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SHORT COMMUNICATION

Complexation of herbicide bentazon with native and modified β-cyclodextrin

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Abstract For first time the complexation of bentazon (Btz) with native β-cyclodextrin (β-CD) and modified sulfobutylether-β-CD (SBE-CD) was studied by differential pulse voltammetry. In addition, a spectrophotometry UV–Visible study was carried out. In presence of CDs there is a decrease of the anodic peak current with the increase of the amount of CD. This decrease is due to the lower diffusion coefficient of Btz/CD complex compared with the free guest. Using the variation in current, association constants of 118 ± 20 and 317 ± 25 M^{-1} for β-CD and SBE-CD were determined. The solubility of bentazon was 8 fold higher with SBE-CD as compared with bentazon-free. Phase solubility diagrams performed using UV–Vis experiments permit to obtain the same association constants which were compared with the values obtained by electrochemical techniques.

Keywords Cyclodextrin · Inclusion complexes · Bentazon · Herbicide

Introduction

Cyclodextrins are water-soluble hosts that contain a hydrophobic cavity which is able to accommodate a variety of organic molecules. Inclusion in these hosts results in many modifications to the properties of the guest compounds such as fixation of volatile materials, masking of odorous compounds, stabilisation against hydrolysis, protection against oxidation and photolysis and the modification of their physical and biological properties [1–7].

However, the application of these hosts in pesticide formulations is very modest. In pesticide formulations, practically the same effects can be attained by CDs as in drug formulations. At the present time, large improvements in cyclodextrin production and purification have been achieved and the price is lower than before. In this way, the application of cyclodextrins on pesticide-formulating industry could be a real possibility [8].

Bentazon is a post-emergence herbicide used for selective control of broadleaf weeds and sedges (a weed) in beans, rice, corn, peanuts, and mint, among others. This herbicide presents a moderate solubility in water (0.5 g/L). To the best of our knowledge, there is little information available about the inclusion complexes of bentazon with CDs.

The aim of this work was to study the formation of inclusion complexes of bentazon by using electrochemical techniques. These techniques are highly sensitive, fast and easy to use, and they have shown be useful in determination of association constants [9, 10]. In addition, for comparative purposes the association constants have been determined by spectrophotometry methods.

Experimental

Chemicals

β-cyclodextrin (β-CD) was obtained from Calbiochem and was used without prior purification. Sulfobutylether-β-CD (SBE-CD) [T.D.S. (total degree of substitution) = 6-7;

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Captisol®] was purchased from CyDex, Inc. Bentazon was supplied by SIGMA. All the other reagents employed were analytical grade. All solutions were prepared with ultrapure water (18.2 MΩ cm) from a Millipore Milli-Q system.

Apparatus

Spectrophotometric measurements were carried out with an ATI Unicam Model UV3, UV–Vis spectrophotometer, using 1 cm quartz cell.

Differential pulse voltammetry (DPV) experiments were performed with a totally automatized workstation BAS CV-50 W (Bioanalytical Systems). A 10 mL BAS measuring cell with a glassy carbon electrode (GCE) (3 mm dia., CHI 104, CH Instruments Inc.) as working electrode were used. A platinum wire and Ag/AgCl (Bioanalytical System) were used as counter and reference electrodes, respectively. Thorough cleaning of the working electrode was carried out before each measurement. Glassy carbon electrode was polished with 0.3 and 0.05 μm alumina slurries (Buehler) and was profusely rinsed with water.

Selected electrochemical parameters for DPV were: potential scan rate 20 mV s^{-1}, pulse amplitude 50 mV, pulse width 50 ms.

Methods

Solubility diagrams were performed in triplicate according to the method reported by Higuchi and Connors [11]. Briefly, excess amounts of solid bentazon (12.5 mg) were added to 5 mL of aqueous solution containing various concentrations of CD (0 to 10 mM for β-CD, 0 to 40 mM for SBE-CD). Samples were shaken for 24 h at 20°C. The samples were kept in store for 4 h at 4 °C, and then filtered through a 0.45 μm membrane filter (Advantec MFS, Inc.). Bentazon concentration in the filtrate was spectrophotometrically determined at 344 nm. The association constant, K_a, was calculated from the phase solubility diagrams according to the equation:

$$K_a = \frac{\text{slope}}{S_0(1 - \text{slope})} \quad (1)$$

where S_0 is the solubility of bentazon in the absence of CD and the slope means the corresponding slope of the phase solubility diagrams.

