodologies; at pH 3 the complexes involving proton dissociation do not explain the whole amount of Cu(II) adsorbed. For pH 4 and 5 the amounts of Cu(II) retained on PYR obtained by the two methodologies are comparable, since the values are included in the error intervals (3s). At these pH values the interaction between the dissociated pyromellitate becomes prevalent over the other types of interaction of PYR with Cu(II) ions. Very probably, at pH 3, some Cu(II) complexes are formed without displacement of proton.

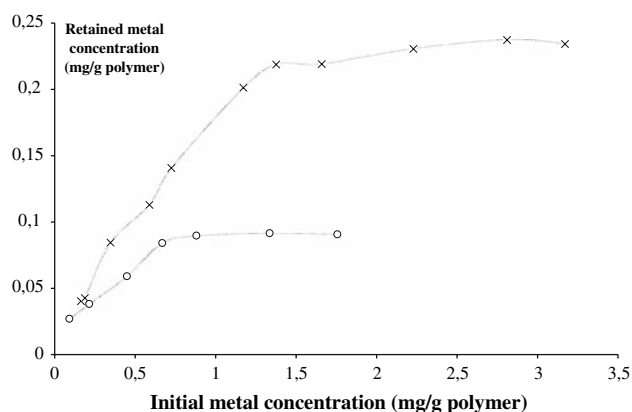
Cu(II) and Cd(II) are chosen as target probes for their different interaction with the organic ligand. To investigate more deeply the PYR-metal ions interaction, the saturation curves of the PYR for Cu(II) or Cd(II) are also studied. The results obtained (Fig. 3) show that in the saturation profile, the concentration retained is  $201.1 \mu\text{mol g}^{-1}$  of polymer for Cd(II), and  $766.0 \mu\text{mol g}^{-1}$  of polymer for Cu(II).

Due to the good results obtained for Cd(II) and due to the fact that the EPA [17] has classified it as a Group B1, probable human carcinogen, further experiments are performed on this metal with the aim of developing an application of PYR in environmental decontamination from cadmium. For this purpose it is important to define the repeatability of the material performance in consecutive steps and in extreme conditions (e.g. low pH by nitric acid required to recover Cd(II) from PYR). Figure 4 shows two IR spectra for PYR: (A) refers to PYR conditioned in nitric acid solution (pH 1) for two months and (B) refers to PYR conditioned in ultra pure water for the same period. As seen, there is not evidence of oxidized functional groups formation in the solid phase after such long contact with nitric acid, suggesting the stability of the material to this

**Table 2** Comparison between the amount of Cu(II) retained (%) at different pH by batch experiments and by exporting pH-metric modelling

| pH | % Cu(II) retained (RSD) |                                    |
|----|-------------------------|------------------------------------|
|    | Batch                   | pH-metric modelling <sup>(a)</sup> |
| 3  | 83.4 (5.51)             | 38.0                               |
| 4  | 85.9 (2.05)             | 91.5                               |
| 5  | 91.8 (1.96)             | 99.6                               |

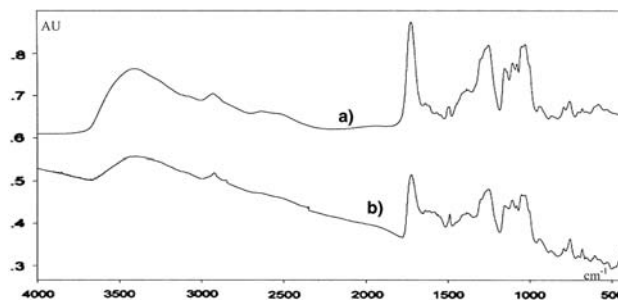
<sup>(a)</sup> calculated value from the chemical model (Table 1)



