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Aptamer-based Electrochemical Sensor for the Monitoring of Carbamazepine in Freshwater Systems

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Summary:

Carbamazepine (CBZ) is an active compound in commonly used drug and is highly durable in the environment, particularly in wastewater, which raises concerns about potential risks to animals and humans. We present an aptamer-based electrochemical sensor labelled with a redox probe which conformational change upon binding event is recorded by square-waved voltammetry. The electrochemical sensor operated in concentrations range from 2.5 pM to 250 µM in buffer. This technology provides a potential method to enable the monitoring of CBZ in treated water.

Keywords: Aptamer, electrochemical sensor, carbamazepine, environment, wastewater

Introduction

Carbamazepine (CBZ) is an anticonvulsant and anti-epileptic drug that was classified in the contaminants of emerging concern (CECs) list due to its unintended persistence in the environment notably in treated wastewater (up to 10 nM for long term exposure) [1]. Commonly used techniques to detect CBZ are liquid chromatography-tandem mass spectroscopy (LC-MS/MS), high-performance liquid chromatography (HPLC), immunoassays and solid-phase extraction (SPE) coupled with chromatography. While these methods are accurate, they are time-consuming and require sophisticated instrumentation. Furthermore, they cannot be applied for on-site detection. Several efforts have been made to develop portable assay formats using electrochemical techniques for rapid detection of carbamazepine (CBZ) and its metabolites, aiming to address this challenge. Direct electrochemical methods utilize target reduction/oxidation (redox) processes for quantification without the need for affinity reagents. While these methods are straightforward, electroactive molecules present in the medium to analyze can lead to a false positive. Molecular imprinted polymers were also reported as artificial biomimetic receptors to improve the low specificity of direct detection however, they are less selective than anti-bodies. Alternatively, aptamers are a class of short single-stranded nucleic acids that can selectively interact with their target rivalling those of antibodies. Specific sequences are generated by an in vitro molecular evolution method known as systematic evolution of ligands by exponential enrichment (SELEX). They are particularly interesting for the detection of small molecules, such as CBZ, that do not have enough immunogenicity to generate a specific antibody. In this work, we developed an electrochemical aptasensor where a conformational change is induced by CBZ target binding within the aptamer structure, which subsequently alters electron transfer between a redox tag appended at a distance and the surface of an electrode. The aptamer was modified with a thiol group on the 5′-end for immobilization on the gold sensing electrode and a methylene blue (MB) tag on the 3′-end for readout [2].

Results

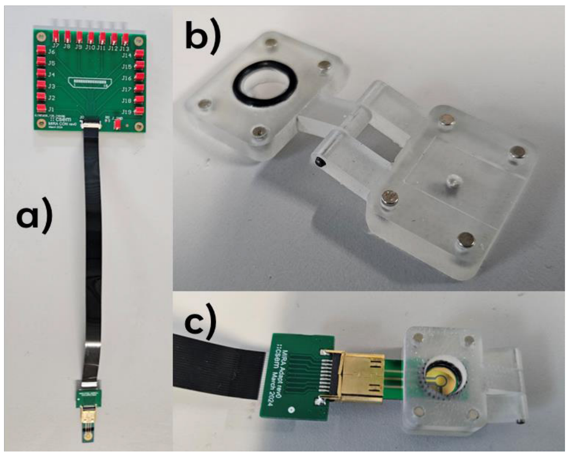

Fig 1. Picture of a) the sensing platform, b) the 3D printing cartridge and c) the sensor plugged in the HDMI mini connector with the cartridge integrated.

The gold electrodes were patterned on a silicon substrate with conventional clean room microfabrication processes. Ag/AgCl electrode was deposited by aerosol jet printing technique. The chip is further integrated in an in-house developed sensing platform with a HDMI mini connector for an easy plug-and-play system. A 3D printed cartridge is integrated for drop-casting the sample on the sensor (see Fig.1). CBZ aptamer was covalently attached with the thiol function on the 3'-end by self-assembled-monolayer (SAM) on the gold working electrode overnight. For the sensor characterization, CBZ was diluted in PBS buffer (pH=7.4) at different concentrations and square-wave voltammetry (SWV) was recorded when the signal was stabilized. In Fig. 2, an increase of CBZ concentration is correlated with a decrease of the current.

