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Influence of boron content on electrochemical properties of boron-doped diamond electrodes and their utilization for leucovorin determination

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A B S T R A C T

Set of the lab-made boron-doped diamond electrodes (BDDEs) prepared with various B/C ratio (1000, 2000, 4000, 8000, 10,000, and 20,000 ppm) in the gas phase was subjected to the detailed characterization in the present paper. It was proved, that the B/C ratio influenced the electrochemical features of the working electrodes like a width of the potential window, which decreased with increasing B/C. Variations of reversibility of two redox systems ($Fe(CN)_6^{3-/4-}$ and $Ru(NH_3)_6^{2+/3+}$) depending on B/C were observed as well. The best electrochemical properties were found for BDDE with B/C 10000 ppm. Moreover, the working electrodes were tested for voltammetric analysis of leucovorin based on its oxidation. The lab-made BDDEs were applied for voltammetric analysis of the pharmaceutical preparation containing leucovorin with excellent results (recovery 97.7–103.3%, $RSD_5 \leq 2.1\%$).

1. Introduction

Boron-doped diamond (BDD) represents remarkable material with various technical applications [1]. Due to the development of the still most used technique for BDD preparation – chemical vapor deposition (CVD) in the eighties of the twentieth century, the possibilities of its application have grown very fast [1–3]. The first mention about the use of a diamond doped with argon and nitrogen as a working electrode appeared in 1983 [4] but the later works focused mainly on boron-doped diamond electrodes (BDDEs) and their possible electroanalytical applications, *e.g.* [5–15]. Their very specific or unique features, like wide potential window, low background current, high mechanical and chemical stability, high resistance to passivation or non-toxicity, are the main reasons, why the use of these electrodes have been so expanded in the last twenty years, *e.g.* [5–15]. It was proved, that properties of the BDDEs depends on many factors, *e.g.* (*i*) concentration and type of the dopant, (*ii*) morphological properties, (*iii*) main crystallographic orientation, (*iv*) surface termination (H, O, F, *etc.*), (*v*) grain boundaries, and (*vi*) presence of the non-diamond carbon phases [16]. The effect of B concentration on the electrochemical features of BDDE have been widely studied, *e.g.* in Refs. [17–35]. It was ascertained, that concentration of B strongly influences the conductivity of the BDD films – heavily doped films have metallic type of conductivity and the lower doped BDD could be found as semiconductive, which intensively affects electrochemical properties of BDDEs [10,19,22,28,31,33–35]. Besides conductivity, B content and a quality of the film in general also affect width of the potential window or the background current [18,26,28,32,35]. Moreover, it was confirmed, that amount of B and B/C, respectively, in the gas phase influences the structure of the prepared films, specifically higher level of B caused smaller formed crystals [19,25,27,28,35].

Voltammetric behavior of the particular redox systems could reveal important information about the surface of used working electrodes, *e.g.* in Refs. [7,36–47]. Heterogeneous transfer of electron (transfer between the redox system and the electrode) can be categorized into two groups: (*i*) *outer sphere reaction*, where the electrode reaction proceeds only by mass transport and the working electrode serves as a donor or an acceptor of electrons. The electrode kinetics is not sensitive to the structure or surface of the electrode; and (*ii*) *inner sphere reaction*, which is strongly dependent on the electrode surface because it proceeds *via* some specific interaction with the surface [36,37]. The most often employed redox system, typical representative of the inner sphere reactions, whose behavior has been widely studied on BDDEs is $Fe(CN)_6^{3-/4-}$ [7,30,31,35,37–39,41–43]. Besides $Fe(CN)_6^{3-/4-}$, voltammetric behavior of aquated ions ($Fe^{3+/2+}$, $Ce^{4+/3+}$ or $Eu^{2+/3+}$), which proceed also through inner sphere reaction mechanism pathway,

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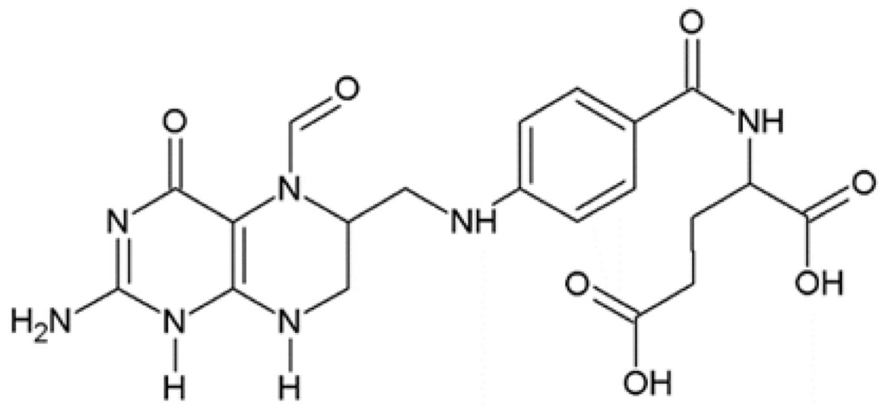

Scheme 1. Chemical structure of leucovorin.

has been investigated on BDDEs as well [37,42–45]. The redox probes, which typically provide outer sphere reaction and have been investigated on BDDEs are particularly $Ru(NH_3)_6^{2+/3+}$ and $IrCl_6^{2-/3-}$ [35,37–41,47].

