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Voltammetric Oxidation of Pharmaceutical Organic Compounds at a New Modified Electrode: The Aluminum Graphite Spray-Covered Electrode

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INTRODUCTION

We have for several years studied the electrochemical oxidation (*3, 4*) and reduction (*5*) of dibenzodiazepines such as clozapine, clothiapine, and loxapine. The electrochemical properties have been determined on graphite electrodes. We have recently described the preparation and properties of the graphite spray electrode (*1, 2*). The carbon-based graphite spray electrode results in improved background currents (*1*), while the metal-based graphite spray electrode offers in addition extended potential ranges and highly reproducible areas (*2*). These electrodes have been applied to cyclic voltammetry and anodic stripping voltammetry, the latter down to 10^{-9} *M* concentrations with 5-min plating times. The extended potential range of the metal-based graphite spray electrode and its high reproducibility make it suitable for application to the determination of electroactive organic compounds. In this study we have investigated the determination of dibenzodiazepines at the graphite spray-aluminum electrode.

MATERIALS AND METHODS

Apparatus. Voltammetric measurements were performed on a Bruker E 100 polarograph with a Hewlett–Packard Type 7004B recorder. Cyclic voltammetric measurements were made using a triangle signal generator constructed in our laboratory. A three-electrode cell thermostated at 25.0 ± 0.1°C was used. A saturated calomel electrode served as the reference electrode while a platinum wire served as the counter electrode. The working electrode was an aluminum-based graphite spray electrode fabricated and prepared as previously described (*2*). The prepared graphite

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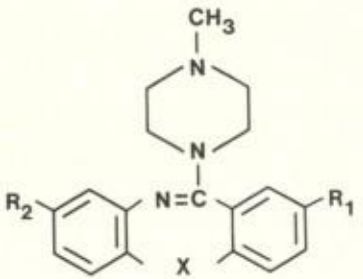
surface was polished as described, before each series of measurements, but no other electrode pretreatment was necessary.

Reagents. The benzodiazepine compounds were graciously furnished by the Wander–Sandoz Company (Switzerland). Supporting electrolyte solutions were prepared from reagent grade chemicals. Water was demineralized and then distilled twice, first from permanganate, and stored in polyethylene bottles.

RESULTS AND DISCUSSION

Oxidation of Clozapine

The general formula for benzodiazepines is



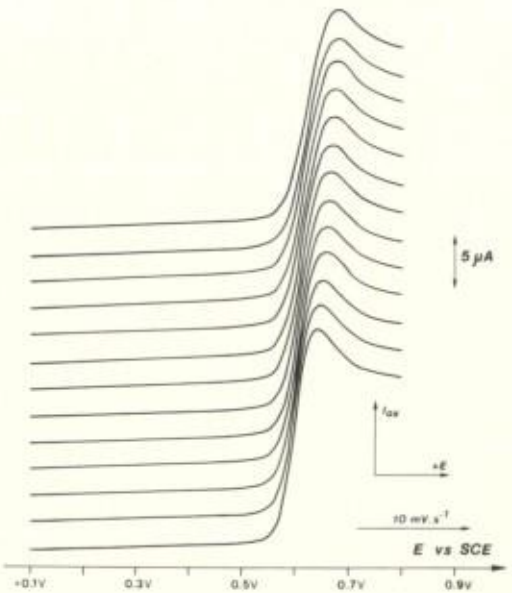


FIG. 1. Current–voltage curves from 5×10^{-4} *M* clozapine in 0.1 *M* H_2SO_4, 0.1 *M* Ac^-. Relative SD = 1.1%, $n = 13$.

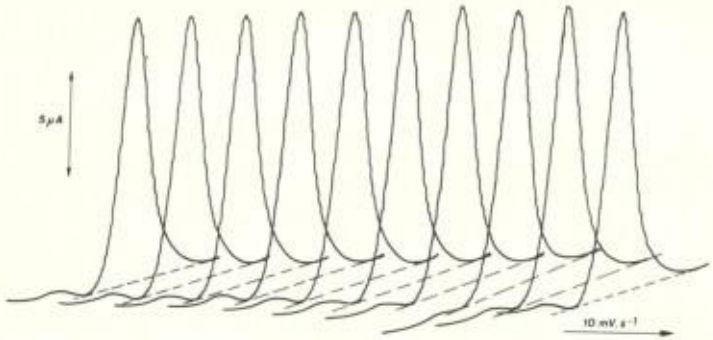


FIG. 2. Replicate differential pulse voltammograms from 5×10^{-5} *M* clozapine solution with the modified aluminum electrode (medium: 0.1 *M* HAc/Ac$^-$ in 20% methanol). Relative SD = 1.9%, n = 10. Same surface without any treatment between the scans. The solution was stirred for 2 min before each measurement.