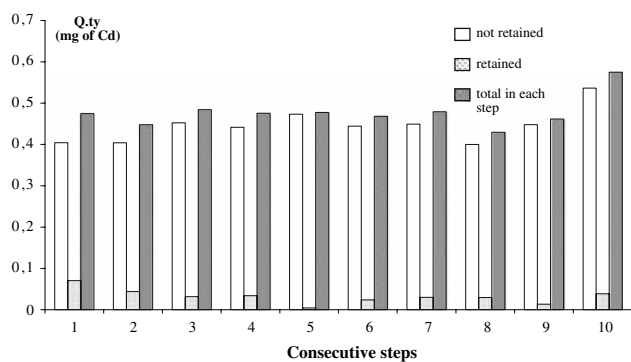
**Fig. 3** Saturation curves of Cd(II)-PYR (O) and Cu(II)-PYR (X) complexes

treatment. Based on the different retention of Cd(II) exhibited by PYR at varying pH, it is possible to move to a dynamic system, where Cd(II) is retained and then released, changing only pH conditions. Cd(II) ( $10 \text{ mg l}^{-1}$ ) is retained loading 50 ml of a solution at pH 2 (nitric acid) on PYR and subsequently released in two steps by aliquots of 10 ml of 0.1 M HNO<sub>3</sub> each. Ten consecutive steps of retention and release are evaluated to determine the repeatability of PYR on Cd(II) retention. The recovery of Cd(II) in the second step of elution is always under the detection limit ( $100 \text{ ng l}^{-1}$ ), supporting that Cd(II) is quantitatively recovered in the first step. The amount of Cd(II) retained and recovered for all the consecutive steps is described in Fig. 5, with RSD = 1.7% ( $n = 30$ ). According to the results obtained, thanks to its repeatability and resistance in oxidizing conditions, PYR can be reused in sequential steps of retention and recovery.

The retention of Cd(II) and Cu(II) on other types of cyclodextrin polymers is then studied. NAF and PCD present a different structure and, in particular, PCD does not have an anion exchange site.



**Fig. 4** IR spectra of PYR conditioned for two months in: (a) 0.1 M HNO<sub>3</sub> and (b) ultrapure water

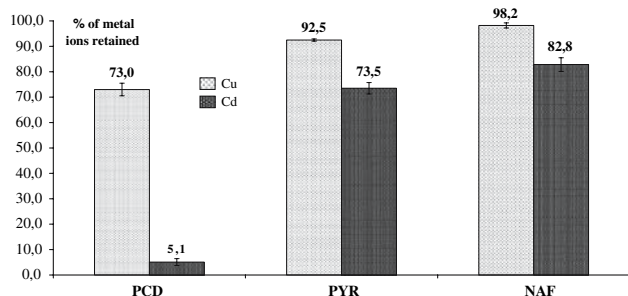


**Fig. 5** Column packed with PYR: average ( $n = 3$ ) quantity of Cd(II) retained and recovered in flow conditions. For details, see text

Solutions containing  $10 \text{ mg l}^{-1}$  of each metal (pH 4) are equilibrated with the materials for 48 h, according to the procedure previously described. After filtration, the solutions are analyzed by voltammetry. The results collected in Fig. 6 show that the best retention is achieved with NAF. PCD does not efficaciously retain Cd(II). Since Cd(II) is retained by both PYR and NAF, it can be supposed that interaction of Cd(II) with the polymers is mainly related to the presence of the ionic group (carboxylate). The retained amount of Cu(II) in the polymers does not show big differences, suggesting that interaction does not only depend upon the presence of acidic groups. These results agree with deduction from pH-metric titrations, where it is found that the cyclodextrin unit is able to complex Cu(II), complexation being not only directly dependent on the presence of carboxylate group (Table 2). That is, the polymer is able to bind also at acidic pH values, whereas the native cyclodextrin that is able to complex Cu(II) only at  $\text{pH} > 12$  [4, 6].

## Conclusion

The new polymer synthesized (PYR) presents a cross-linker which confers cation exchange and coordinating



**Fig. 6** Amount of Cd(II) and Cu(II) retained on PCD, PYR and NAF after equilibration with  $10 \text{ mg l}^{-1}$  of each metal ion (pH 4)

properties, enhancing the complexing activity of the native cyclodextrin towards metal ions. Cu(II) retention on the polymer has been characterised at different pH values and by pH-metric titrations. Through the modelling of pH-metric data, the presence of four different complexes has been proposed, one of these involves dissociated alcoholic groups present on the cyclodextrin structure. This complex is present in the range of pH 5.5–7. The retention of Cd(II) on PYR is exploited in flow system; the PYR packed column shows the possibility of retaining and releasing Cd(II) by simply changing pH conditions of the eluent. Furthermore, the polymer maintains its properties unchanged after ten consecutive steps of adsorption and desorption. These data support the possibility of using PYR in environmental applications. The comparison of Cd(II) complexation by PYR, NAF and PCD shows that the anion exchange moiety is crucial for retention of metal ions that do not interact with the native cyclodextrin.

