

Electrochemical DNA sensors with layered polyaniline–DNA coating for detection of specific DNA interactions

Kulikova T., Porfireva A., Evtugyn G., Hianik T.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2019 by the authors. Licensee MDPI, Basel, Switzerland. A DNA sensor has been proposed on the platform of glassy carbon electrode modified with native DNA implemented between two electropolymerized layers of polyaniline. The surface layer was assembled by consecutive stages of potentiodynamic electrolysis, DNA drop casting, and second electrolysis, which was required for encapsulation of the DNA molecules and prevented their leaching into the solution. Surface layer assembling was controlled by cyclic voltammetry, electrochemical impedance spectroscopy, atomic force, and scanning electron microscopy. For doxorubicin measurement, the DNA sensor was first incubated in the Methylene blue solution that amplified signal due to DNA intercalation and competition with the doxorubicin molecules for the DNA binding sites. The charge transfer resistance of the inner layer interface decreased with the doxorubicin concentration in the range from 1.0 pM to 0.1 μM (LOD 0.6 pM). The DNA sensor was tested for the analysis of spiked artificial urine samples and showed satisfactory recovery in concentration range of 0.05–10 μM. The DNA sensor developed can find application in testing of antitumor drugs and some other DNA damaging factors.

<http://dx.doi.org/10.3390/s19030469>

Keywords

DNA intercalator, Doxorubicin, Electrochemical DNA sensor, Electrochemical impedance spectroscopy, Electropolymerization, Polyaniline

References

- [1] Teles, F.R.R.; Fonseca, L.P. Trends in DNA biosensors. *Talanta* 2008, **77**, 606–623. [CrossRef]
- [2] Yu, H.L.L.; Maslova, A.; Hsing, I.-M. Rational design of electrochemical DNA biosensors for point-of-care applications. *ChemElectroChem* 2017, **4**, 795–805. [CrossRef]
- [3] Palchaudhuri, R.; Hergenrother, P.J. DNA as a target for anticancer compounds: Methods to determine the mode of binding and the mechanism of action. *Curr. Opin. Biotechnol.* 2007, **18**, 497–503. [CrossRef] [PubMed]
- [4] Mervin, L.H.; Cao, Q.; Barrett, I.P.; Firth, M.A.; Murray, D.; Mc Williams, L.; Haddrick, M.; Wigglesworth, M.; Engkvist, O.; Bender, A. Understanding cytotoxicity and cytostaticity in a high-throughput screening collection. *ACS Chem. Biol.* 2016, **11**, 3007–3023. [CrossRef] [PubMed]
- [5] Hurley, L.H. DNA and its associated processes as targets for cancer therapy. *Nat. Rev. Cancer* 2002, **2**, 188–200. [CrossRef] [PubMed]