For clozapine, X = N–H, R_1 = H, and R_2 = Cl. Clozapine is easily electrochemically oxidized. The electrochemical products are very little adsorbed on the graphite spray electrode surface with negligible poisoning of the surface for numerous runs. Figs. 1 and 2 illustrate the reproducibility of repetitive voltammetric measurements on the electrode using either linear scan voltammetry or differential pulse voltammetry. It was not necessary to repolish the electrode between runs. Figures 3 and 4

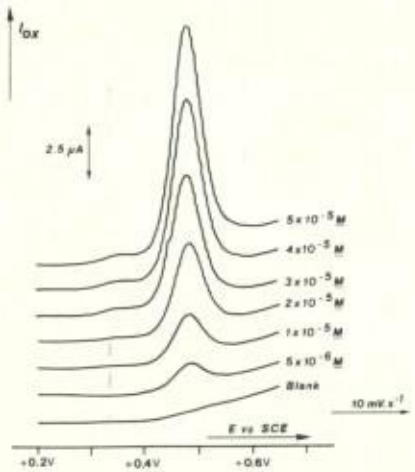


FIG. 3. Differential pulse voltammograms from clozapine solutions of increasing concentration with the modified aluminum electrode, dpp = 40 mV, 0.5 sec. HAc/Ac$^-$ (20% methanol): pH 4.7.

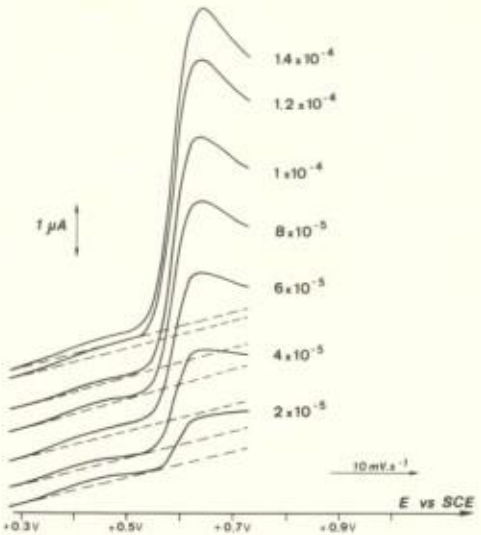


FIG. 4. Linear scan voltammograms for clozapine solutions of increasing concentration in 0.1 *M* H_2SO_4, 0.1 *M* Ac^-. Scan rate = 10 mV sec^{-1}.

show the linear dependence of the peak currents on concentration for microquantities of clozapine by the two techniques. The calibration curve from these peaks was linear, passing through zero with a correlation coefficient of 0.9994 for differential pulse voltammetry and 0.9995 for linear scan voltammetry.

TABLE 1
CYCLIC VOLTAMMETRIC DATA FOR 1×10^{-4} *M* CLOZAPINE OXIDATION IN 0.1 *M* PHOSPHATE BUFFER

	$E_p - E_{p/2}$ (mV)		I_{pa} (μA)		$E_{pa} - E_{pc}$ (mV)	
pH	Carbon paste electrode[a]	Al-modified electrode[a]	Carbon paste electrode	Al-modified electrode	Carbon paste electrode	Al-modified electrode
6.7	35	40	8.5	8.7	80	50
5.9	35	35	8.7	8.8	100	44
5.1	35	30	7.6	8.4	90	44
3.8	40	30	7.5	7.4	44	40
2.95	34	32	6.7	7.45	50	38
1.90	40	35	6.5	7.2	56	40
1.10	35	32	6.8	7.5	56	40

Note. Scan rate 10 mV/sec, temperature 25.0 ± 0.1°C. Data taken immediately after placing the electrode in solution (deoxygenated). Surface polished between measurements.
[a] Internal diameter: 8 mm.