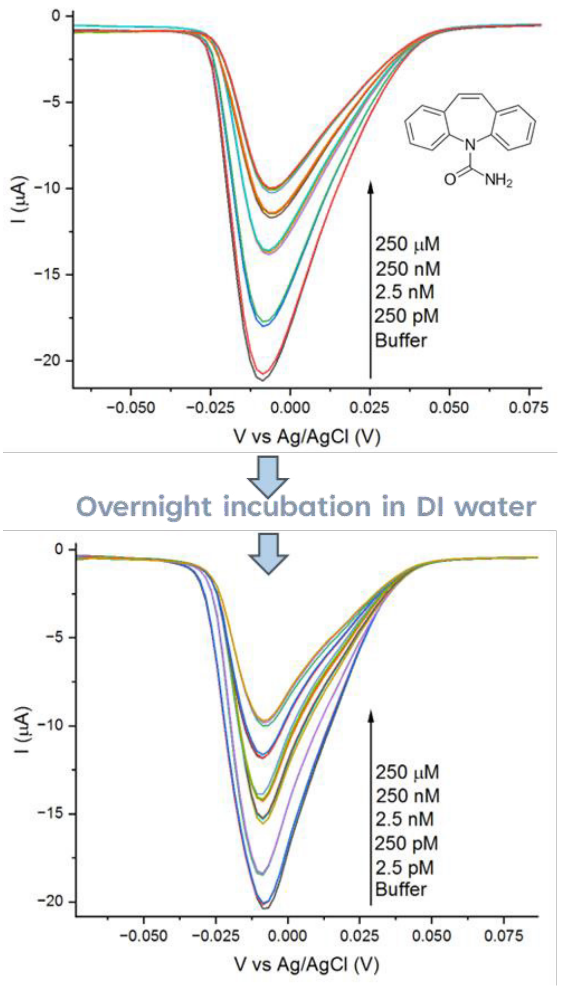

Fig. 2 SWV of the aptasensor showing its reversibility after overnight incubation in DI water.

It can be explained with the initial aptamer state being close to the gold electrode and allowing high-electron transfer rate with the MB. Upon binding with CBZ, the aptamer conformation switching moves the MB further away from the electrode which is transduced by a decrease of the current. A consequent advantage of aptamers is their reversible denaturation. By incubating the sensor in deionized (DI) water, the aptamer loses its conformation and CBZ is released in the solution. When it is reintroduced in PBS buffer, the aptamer goes back to its initial conformation and similar performances are observed as shown in Fig. 3.

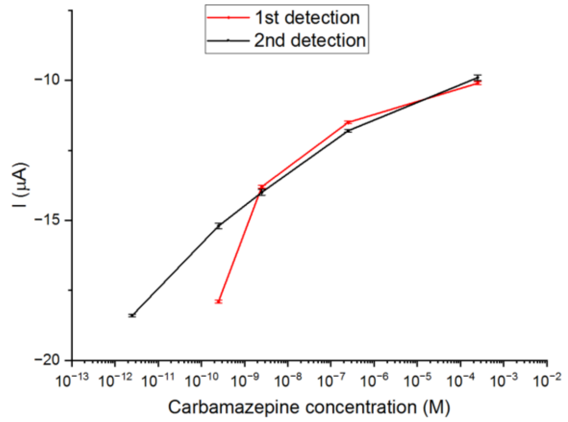

Fig. 3 Calibration curves of the aptasensor before (1st detection) and after (2nd detection) incubation in water

Conclusion

In this study, we have demonstrated the reversible detection of CBZ with a MB labelled aptamer electrochemical sensor. The developed sensor showed high sensitivity to CBZ down to 2.5 pM. Therefore, it holds great potential for the development of the next generation of portable on-site assays for the monitoring of CBZ in the environment.

References

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