CYCLIC VOLTAMMETRY AS A SENSITIVE APPROACH IN INVESTIGATION OF DOXORUBICIN

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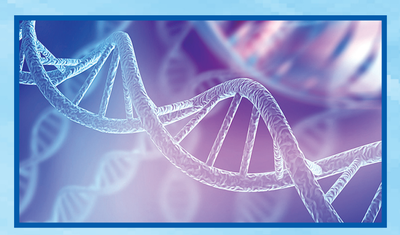
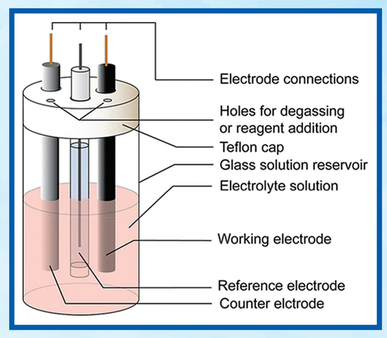
INTRODUCTION AND OBJECTIVE

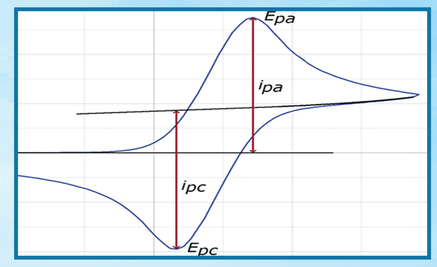


Doxorubicin is an anthracycline drug possessing a strong chemotherapeutic effect due to two possible mechanisms, 1)disruption of topoisomerase-II-mediated DNA repair due to its intercalation into DNA helix and 2)generation of free radicals and their damage to cellular membranes, DNA, and proteins. This can be a result of its planar aromatic chromophore which intercalates between two base pairs of DNA [1]. Therefore, its pharmacological/toxicological characteristics are largely dependent on its oxidative properties, and the aim of this study is to summarize the methods and data based on its electrochemical behavior of doxorubicin, obtained by the means of cyclic voltammetry (CV) [2].

METHODS

Cyclic voltammetry is a versatile electrochemical method where the redox reactions occurring at the working electrode result in a flow of current. The potentiostat measures this current and plots it as a function of the applied potential. Each successful forwards and backwards potential sweep produces a a cyclic voltammogram characterized by anodic and cathodic peak currents, peak potentials, and the oxidation and reduction onset potentials.

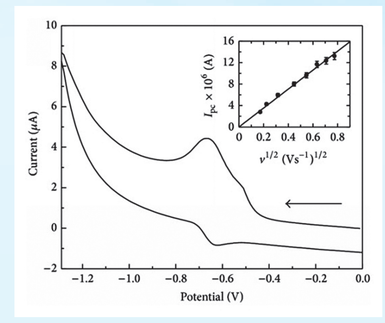




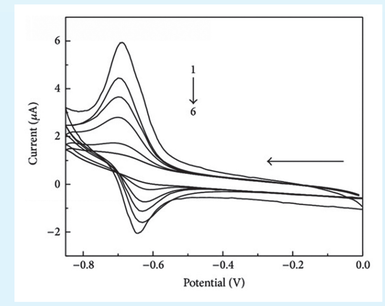
RESULTS

Our research revealed several studies that feature the electrochemical behavior of doxorubicin. CV in pH~7.4 has shown that doxorubicin undergoes a reversible two-electron reduction with value E1/2 = -665 mV(versus Ag/AgCl, saturated KCl). This process was defined as quasi reversible, at low scan rates. Further, the interaction of doxorubicin hydrochloride with calf thymus DNA was studied by measuring cathodic peak current, which gradually decreased as more DNA was added into the cell [3].

The interaction of doxorubicin with calf thymus DNA, was mostly assessed by electrochemical sensors using surface modified working electrodes [4,5,6]. Electrochemical sensor based on multi-walled carbon nanotubes modified platinum electrode (Pt/MWCNTs) [4], electrodeposition of silver nanoparticles and electro-polymerization of alginate layers on the surface of a glassy carbon electrode have been also used in this purpose [5]. CV of doxorubicine on a screen-printed electrodes modified with single-wall carbon nanotubes (SPE/CNT) have shown linear dependence of the intensity of electro reduction/oxidation on the square root of the scan rate which proved that the process is a controlled by diffusion. Moreover, thay imployed differential pulse voltammetry to validate a sensitive method for doxorubicine quantification. The drug binding processes were examined by DPV via the registration of a decrease in peak current intensity of guanine, adenine, and thymine of DNA in the presence of doxorubicin [6].



Cyclic voltammogram of doxorubicin hydrochloride in aqueous buffer at pH 7.4 on glassy carbon electrode. [Doxorubicin hydrochloride] = 33 μM, [NaCl] = 0.160 M, scan rate = 0.1 V s-1, and temperature = 25°C. Inset: plot of cathodic peak current versus square root of scan rate for the two-electron reduction of doxorubicin hydrochloride in aqueous buffer at pH 7.4.



Cyclic voltammogram of doxorubicin hydrochloride in the absence (1) and presence of different CT DNA concentrations: 19.9 μM (2), 59.31 μM (3), 98.2 μM (4) 174.47 μM (5), and 230.85 μM (6). Scan rate = 0.100 V s-1, pH = 7.4, [NaCl] = 0.160 M , and temperature = 25°C.

(Doxorubicine voltamogramms addopted from Guin P.S, and Das S., 2014)

CONCLUSION

Cyclic voltammetry can be used as an efffective tool for quantification of doxorubicine and its interactions with DNA or other metals. Reverible oxidation of doxorubicin to semiquinone and back, releases reactive oxygen species that cause DNA damage and lipid peroxidation. The effectivness of the therapeutic effect of doxorubicine depends on its interaction with DNA. These interactions were mostly assessed by using an electrochemical surface modified sensor, in the presence of DNA. These data lead to a conclusion that electrochemical platforms represent a sensitive approach for the investigation of DNA–drug interaction in electrode systems. Examining the electrochemical signals doxorubicin or DNA–doxorubicin complex before and after binding establishes the interaction and helps in mechanism elucidation.

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