CAPSULES
notes and applications from Bioanalytical Systems, Inc.
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Detection of Dacarbazine and Its Major Metabolite Using Differential Pulse Voltammetry

Purpose

In general, the redox potentials of electroactive pharmaceuticals and their metabolites are similar. Therefore, their simultaneous detection requires separation (e.g., by HPLC) followed by electrochemical detection. However, the redox potentials of Dacarbazine and its major metabolite are sufficiently resolved that both can be accurately determined from the same sample using differential pulse voltammetry.

Reference

Electrochemical Oxidation of Dacarbazine and Its Major Metabolite (AIC) on Carbon Electrodes, J.R.B. Rodriguez, A.C. Garcia, A.J.M. Ordieres and P.T. Blanco, Electroanalysis 1 (1989) 529-534.

Method

Differential pulse voltammetry is one of the electrochemical techniques preferred for concentration measurements, due to its relatively low detection limit (which is due to good discrimination against the charging current). In this particular study, the pulse amplitude used had to be optimized in order to obtain a sensitive current response while maintaining good resolution between the two peaks.

Results

Dacarbazine [5-(3,3-dimethyl-1-triazenyl)imidazole-4-carboxamide] (DTIC) ***(F1)*** is used as an anti-tumor agent. Its major metabolite is 5-aminoimidazole-4-carboxamide (AIC) ***(F2)***. Cyclic voltammograms of both DTIC and AIC using carbon paste electrodes show an irreversible oxidation ***(F3)***, which was shown by controlled potential electrolysis to involve the transfer of two electrons. The best sensitivity was found under acidic conditions, and hence solutions of 0.1 M perchloric acid were used for the subsequent analyses.

Due to the difference in the redox potentials of DTIC and AIC, the two redox processes could be resolved when using differential pulse voltammetry ***(F4)***. Although increasing the pulse amplitude increased the sensitivity of the current response, it also increased the peak width, thereby decreasing the resolution. A pulse amplitude of 20 mV was found to be optimum. The detection limit for both molecules using differential pulse voltammetry (5×10^{-7} M) was lower than that measured using cyclic voltammetry.

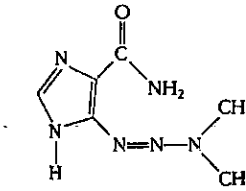

Figure 1. *Molecular structure of DTIC.*

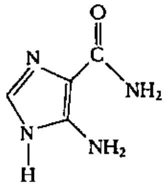

Figure 2. *Molecular structure of AIC.*

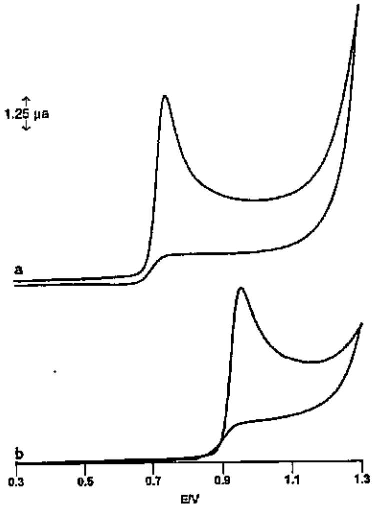

Figure 3. *Cyclic voltammograms of 0.1 mM AIC (a) and DTIC (b) in 0.1 M perchloric acid. Scan rate = 50 mV/s, all potentials measured with reference to the saturated calomel electrode. Figure adapted from reference.*

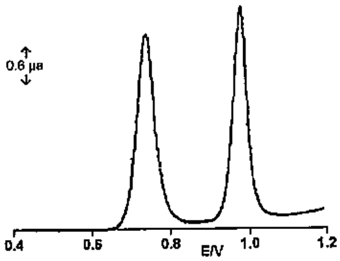

Figure 4. *Differential pulse voltammogram of a mixture of 0.1 mM DTIC and 0.1 mM AIC in 0.1 mM perchloric acid. All potentials measured with reference to the saturated calomel electrode. Figure adapted from reference.*