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Short communication

Voltammetric investigation of Olanzapine: mechanistic insights into its electrochemical behavior

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Introduction

The atypical antipsychotic olanzapine has attracted significant interest in electroanalytical chemistry due to its distinct electroactive functional groups (Yilmaz et al., 2017). Its electrochemical behavior is strongly influenced by protonation state, electron-transfer kinetics and electrode-surface properties (Bacil et al., 2021). This study investigated the redox behavior of olanzapine at glassy carbon (GC) and edge-plane pyrolytic graphite (EPPG) electrodes, focusing on the effects of pH and scan rate (v) to obtain mechanistic insight into its electrochemical transformation. To the best of our knowledge, this is the first comparative voltammetric investigation of olanzapine at bare GC and EPPG electrodes.

Materials and methods

A 10^{-2} mol/L olanzapine stock solution was prepared in dimethyl sulfoxide and diluted to 10^{-3} mol/L in 0.1 mol/L HCl, acetate (pH = 4.50), citrate (pH = 6.00) or phosphate (pH = 7.35) buffer. Cyclic (CV) and square-wave voltammetry (SWV) were performed using a PalmSens potentiostat with PSTrace 4.8 software. Bare GC and EPPG served as working electrodes, Ag/AgCl (3 mol/L KCl) as reference electrode and a graphite rod as counter electrode.

Results and discussion

Olanzapine exhibited a pronounced pH-dependent voltammetric response at both investigated carbon electrodes. In strongly acidic medium, the principal anodic process was located at approximately 0.49-0.50 V. Increasing the pH caused a progressive displacement of the oxidation toward less positive potential. At the GC electrode, representative anodic peak-potentials ($E_{p,a}$) values at a scan rate of 50 mV/s were: 0.490 V in 0.1 M HCl; 0.330 V in acetate buffer; 0.200 V in citrate buffer and 0.145 V in phosphate buffer. A comparable trend was obtained at EPPG, with corresponding potentials of 0.495, 0.330, 0.200 and 0.135 V, respectively. Thus, increasing the pH from strongly acidic to near-neutral conditions decreased the potential required for olanzapine oxidation by approximately 0.35 V.

The systematic negative displacement with increasing pH demonstrates direct involvement of proton transfer in the electrode process. The magnitude of this shift approaches theoretical Nernstian dependence expected when the numbers of protons and electrons involved in the potential-determining step are equal. Previous mechanistic

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studies of olanzapine at carbon electrodes have proposed a one-electron/one-proton oxidation step followed by chemical transformation of the initially generated species (Bacil et al., 2021). Accordingly, the present pH dependence is consistent with a proton-coupled electron-transfer (PCET) process involving one electron and one proton in the principal oxidation step. The progressively lower oxidation potential at higher pH further indicates that oxidation of olanzapine becomes energetically more favorable as its protonation state changes.

Comparison of the two carbon electrodes showed remarkably similar anodic peak potentials. At scan rates of 10, 50 and 100 mV/s, differences in $E_{p,a}$ between GC and EPPG were generally within 0-10 mV in HCl, acetate and citrate media. These results indicate that the fundamental oxidation pathway of olanzapine is retained at both carbon materials. Differences between the electrodes were more apparent in peak current and peak morphology, suggesting that surface structure predominantly affects the interfacial response rather than the thermodynamic position of the oxidation process.

The scan rate also influenced the voltammetric response. At GC in 0.1 M HCl, anodic peak-current ($I_{p,a}$) increased from 9.95 μA at 10 mV/s to 31.49 μA at 100 mV/s, while the anodic peak remained within 0.490-0.500 V over most of the investigated range. In acetate buffer, $I_{p,a}$ increased from 8.00 to 22.55 μA and $E_{p,a}$ shifted from 0.310 to 0.340 V. A similar behavior was observed in citrate buffer, where $I_{p,a}$ increased from 4.59 to 22.75 μA, accompanied by a shift of $E_{p,a}$ from 0.190 to 0.210 V. The increase in peak current with scan rate, together with the positive displacement of the anodic peak potential, particularly in buffered media, indicates kinetic limitations and deviation from an ideal reversible redox system. These results are in agreement with previous voltammetric studies of olanzapine at graphite electrodes (Yilmaz et al., 2017).

Cathodic responses were also observed during the reverse scan under several experimental conditions. In HCl, well-defined anodic and cathodic processes were obtained at both electrodes, with peak separations of approximately 45-65 mV over the investigated scan-rate range. Greater peak separations were observed under some buffered conditions, together with changes in the relative anodic and cathodic currents. These observations indicate that the apparent reversibility of the olanzapine redox process is dependent on the solution environment. The combined pH and scan-rate effects therefore suggest a proton-coupled electrochemical transformation accompanied by kinetic and possibly subsequent chemical contributions rather than a simple, fully reversible electron-transfer process.

Analysis of the scan-rate dependence suggested contributions from both diffusion and adsorption, as comparable correlations were obtained for $I_{p,a}$ versus $v^{1/2}$ and $I_{p,a}$ versus v. The adsorption contribution was further supported by the pronounced surface-dependent behavior observed in SWV.

Conclusion

The voltammetric investigation of olanzapine revealed a strong pH-dependent electrochemical behavior that was largely preserved at both GC and EPPG electrodes. The systematic shift of the oxidation potential toward less positive values with increasing pH supports a proton-coupled electron-transfer mechanism, consistent with a one-electron/one-proton process. Scan-rate studies indicated mixed diffusion and adsorption-controlled behavior, with surface interactions further evidenced by SWV measurements. The relatively smaller peak separation observed in strongly acidic medium suggests slightly faster apparent electron-transfer kinetics in HCl. Overall, the results demonstrate that proton activity primarily governs the oxidation potential of olanzapine, while mass transport, adsorption and electrode-surface characteristics contribute to the kinetics and overall voltammetric response.

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