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ARTICLES

An Electrochemical DNA Sensor for Doxorubicin Based on a Polyelectrolyte Complex and Aminated Thiacalix[4]Arene

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Abstract—An impedimetric DNA sensor is developed for the highly sensitive determination of doxorubicin; the signal is charge transfer resistance recorded by electrochemical impedance spectroscopy using a glassy carbon electrode modified by electropolymerized Neutral Red or polyaniline and polyelectrolyte complexes including DNA. The nature of the polymer layer and the composition of the polyelectrolyte complex affect the sensitivity of the determination of doxorubicin. The role of a macrocycle capable of shielding the DNA negative charge and interacting with cationic centers of the substrate is shown. With an optimal composition of polyelectrolytes, the DNA sensor ensures the determination of down to 0.1 nM of doxorubicin.

Keywords: DNA sensor, biosensor, electropolymerization, Neutral Red, polyaniline, DNA intercalation, determination of doxorubicin

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The development of modern electroanalytical chemistry creates new possibilities for highly sensitive and selective detection of compounds that are in demand in medical diagnostics and pharmaceuticals. These include metabolites, residual amounts of pollutants, biomarkers of diseases, pharmaceutical preparations, and products of their transformation [1]. Currently, most of these compounds are determined using various methods of chromatography and optical spectroscopy [2, 3]. Being sensitive and selective, universal methods of instrumental analysis require stationary chemical laboratory conditions, time- and labor-consuming sample preparation, and highly skilled personnel for their implementation The development of personalized medicine, in particular, diagnostic equipment for use outside the medical facility (point-of-care, at the patient's bed [4]) suggests a transition from such universal equipment to individual sensors. Such devices also include biosensors that use the reaction of the analyte with the participation of biochemical recognition elements (enzymes, antibodies, nucleic acids) to determine it. Medical biosensors are currently most often based on electrochemical signal transducers. Their advantages include compact design, ease of operation, compatibility with most versions of biochemical analysis, a well-developed theory of application, and an intuitive interpretation of the signal [5].

The development of biosensors and the prospects for their introduction into medical diagnostics largely depend on the possibilities of improving the principles of signal measurement, associated with the interaction of the analyte and the biochemical receptor. The search for more sensitive signal transducers and new strategies for recording biochemical interactions can expand the field of application of biosensors and improve their analytical and performance characteristics. This is fully applied to DNA sensors. At present, they are mainly used to determine the complementary sequences of oligonucleotides by the reaction of their hybridization on the surface of the signal converter [6]. The signal of hybridization is a change in the current of a diffusion-free indicator (redox probe) added to the solution or the transfer resistance of the same probe, calculated from the results of measuring the electrochemical impedance. The change in the signal of the redox probe is associated with the introduction of bulk oligonucleotides into the surface layer, which decreases the rate of transfer of the probe molecules to the electrode. In the case of low-molecular-weight analytes, the sensitivity of this method of detection may be insufficient because the binding of the analyte in the surface layer does not change its volume and permeability [7]. Such problems can arise, for example, when determining anticancer preparations of cytostatic action that interact with native DNA, being inserted between pairs of nucleic bases [8]. It was previously shown that the recording of the electrochemical response of hybrid materials consisting of DNA and electropolymerization products, exhibiting redox