- [6] Doménech-Carbó, A.; Cebrián-Torrejón, G.; Montoya, N.; Ueberschaar, N.; Scotti, M.T.; Benfodda, Z.; Hertweck, C. Electrochemical monitoring of ROS generation by anticancer agents: The case of chartreusin. *RSC Adv.* 2017, 7, 45200-45210. [CrossRef]
- [7] Muti, M.; Muti, M. Electrochemical monitoring of the interaction between anticancer drug and DNA in the presence of antioxidant. *Talanta* 2018, 178, 1033-1039. [CrossRef]
- [8] Kara, H.E.S. Redox mechanism of anticancer drug idarubicin and in-situ evaluation of interaction with DNA using an electrochemical biosensor. *Bioelectrochemistry* 2014, 99, 17-23. [CrossRef]
- [9] Bagni, G.; Osella, L.; Sturchio, E.; Mascini, M. Deoxyribonucleic acid (DNA) biosensors for environmental risk assessment and drug studies. *Anal. Chim. Acta* 2006, 573-574, 81-89. [CrossRef]
- [10] Ilkhani, H.; Hughes, T.; Li, J.; Zhong, C.J.; Hepel, H. Nanostructured SERS-electrochemical biosensors for testing of anticancer drug interactions with DNA. *Biosens. Bioelectron.* 2016, 80, 257-264. [CrossRef]
- [11] Trnkova, L.; Huska, D.; Adam, V.; Kizek, R.; Eckschlager, T.; Stiborova, M.; Hubalek, J. Electrochemical biosensor for investigation of anticancer drugs interactions (doxorubicin and ellipticine) with DNA. In Proceedings of the SENSORS, Christchurch, New Zealand, 25-28 October 2009; pp. 1200-1203.
- [12] Huska, D.; Adam, V.; Babul, P.; Hrabela, J.; Stiborova, M.; Eckschlager, T.; Trnkova, L.; Kizek, R. Square-wave voltammetry as a tool for investigation of doxorubicin interactions with DNA isolated from Neuroblastoma cells. *Electroanalysis* 2009, 21, 487-494. [CrossRef]
- [13] Hynek, D.; Krejcova, L.; Zitka, O.; Adam, V.; Trnkova, L.; Sochor, J.; Stiborova, M.; Eckschlager, T.; Hubalek, J.; Kizek, R. Electrochemical study of doxorubicin interaction with different sequences of double stranded oligonucleotides. Part II. *Int. J. Electrochem. Sci.* 2012, 7, 34-49.
- [14] Paziewska-Nowak, A.; Jankowska-Śliwińska, J.; Dawgul, M.; Pijanowska, D.G. Selective electrochemical detection of pirarubicin by means of DNA-modified graphite biosensor. *Electroanalysis* 2017, 29, 1810-1819. [CrossRef]
- [15] Rauf, S.; Gooding, J.J.; Akhtar, K.; Ghauri, M.A.; Rahman, M.; Anwar, M.A.; Khalid, A.M. Electrochemical approach of anticancer drugs-DNA interaction. *J. Pharm. Biomed. Anal.* 2005, 37, 205-217. [CrossRef] [PubMed]
- [16] Li, C.-Z.; Luong, J.H.T. Impedance sensing of DNA binding drugs using gold substrates modified with gold nanoparticles. *Anal. Chem.* 2005, 77, 478-485. [CrossRef] [PubMed]
- [17] Ensaifi, A.A.; Amini, R. Impedimetric DNA-biosensor for the study of anti-cancer action of mitomycin C: Comparison between acid and electroreductive activation. *Biosens. Bioelectron.* 2014, 59, 282-288. [CrossRef] [PubMed]
- [18] Mousavisan, S.Z.; Raoof, J.B.; Ojani, R.; Bagheryan, Z. An impedimetric biosensor for DNA damage detection and study of the protective effect of deferoxamine against DNA damage. *Bioelectrochemistry* 2018, 122, 142-148. [CrossRef]
- [19] Evtugyn, G.; Hianik, T. Electrochemical DNA sensors and aptasensors based on electropolymerized materials and polyelectrolyte complexes. *TrAC Trends Anal. Chem.* 2016, 79, 168-178. [CrossRef]
- [20] Sui, J.; Zhang, L.; Peng, H. Label-free DNA sensor construction using self-assembled poly(o-methoxyaniline) hollow nanospheres. *Eur. Polym. J.* 2013, 49, 139-146. [CrossRef]
- [21] Shinkai, S.; Takeuchi, M.; Bae, A.-H. Rational design and creation of novel polymeric superstructures by oxidative polymerization utilizing anionic templates. *Supramol. Chem.* 2006, 17, 181-186. [CrossRef]
- [22] Wang, X.; Xuan, H.; Zhang, J.; Chen, S.; Zhang, F.; Zou, W. Facile synthesis of fluorescent polyaniline microspheres and their use for the detection of mercury ions. *New J. Chem.* 2015, 39, 6261-6266. [CrossRef]
- [23] Iqbal, S.; Ahmad, S. Recent development in hybrid conducting polymers: Synthesis, applications and future prospects. *J. Ind. Eng. Chem.* 2018, 60, 53-84. [CrossRef]
- [24] Mazeikiene, R.; Malinauskas, A. Deposition of polyaniline on glass and platinum by autocatalytic oxidation of aniline with dichromate. *Synth. Met.* 2000, 108, 9-14. [CrossRef]
- [25] Radhakrishnan, S.; Muthukannan, R.; Kamatchi, U.; Rao, C.R.K.; Vijayan, M. Performance of phosphoric acid doped polyaniline as electrode material for aqueous redox supercapacitor. *Indian J. Chem.* 2011, 50A, 970-978.
- [26] Mondal, S.K.; Prasad, K.R.; Munichandraiah, N. Analysis of electrochemical impedance of polyaniline films prepared by galvanostatic, potentiostatic and potentiodynamic methods. *Synth. Met.* 2005, 148, 275-286. [CrossRef]
- [27] Can, M.; Pekmez, N.O.; Yildiz, A. Theoretical investigation of the proton effect on electropolymerization of aniline. *Polymer* 2003, 44, 2585-2588. [CrossRef]
- [28] Prakash, R. Electrochemistry of polyaniline: Study of the pH effect and electrochromism. *J. Appl. Polym. Sci.* 2002, 83, 378-385. [CrossRef]
- [29] Piccinini, E.; Bliem, C.; Reiner-Rozman, C.; Battaglini, F.; Azzaroni, O.; Knoll, W. Enzyme-polyelectrolyte multilayer assemblies on reduced graphene oxide field-effect transistors for biosensing applications. *Biosens. Bioelectron.* 2017, 92, 661-667. [CrossRef]
- [30] Dhand, C.; Das, M.; Datta, M.; Malhotra, B.D. Recent advances in polyaniline based biosensors. *Biosens. Bioelectron.* 2011, 26, 2811-2821. [CrossRef]