Much less publications have been so far focused on the electroanalytical features of BDDEs with different boron content and their influence of analysis of specific electroactive compounds like nitrates [18,23], benzophenone-3 [31], linuron [32], 4-chloro-3-methylphenol [33], 5-nitroquinoline [34], and 2-aminobiphenyl [35].

Leucovorin (LV, Scheme 1) is a reduced derivative of folic acid [48]. It is administrated with methotrexate to reduce its negative side effects [49–51] or in combination with 5-fluorouracil to enhance its effectiveness during treatment of various serious diseases [52,53]. It was chosen as a representative electroactive compound, because its voltammetric behavior has been already described only on mercury [54–56] and silver solid amalgam electrodes [56]. Considering the used working electrodes, the papers were focused on recording of LV reduction and thus interested in cathodic signals [54–56]. Our proposed voltammetric methods based on application of silver solid amalgam electrodes provided low detection limits specifically 2.2×10^{-8} and 5.0×10^{-8} mol L^{-1} for mercury meniscus modified (m-AgSAE) and polished silver solid amalgam electrode (p-AgSAE), respectively [56]. The obtained results were compared also with outputs from measuring with hanging mercury drop electrode (HMDE), which provided significantly higher limit of detection (9.8×10^{-7} mol L^{-1}) [56].

The present paper deals with characterization of the electrochemical features of BDDEs prepared under different conditions particularly with different B/C in the gas phase. Moreover, their applicability as an analytical tool for determination of the chemoprotectant drug LV based on its electrochemical oxidation is examined as well.

2. Experimental

2.1. Chemicals

All of the used chemicals were of analytical grade purity and were obtained from Sigma Aldrich, if not stated otherwise. Standard solution of 0.001 mol L^{-1} leucovorin was prepared by simple dissolution of its calcium salt powder in the distilled water. It was stored in a refrigerator. Solutions of lower concentration were prepared by dilution with distilled water or the supporting electrolyte directly before analysis.

Britton-Robinson buffer (BRB) consisting of the mixture of acidic (H_3PO_4, H_3BO_3, and CH_3COOH – all three of the same concentration 0.4 mol L^{-1}) and alkaline component (0.2 mol L^{-1} NaOH from Lachema, Czech Republic) was used as a supporting electrolyte. 0.5 and 0.05 mol L^{-1} H_2SO_4 was prepared from 96% H_2SO_4 (Penta-Švec, Czech Republic). 0.1 mol L^{-1} KCl was prepared by dissolution of its powder (Penta-Švec, Czech Republic) in the distilled water. Standard solutions of 2.5×10^{-3} mol L^{-1} $K_3[Fe(CN_6)]$ and $[Ru(NH3)_6]Cl_3$ (both of purity ≤ 99%) were prepared in the solution of 0.1 mol L^{-1} KCl.

"Leucovorin Ca LACHEMA 10" for preparation of the injection solution originated from Pliva-Lachema, Czech Republic.

2.2. Instrumentation

Voltammetric measurements were carried out by computer controlled analyzer Eco-Tribo Polarograph (Polaro-Sensors, Czech Republic) and employing software POLAR.PRO version 5.1. The measuring system consisted of three electrodes – BDDE as a working electrode, Ag|AgCl|KCl (sat.) as a reference (Monokrystaly, Czech Republic), and platinum wire (Monokrystaly, Czech Republic) as an auxiliary electrode. As a working BDD electrode, we have used the commercially available one with working surface of 7.07 mm^2 and B/C ratio in the gas phase of 1000 ppm as declared by the producer Windsor Scientific (UK) or one of the laboratory prepared electrodes (Slovak University of Technology in Bratislava, Faculty of Electrical Engineering and Information Technology, Institute of Electronics and Photonics) with working surface of 0.43 mm^2 and B/C ratio in gas phase of 1000, 2000, 4000, 8000, 10,000, and 20,000 ppm. All measurements were carried out at laboratory temperature of 23 ± 2 °C. Values of pH were measured by pH-meter Accumet AB150 (Fisher Scientific, Czech Republic).

All graphical dependences were constructed using Excel software (Microsoft, USA). Parameters of calibration curves and confidence intervals were calculated using OriginPro 9 software (OriginLab Corporation, USA) on the level of significance 0.05. Statistical parameters like limit of detection (LOD) and limit of quantification (LOQ) were calculated from the calibration dependences as three times and ten times, respectively, of standard deviation of intercept divided by the slope.

2.3. Procedures

2.3.1. Electrochemical characterization of BDDEs

Preparation and surface characterization of the lab-made BDD electrodes is described in our previous paper [57]. All of the used working BDD electrodes (the lab-made and the commercial one as well) were activated and regenerated employing the same procedure. The chosen electrode underwent activation in 0.5 mol L^{-1} H_2SO_4 by applying negative (cathodic) potential (E_c = −2000 mV) for 60 s followed by insertion of positive (anodic) potential (E_a = +2000 mV) of the same duration. Then, 20 cyclic voltammograms between −1000 mV and +2000 mV were recorded to ensure stabilization of the activated electrode. After this step, the working electrode was ready for analysis. Besides the activation, the regeneration step, which consisted of the