Differential pulse voltammetry

Polarographic experiments were carried out by keeping constant concentration 5.0×10^{-4} M of bentazon in 0.1 M Britton Robinson (pH 6.0) while varying concentrations of CD. The solutions were shaked thoroughly for 20 min and allowed to equilibrate at room temperature. The current titration equation has been described as follows [12–15]:

$$\frac{1}{[\text{CD}]} = K_a \frac{(1 - A)}{1 - I/I_0} - K_a \quad (2)$$

where K_a is the complex association constant, I_0 and I are the peak currents without and with CD, respectively, [CD] is molar concentration of CD and A is a proportional constant. The condition for using this equation is that a 1:1 association complex is formed and CD concentrations are much larger than the total concentration of the guest.

All the voltammetric experiments were performed after flushing the cell with N_2 for 10 min before each run. Temperature was kept constant at 20 ± 0.1 °C in all experiments.

Results and discussion

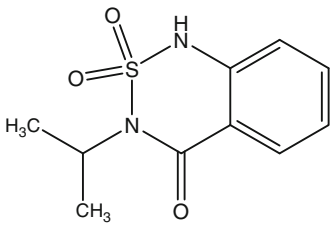
Spectrophotometric study

The maximun concentration of bentazon in aqueous solution determined in absence of CDs at 20 °C, was of 2.1 ± 0.1 mM. A low increase in bentazon solubility was observed with increasing β-CD concentration and a solubility limit was determined at 5 mM β-CD. Higher β-CD concentrations do not produced more solubility of bentazon. On the other hand, solubility increase was highest when SBE-CD was used (Fig. 2) being 8 fold higher than that of bentazon with 30 mM SBE-CD. The results obtained with both CDs are summarized in Table 1; Fig. 1.

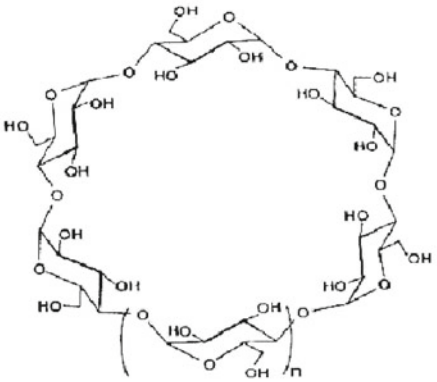
The phase solubility diagram show a linear increment of bentazon concentration in presence of SBE-CD with a slope lower than 1 (Fig. 3), which may be ascribed to the formation of complexes in solution with 1:1 stoichiometry. In spite of solubility limit found with β-CD, a linear relationship between bentazon and β-CD concentrations was also observed in the range of 0–5 mM β-CD. The association constants were calculated from Eq. 1 and shown in Table 2. The association constant for Btz/SBE-CD complex was 430 M^{-1} which was nearly three fold higher than that obtained for Btz/β-CD complex, indicating that the interaction of SBE-CD with bentazon is stronger than β-CD. This result reflects the interaction of sulphonate groups with bentazon at this pH value. According to Zia et al. [16, 17], neutral molecules displayed a stronger interaction with SBCD as compared with other CD.

Table 1 Solubility of bentazon in absence and presence of β-CD (5 mM) and SBE-CD (30 mM)

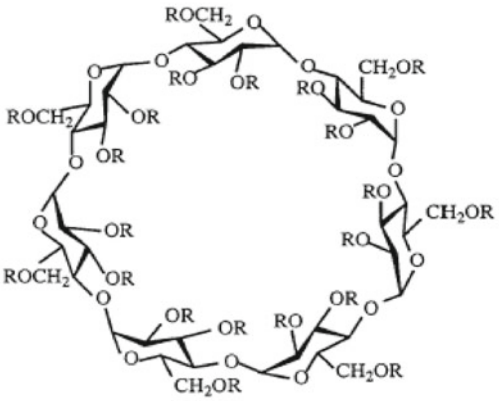
Bentazon (g L^{-1})	Btz/β-CD (g L^{-1})	Btz/SBE-CD (g L^{-1})
0.50	0.96	4.1



bentazon



β-cyclodextrin (n=7)



Sulphobutylether-β-cyclodextrin (R= $(CH_2)_4$ SO_3Na)

Fig. 1 Molecular structures of bentazon, *β*-CD and SBE-CD

Differential pulse voltammetry study

The electrochemical oxidation of bentazon at glassy carbon electrode in aqueous solution has been previously studied [18]. According to this study, bentazon is susceptible to be oxidized on the glassy carbon electrode. As can be seen in Fig. 4, bentazon shows a well resolved oxidation peak, with a peak potential (E_p) at 0.93 V (versus Ag/AgCl), when was submitted to a differential pulse voltammetry experiment in buffer phosphate at pH 6.0 (line a, Fig. 4).