- [31] Azmi, U.Z.M.; Yusof, N.A.; Kusnin, N.; Abdullah, J.; Suraiya, S.; Ong, P.S.; Raston, N.H.A.; Rahman, S.F.A.; Fathil, M.F.M. Sandwich electrochemical immunosensor for early detection of tuberculosis based on graphene/polyaniline-modified screen-printed gold electrode. *Sensors* 2018, 18, 3926. [CrossRef]
- [32] Ates, M. A review study of (bio)sensor systems based on conducting polymers. *Mater. Sci. Eng. C* 2013, 33, 1853–1859. [CrossRef] [PubMed]
- [33] Hur, J.; Im, K.; Kim, S.W.; Kim, U.J.; Lee, J.; Hwang, S.; Song, J.; Kim, S.; Hwang, S.; Park, N. DNA hydrogel templated carbon nanotube and polyaniline assembly and its applications for electrochemical energy storage devices. *J. Mater. Chem. A* 2013, 1, 14460–14466. [CrossRef]
- [34] Wang, Z.-G.; Ding, B. Engineering DNA self-assemblies as templates for functional nanostructures. *Acc. Chem. Res.* 2014, 47, 1654–1662. [CrossRef] [PubMed]
- [35] Hao, Y.; Zhou, B.; Wang, F.; Li, J.; Deng, L.; Liu, Y.-N. Construction of highly ordered polyaniline nanowires and their applications in DNA sensing. *Biosens. Bioelectron.* 2014, 52, 422–426. [CrossRef] [PubMed]
- [36] Shamagsumova, R.; Porfireva, A.; Stepanova, V.; Osin, Y.; Evtugyn, G.; Hianik, T. Polyaniline-DNA based sensor for the detection of anthracycline drugs. *Sens. Actuators B* 2015, 220, 573–582. [CrossRef]
- [37] Nishida, Y.; Domura, R.; Sakai, R.; Okamoto, M.; Arakawa, S.; Ishiki, R.; Salick, M.R.; Turng, L. Fabrication of PLLA/HA composite scaffolds modified by DNA. *Polymer* 2015, 56, 73–81. [CrossRef]
- [38] Guschlauer, W.; Courtois, Y. pH induced changes in optical activity of guanine nucleosides. *FEBS Lett.* 1968, 1, 183–186. [CrossRef]
- [39] Haque, L.; Bhuiya, S.; Giri, I.; Chowdhury, S.; Das, S. Structural alteration of low pH, low temperature induced protonated form of DNA to the canonical form by the benzophenanthridine alkaloid nitidine: Spectroscopic exploration. *Int. J. Biol. Macromol.* 2018, 119, 1106–1112. [CrossRef]
- [40] Ma, Y.; Zhang, J.; Zhang, G.; He, H. Polyaniline nanowires on Si surfaces fabricated with DNA templates. *J. Am. Chem. Soc.* 2004, 126, 7097–7101. [CrossRef] [PubMed]
- [41] Becerril, H.A.; Woolley, A.T. DNA-templated nanofabrication. *Chem. Soc. Rev.* 2009, 38, 329–337. [CrossRef]
- [42] Bardavid, Y.; Ghabboun, J.; Porath, D.; Kotylar, A.B.; Yitzchaik, S. Formation of polyaniline layer on DNA by electrochemical polymerization. *Polymer* 2008, 49, 2217–2222. [CrossRef]
- [43] Radhakrishnan, S.; Sumathi, C.; Dharumana, V.; Wilson, J. Polypyrrole nanotubes-polyaniline composite for DNA detection using methylene blue as intercalator. *Anal. Methods* 2013, 5, 1010–1015. [CrossRef]
- [44] Yau, H.C.M.; Chan, H.L.; Yang, M. Electrochemical properties of DNA-intercalating doxorubicin and methylene blue on n-hexadecyl mercaptan-doped 5-thiol-labeled DNA-modified gold electrodes. *Biosens. Bioelectron.* 2003, 18, 873–879. [CrossRef]
- [45] Pauliukaite, R.; Ghica, M.E.; Barsan, M.M.; Brett, C.M.A. Phenazines and polyphenazines in electrochemical sensors and biosensors. *Anal. Lett.* 2010, 43, 1588–1608. [CrossRef]
- [46] Kulikova, T.N.; Porfireva, A.V.; Shamagsumova, R.V.; Evtugyn, G.A. Voltammetric sensor with replaceable polyaniline-DNA layer for doxorubicin determination. *Electroanalysis* 2018, 30, 2284–2292. [CrossRef]
- [47] Hajian, R.; Tayebi, Z.; Shams, N. Fabrication of an electrochemical sensor for determination of doxorubicin in human plasma and its interaction with DNA. *J. Pharm. Anal.* 2017, 7, 27–33. [CrossRef]
- [48] Peng, A.; Xu, H.; Luo, C.; Ding, H. Application of a disposable doxorubicin sensor for direct determination of clinical drug concentration in patient blood. *Int. J. Electrochem. Sci.* 2016, 11, 6266–6278. [CrossRef]
- [49] Evtugyn, A.; Porfireva, A.; Stepanova, V.; Budnikov, H. Electrochemical biosensors based on native DNA and nanosized mediator for the detection of anthracycline preparations. *Electroanalysis* 2015, 27, 629–637. [CrossRef]
- [50] Fojta, M.; Daňhel, A.; Havran, L.; Vyskočil, V. Recent progress in electrochemical sensors and assays for DNA damage and repair. *Trends Anal. Chem.* 2016, 79, 160–167. [CrossRef]