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Paper-Based Microfluidic Analytical Device Based on Molecularly Imprinted Polymer for Detection of Carcinoembryonic Antigen

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Abstract:

This paper describes a novel strategy to fabricate a low-cost microfluidic paper-based analytical device (μPAD) readily based on surface molecularly imprinted technology for clinical detection of carcino-embryonic antigen (CEA). The movable valve fabrication was realized using hollow rivets as the holding center to control the electrode and channel of the μPAD in different layer movement, so the entire process of synthesis and testing could be completed easily. Graphene oxide, chitosan and CEA templates were assembled on the μPAD as a substrate, and subsequently the molecularly imprinted membranes were formed by electropolymerization of dopamine. Finally, the novel μPAD was obtained after removal of CEA templates. Because the entire manufacturing process was done on the μPAD without any external treatment, the μPAD has the characteristics of easy synthesis, low cost and low toxicity. Moreover, the μPAD gave a flexible and easy way to operate the entire detection process conveniently. Experimental parameters such as equilibration time, scan cycles, template concentration and pH value were optimized. A good linearity was obtained in the range of 1 − 500 ng mL^{-1} (R^2= 0.994) with the limit of detection (LOD) of 0.21 ng mL^{-1}.

Key words: microfluidic paper-based devices, electrochemical sensor, molecularly imprinted technology, carcinoembryonic antigen

Introduction

Microfluidic paper-based analytical device (μPAD) technology has been developing quickly like the bamboo shoots after a spring rain. However, most studies require the help of external conditions to synthesize complex materials to support the operation of the μPAD. Therefore, finding a simple and low-carbon synthesis method has become a major challenge for μPAD development. On the other hand, accurate and sensitive determination of CEA by the application of μPAD in human body is very important in early diagnosis, screening disease recurrence, and healing the patients with certain tumor-associated disease [1].

Fabrication of μPAD

Firstly, we designed a structure that contains hydrophobic and hydrophilic areas on the paper chip, as shown in Fig. 1. Secondly, graphene oxide (GO), chitosan and CEA templates were assembled on the working electrode pool of μPAD to synthsize molecularly imprinted polymer by electropolymerization of dopamine [2]. Lastly, μPAD was obtained after removal of CEA templates.

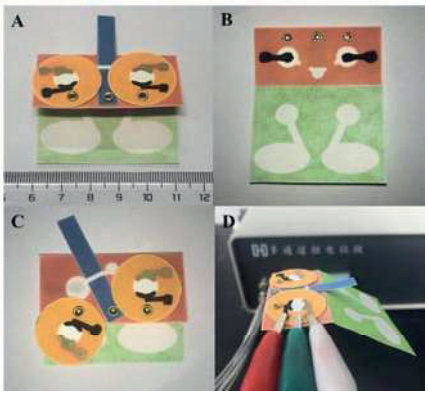

Fig. 1. Photograph of μPADs prepared on filter paper.

Electrochemical characterization

Cyclic voltammetric responses at bare paper electrode and modified paper electrode are shown in Fig. 2. The bare paper electrode showed a couple of redox peaks at 0.11 and 0.27 V in a solution of 5 mM $[Fe(CN)_6]^{3-/4-}$ (0.1 mol/L PBS, pH 7.4). An obvious increase of peak current could be observed when GO was used on bare paper due to the large surface area and high conductivity of GO. Then a further increase was obtained after chitosan was coated. This could be attributed to that the electrostatic attraction between positively charged chitosan amino group and negatively charged $[Fe(CN)_6]^{3-/4-}$ accelerated electron transfer on the electrode surface. The peak current of molecularly imprinted polymer modified paper was very weak before elution, but recovered after templates removal.

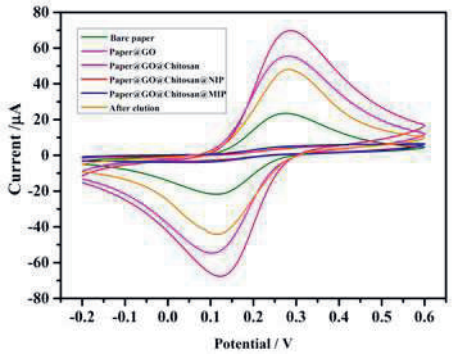

Fig. 2. Cyclic voltammograms of paper electrodes at the different steps of fabrication process.

Performance of μPAD

Because CEA was not electrochemically active, a blocking effect was caused by the presence of the CEA, resulting in the reduction of electron transfer. The relationship between the peak current variation and the CEA concentration was detected using differential pulse voltammetry (DPV) under the optimal conditions. As shown in Fig. 3, the differences of peak current were proportional to the logarithm concentration of CEA in the range of 1−500 ng mL^{-1} and the regression equation was ΔI (μA) = 19.342 lgC (ng mL^{-1}) + 6.933 with correlation coefficient of 0.994.

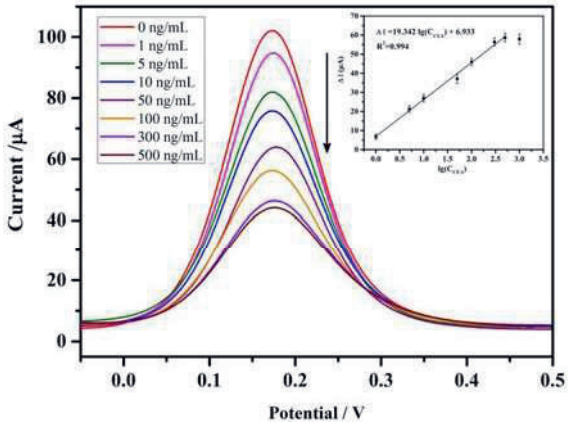

Fig. 3. DPVs of μPADs in 5 mM $[Fe(CN)_6]^{3-/4-}$ + 0.1 M PBS (pH 7.4) with different concentration of CEA. Inset is the calibration curve.

Conclusion

This paper describes a novel strategy to fabricate a low-cost electrochemical μPAD readily based on surface molecularly imprinted technology. The electrochemical μPAD is successfully applied for detection of CEA, showing promising prospect in the field of clinical diagnostics and healthcare in the future.

Acknowledgements

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