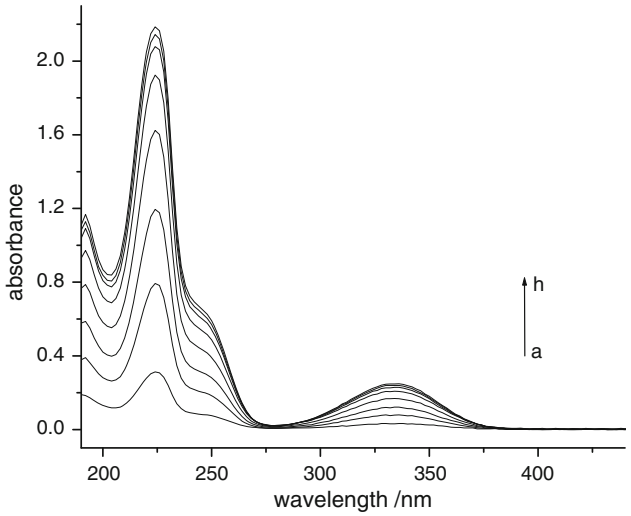


Fig. 2 Absorption spectra of bentazon in absence and presence of SBE-CD. Curves a–h: 0, 5, 10, 15, 20, 25, 30, 50 mM SBE-CD

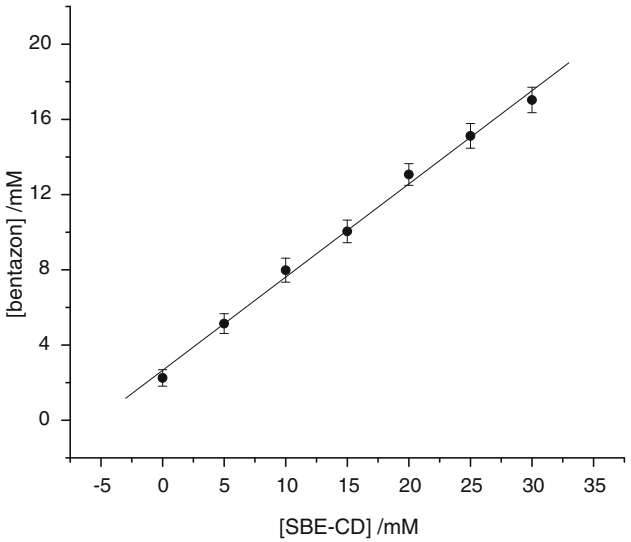


Fig. 3 Phase solubility diagrams for bentazon with increasing concentrations of SBE-CD

Table 2 Association constant of the inclusion complexes (K_a) of bentazon with CD determined by differential pulse voltammetry and spectrophotommetry UV–Vis

Complex	K_a/M^{-1}	
	Spectrophometry	DPV
Btz/*β*-CD	140 ± 7	118 ± 20
Btz/SBE-CD	430 ± 18	317 ± 25

Standard deviations are calculated on triplicate trials

The electrochemical behavior of bentazon in presence of CD exhibit similar characteristics to those observed for free bentazon, i.e. only one oxidation peak around 0.95 V, with a clear decrease in the current intensity with increasing of

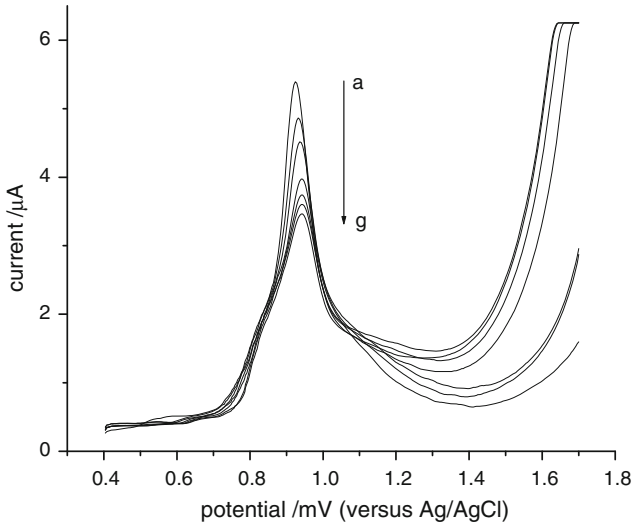


Fig. 4 Differential pulse voltammetry curves for 5.0×10^{-4} M bentazon in buffer phosphate pH 6.0 in the absence and the presence of different β-CD concentrations. Curves a–g: 0, 2, 4, 6, 8, 10, 14 mM β-CD