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## References

- Berto, S., Bruzzoniti, M.C., Cavalli, R., Perrachon, D., Prenesti, E., Sarzanini, C., Trotta, F., Tumiatti, W.: Synthesis of new ionic  $\beta$ -cyclodextrin polymers and characterization of their heavy metals retention. *J. Incl. Phenom. Macrocycl. Chem.* (2007). DOI: 10.1007/s10847-006-9273-0
- Martin Del Valle, E.M.: Cyclodextrins and their use: a review. *Process Biochem.* **39**, 1033–1046 (2004)
- Duchêne, D., Wouessidjewe, D., Ponchel, G.: Cyclodextrins and carrier systems. *J. Controlled Release* **62**, 263–268 (1999)
- Bender, M.L., Komiyama, M.: *Cyclodextrin Chemistry*. Springer-Verlag, Berlin Heidelberg New York, Chapter II, pp. 2–8 (1978)
- Måsson, M., Loftsson, T., Jónsdóttir, S., Fridriksdóttir, H., Petersen, D.S.: Stabilisation of ionic drugs through complexation with non-ionic and ionic cyclodextrins. *Int. J. Pharm.* **164**, 45–55 (1998)
- Matsui Y., Kurita T., Yagi M., Okayama T., Mochida K., Date Y.: The formation and structure of Copper(II) complexes with cyclodextrins in an alkaline solution. *Bull. Chem. Soc. Jpn.* **48** (7), 2187–2191 (1975)
- Stoddart, J.F., Zarzycki, R.: Cyclodextrins as second-sphere ligands for transition metal complexes. *Recl. Trav. Chim. Pays-Bas* **107**, 515–528 (1988)
- Heck, R., Marsura, A.: A new symmetrically modified  $\alpha$ -cyclodextrin tripod: selective metal complexation and fluorescence properties. *Tetrahedron. Lett.* **45**, 281–284 (2004)
- Campagna, T., Grasso, G., Rizzarelli, E., Vecchio, G.: L- and D- Cysteine derivatives of  $\beta$ -cyclodextrin: different molecular recognition properties of their copper(II) complexes for amino acids. *Inorg. Chim. Acta* **275–276**, 395–400 (1988)
- Rizzarelli, E., Vecchio, G.: Metal complexes of functionalized cyclodextrins as enzyme models and chiral receptors. *Coord. Chem. Rev.* **188**, 343–364 (1999)

11. Burgos, A.E., Belchior, J.C., Sinisterra, R.D.: Controlled release of rhodium (II) carboxylates and their association complexes with cyclodextrins from hydroxyapatite matrix. *Biomaterials* **23**, 2519–2526 (2002)
12. Reetz, M.T., Kostas, I.D., Waldvogel, S.R.: Synthesis of gold(I) complexes with a (thio)phosphine-modified  $\beta$ -cyclodextrin. *Inorg. Chem. Comm.* **5**, 252–254 (2002)
13. De Stefano, C., Princi, P., Rigano, C., Sammartano, S.: Computer analysis of equilibrium data in solution. ESAB2M: an improved version of the ESAB program. *Ann. Chim. (Rome)* **77**, 643–675 (1987)
14. De Stefano, C., Mineo, P., Rigano, C., Sammartano, S.: Ionic strength dependence of formation constants. XVII. The calculation of equilibrium concentrations and formation constants. *Ann. Chim. (Rome)* **83**, 243–277 (1993)
15. Smith, R.M., Martell, A.E., Motekaitis, R.J.: NIST Critical Selected Stability Constant of Metal Complexes Databases, version 6.0 (2002)
16. Casale, A., Daniele, P.G., De Robertis, A., Sammartano, S.: Ionic strength dependence of formation constants. Part XI. An analysis of literature data on carboxylate ligand complexes. *Ann. Chim. (Rome)* **78**, 249–260 (1988)
17. <http://www.epa.gov/ttn/atw/hlthef/cadmium.html>. EPA, Cadmium compounds, Hazard Summary-(April 1992, Revised in January 2000)