CAPSULES
notes and applications from Bioanalytical Systems, Inc.
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Determination of Carboplatin in Serum

Purpose

The direct electrochemical detection of the anticancer platinum(II) complex Carboplatin ((cis-diamine-1,1-cyclobutanedicaroxylate)platinum(II)) is difficult, due to its high oxidation potential. Previous attempts at indirect electrochemical detection have involved its conversion to Cisplatin (cis-dichloroamineplatinum(II)) (1), which has a lower oxidation potential. In this study, another indirect electrochemical method is discussed, based on interaction of Carboplatin with DNA (which is also the basis for its pharmacological activity).

Reference

Electrochemical Determination of Carboplatin in Serum Using a DNA-Modified Glassy Carbon Electrode, A.M. Oliveira Brett, S.H.P. Serrano, T.A. Macedo, D. Raimundo, M.H. Marques and M.A. La-Scalea, Electroanalysis 8 (1996) 992-995.

Method

Differential pulse voltammetry is one of the electrochemical techniques preferred for concentration measurements, due to its relatively low detection limits (which are due to good discrimination against the charging current). In this study, absolute concentrations are obtained using the method of standard additions.

Results

The differential pulse voltammogram of single stranded DNA (ss DNA) at a DNA-modified glassy carbon electrode shows two peaks, due to the oxidation of guanine and adenine residues ***(F1a)***. The addition of Carboplatin to the solution of ss DNA causes a significant decrease in the peak current for the oxidation of the adenine residues, whereas there is only a slight change in the peak current for the oxidation of the guanine residues ***(F1b-d)***. The decrease in current was attributed to the interaction of the adenine residues with the Carboplatin. Similar results were obtained for samples containing serum from patients undergoing Carboplatin therapy ***(F2)***,

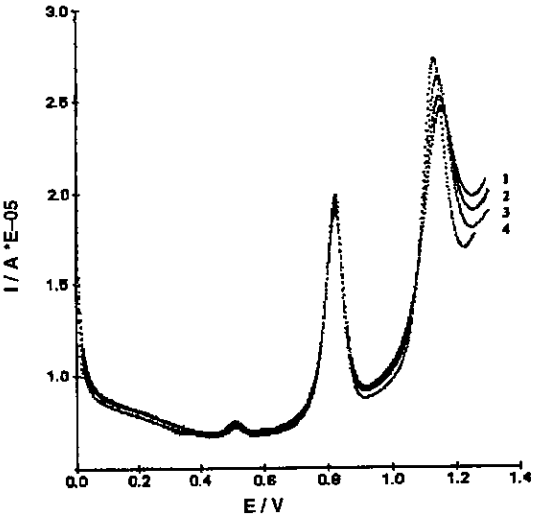

Figure 1. *Differential pulse voltammograms of a solution of ss DNA (78 μg/mL) and 0 (a), 84.4 μM (b), 161 μM (c), and 236 μM (d) Carboplatin in acetate buffer (pH 4.6) using a DNA-modified electrode. Pulse amplitude = 50 mV, pulse width = 50 ms, and scan rate = 5 mV/s. All potentials measured with reference to the SCE.*
Figure adapted from primary reference.

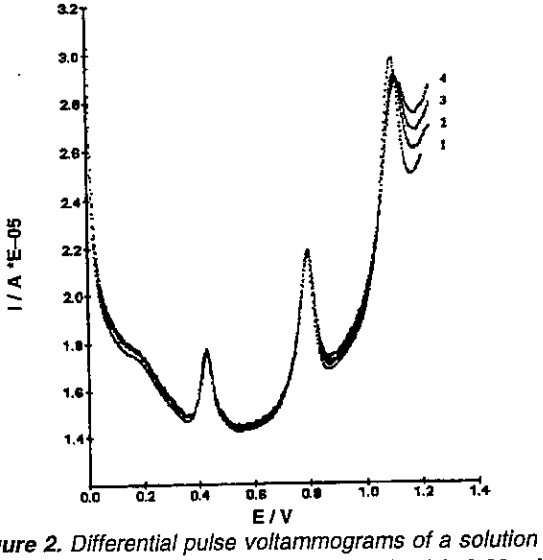

Figure 2. *Differential pulse voltammograms of a solution of ss DNA (78 μg/mL), 400 μL of serum, and 0 (a), 0.39 mM (b), 1.1 mM (c), and 1.5 mM (d) Carboplatin in acetate buffer (pH 4.6) using a DNA-modified electrode. Pulse amplitude = 50 mV, pulse width = 50 ms, and scan rate = 5 mV/s. All potentials measured with reference to the SCE.*
Figure adapted from primary reference.

and this method was used to study the in vivo pharmacokinetics of this drug ***(F3)***.