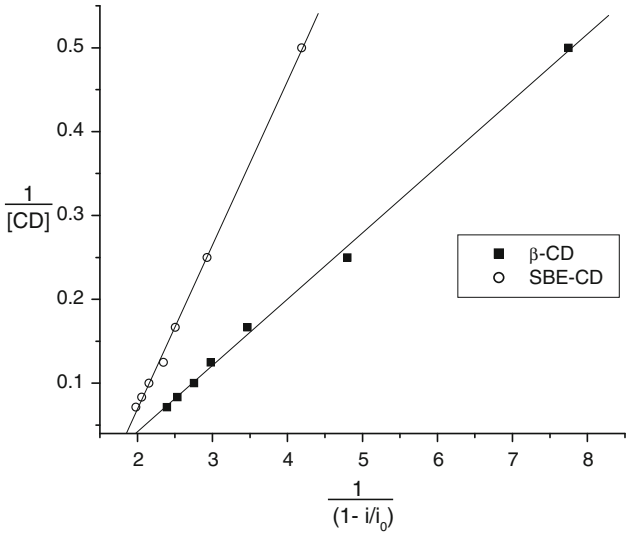


Fig. 6 Plot of 1/[CD] versus $1/(1 - I/I_0)$ for bentazon in buffer phosphate pH 6.0

β-CD concentration. Similar behavior is observed upon addition of SBE-CD. The oxidation peak potentials (E_p) are lightly shifted in a positive direction up to 20 mV. The decrease of peak current as a function of the concentration of each CD is shown in Fig. 5. The lowest values of current are obtained when SBE-CD is added to the solution. The change in the peak current can be ascribed to a lower value of the diffusion current due to a decrease of the apparent diffusion coefficient of bentazon included into the CD cavity, compared with the apparent diffusion coefficient of bentazon-free form. Electrochemical measurements have confirmed the difference between apparent diffusion coefficients in some other systems, as estradiol complexed with CDs [19].

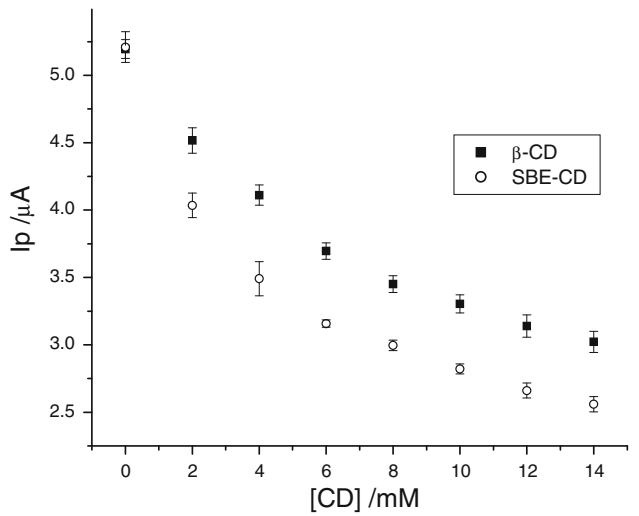


Fig. 5 Current dependence on the concentration of CD for bentazon in buffer phosphate pH 6.0. Current values obtained from DPV measurements

Using the equation described for current titration (Eq. 2), the association constants (K_a) for Btz/βCD and Btz/SBE-CD complexes were obtained. Linear relationships were obtained in 1/CD vs $1/(1 - I/I_0)$ plots, confirming the existence of a stoichiometry 1:1 for both complexes (Fig 6). The association constants values (K_a) obtained by DPV are shown in Table 2. Although K_a values obtained by DPV are slightly lower than those obtained by UV–Vis, can be seen that the association constant obtained for the Btz/SBE-CD complex is almost three fold higher than that of Btz/β-CD complex in both cases. Electrochemical technique was quite fast and gave a very good approach to determine the association constants of inclusion complexes.

Conclusions

For first time the study of complexation of bentazon with CDs performed by electrochemical techniques is reported. The peak current of oxidation of bentazon decreased when CD concentration was increased. This change was applied to quantify the interaction between CDs and bentazon obtaining the association constant of both inclusion complexes. Therefore, electrochemical techniques, which have the advantage that are fast, give a good estimation of the association constant of inclusion complexes.

Besides, an increase in the solubility of bentazon due to its complexation with native β-CD and modified β-cyclodextrin is reported. A slight increases was observed with

β-CD, whereas the Btz solubility was 8 fold higher in presence of SBE-CD.

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