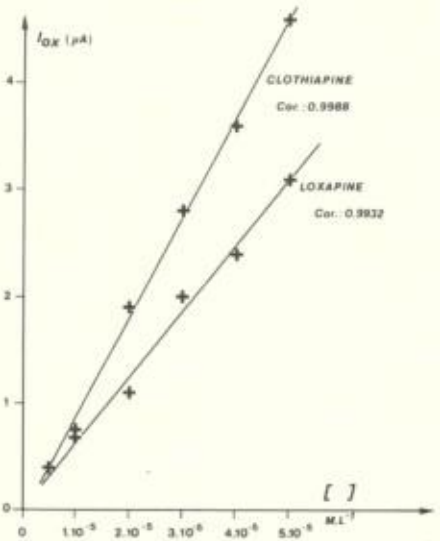


FIG. 5. DPV calibration curves for two pharmaceutical organic compounds. Modified aluminum electrode. dpp = 40 mV, 0.5 sec. Scan rate = 10 mV sec^{-1}. 0.1 *M* HAc/Ac$^-$ in 20% methanol solution.

Cyclic voltammetry at the electrode shows that in comparison to the carbon paste electrode the anodic peak potentials are slightly less positive and the cathodic peak is much better defined. In addition, the reversibility is markedly increased, especially in alkaline media as shown in Table 1.

Clothiapine and Loxapine

For clothiapine, X = S, R_1 = Cl, and R_2 = H, while for loxapine, X = O, R_1 = Cl, and R_2 = H. These two molecules are more difficult to oxidize than clozapine, with the electrochemical oxidation occurring close to the oxidation of the solvent. Also the oxidation products appear to be strongly adsorbed on the electrode surface; if subsequent runs are performed, peak heights diminish markedly. However, if the electrode is repolished after each run, reproducible peak heights are obtained, allowing quantitative determinations (see Fig. 5).

The above studies demonstrate that the graphite spray-modified aluminum electrode is suitable for the quantitative determination of organic compounds, and compares favorably with all other solid electrodes. Even with strong adsorption and poisoning of the electrode, the electrode surface is readily refurbished by simple polishing. Ongoing studies show that the electrode can be used in certain organic solvents such as acetonitrile. Solvents such as benzene or acetone cannot be used but are employed for cleaning the graphite from the electrode.

SUMMARY

A new graphite spray-modified aluminum electrode has been used to determine clozapine, clothiapine, and loxapine in acetate buffer at pH 4.7 and 20% methanol, down to 5×10^{-6} *M* concentrations using differential pulse voltammetry. Reproducibility exceeds that of other solid electrodes, being in the range of 1 to 2%. The electrochemical oxidation products of the latter two compounds are strongly adsorbed, causing diminished electrode response, but response is readily restored by polishing of the sprayed electrode.

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REFERENCES

1. Kauffmann, J.-M., Laudet, A., Patriarche, G. J., and Christian, G. D., The graphite spray electrode and its application in the anodic stripping voltammetry of bismuth. *Anal. Chim. Acta* **135**, 153–158 (1982).
2. Kauffmann, J.-M., Laudet, A., Patriarche, G. J., and Christian, G. D., Preparation and characterization of graphite modified metallic electrodes: the graphite spray electrode. *Talanta* **29**, 1077–1082 (1982).
3. Kauffmann, J.-M., Patriarche, G. J., and Christian, G. D., Electrochemical oxidation of derivatives of dibenzodiazepin, dibenzothiazepin and dibenzoxazepin. *Anal. Lett.* **12**, 1217–1234 (1979).
4. Kauffmann, J.-M., Patriarche, G. J., and Genies, M., Comportment électrochimique anodique de divers neuroleptiques en milieu aqueux et non-aqueux. *Eletrochim. Acta* **27**, 721–727 (1982).
5. Viré, J.-C., Patriarche, G. J., and Patriarche-Sépulchre, J., Etude electrochimique et differenciation de derives des dibenzodiazepines et des dibenzothiazepines. *Anal Lett.* **11**, 681–695 (1978).