The proposed mechanism for the above method (i.e., the interaction of adenine residues with the ss DNA) is in apparent contradiction to the mechanism proposed on the basis of previous NMR studies, which suggested a preferential interaction between the guanine residues and the ss DNA (2). This difference was further investigated by examining the interaction between Carboplatin and the nucleotides adenosine 5'-monophosphate and guanosine 5'-monophosphate (the interaction of each nucleotide was investigated separately). It was found that there was a preferable interaction with adenosine 5'-monophosphate at micromolar concentrations of Carboplatin, giving rise to a linear current response over the concentration range of 5.7 µM to 40 µM. However, this interaction became saturated at about 70 µM. In contrast, the interaction between guanosine 5'-monophosphate and Carboplatin was relatively small at micromolar concentrations, but it did not saturate at higher concentrations ***(F4)***. Since the NMR studies were conducted using millimolar concentrations of Carboplatin, it would be therefore be expected that these investigations should show a preferential interaction with the guanine residues. The linear relationship between peak current for the oxidation of adenosine 5'-monophosphate and Carboplatin at low Carboplatin concentrations indicates that this oxidation peak could also be used for the determination of Carboplatin in serum samples.

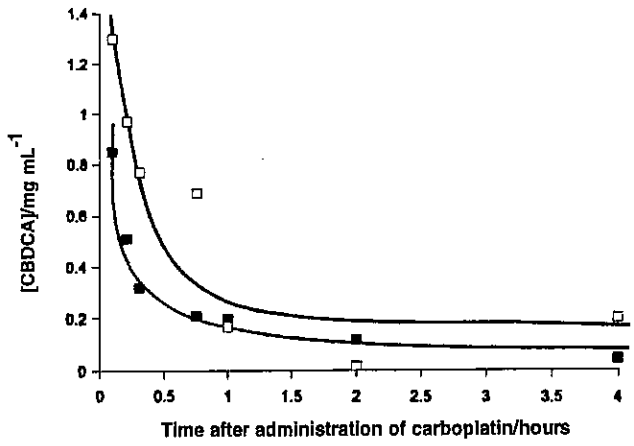

Figure 3. *Pharmacokinetic curves recorded using a DNA-modified electrode in a solution of ss DNA and serum from two patients undergoing Carboplatin therapy. Figure adapted from primary reference.*

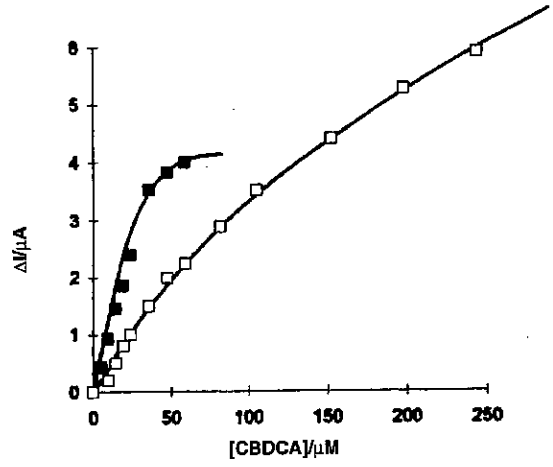

Figure 4. *Calibration plots for the decrease in the adenosine (■) or guanosine (□) peak currents in the presence of Carboplatin. Figure adapted from primary reference.*

References

1. *I.S. Krull, X.-D. Ding, S. Bravermen, C. Selavka, F. Hochberg and L.A. Sternston, J. Chromatogr. Sci. 21 (1983) 166.*
2. *S.E. Sherman and S.J. Lippard, Chem. Rev. 87 (1987) 1153.*

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