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Impedimetric immunosensor for the detection of amyloid beta (1-40) on ortho-polyphenyldiamine modified Platinum micro disk electrode

Abstract

The development of an electrochemical detection of amyloid beta (Aβ (1-40)) peptides as a bio marker of Alzheimer's disease (AD) was carried out. A Pt disk microelectrode was modified with poly-ortho- Phenylenediamine (PPD) and mouse monoclonal beta amyloid antibody (mAβA) was immobilized to form Pt/PPD/mAβA immunosensor. Studies on the optimal conditions for the sensor real application like the antibody-antigen reaction and the concentration effect of Aβ (1-40) solutions, among others, were determined. Detection evaluation was observed through the changes in the Nyquist spectra and values of charge transfer resistance (Rct) were extracted from a modified Randles equivalent circuit. A semi circle Nyquist plot was observed in the presence of Aβ (1-40) whereas a linear spectra were exhibited in the absence of Aβ (1-40). In addition, as the concentrations of Aβ (1-40) solution increased, the diameter of Nyquist plots were also increased. A promising in vivo immunosensor for Aβ (1-40) detection is anticipated to be used as an alternative in monitoring inhibitors of Aβ (1-40) aggregation research.

Keywords: electrochemical impedance spectroscopy, amyloid beta, alzheimer's disease, platinum, biosensor

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Introduction

Due to the awareness of the AD present among the society, the growing of many diagnoses, treatments, researches and methods are developing for the AD treatment. Rapid technological development that associates with AD biomarkers and treatments has been started since the last decade. In addition, there are advance techniques and studies on Aβ determination that have been used such as the Centrifuging and mass-based analyses, Black lipid membranes, Microscopy technique, Nuclear Magnetic Resonance (NMR), Langmuir Monolayers, Infrared Spectroscopy and others.[1] Meanwhile, Conventional enzyme-linked immunosorbent assay is currently available to detect Aβ, but it is costly, labor-intensive, and has not been proven very effective when given in the clinical sample analysis in practice.[2] In contrary, biosensor technology has provided a wide platform to study the degeneration of proteins in brain. Biosensor can be defined as a device that uses biological or chemical receptor to detect analyte by converting from biochemical reaction to the electrical signal and the result will give detailed information on the binding affinity.[3] Biosensors are constructed for monitoring a biological reaction at the surface of electrodes. Varieties of biomolecules such as enzymes, nucleic acid, cells, DNA, RNA and microorganisms have been successfully immobilized on the surface of electrodes in the way of biosensors development.

An immunosensor which is a one of a type of affinity biosensor has been developed. Immunosensor is specifically detecting the binding between the antigen and antibody and more sensitive to the subtle physiochemical changes during the antigen antibody interaction. Electrochemical impedance spectroscopy (EIS) have been widely used in the characterization and analysis of immunosensors. The main reason of using EIS technique is due to the changes on the impedance during the sensor's surface modifications and analyte binding can be identified. Impedimetric immunosensing assay, based on the integration of specific surface antibodies such as a biorecognition element and an impedimetric signal transducer presents will offer a promising alternative for detection of Aβ. This type of assay not only has inherent specificity and selectivity provided by antibody-antigen biospecific interaction on electrode surfaces, but also many advantages offered by the impedimetric-based biosensing technology, such as high sensitivity, label-free detection capability, cost-effectiveness in mass production, and the possibility of miniaturization. Due to these merits, impedimetric immunosensing has attracted a tremendous amount of attention in biosensors scientific community in developing biospecific detection of various disease biomarkers and has been shown to be superior to both conventional and modern assay methods. The sensor performance depends on several factors such as the architecture on the Pt/PPD surface, potential applied , mAβA-antigen interaction, the concentration of Aβ(1-40) as well EIS equivalent circuit as described elsewhere.[4]

The interaction of mAβA to amyloid beta (1-40) under EIS monitoring

The mAβA-Aβ (1-40) coupling was investigated by tracking the changes in impedance response over time before and after the presence of the Aβ (1-40) solution on the Pt/PPD/mAβA surface in PBS solution at the frequency range from 100 kHz to 0.1 Hz. The resulting curves are as illustrated in Figure 1 were due to the mAβA immobilized on the sensor's surface and the effect of coupling binding between the mAβA and Aβ (1-40). From this observation, a Nyquist plot showed almost a straight plot as seen in Figure 1a with the absence of Aβ (1-40) immobilized. Nevertheless, it was clearly illustrated that as the Aβ (1-40) solution was dip on a sensor surface, the Warburg behavior was minimized and a clear large semicircle displayed at the higher frequency (Figure 1b). This decreasing of impedance is due to the specific mAβA- Aβ (1-40) reaction and could be attributed from the difference of dielectric and conductivity properties of electrode surface. Therefore, the changes in interface properties became an evident as the mAβA- Aβ (1-40) interaction occurred on the surface since the differences in impedance spectrum were generated. In

summation, the most significant changes that observed in the real part of impedance are the Rct value which is extracted from the equivalent circuit. The Rct value is higher for Pt/PPD/mAβA linked which is 30.6MΩ. This large value in Rct is because of the mAβA, a large molecule complex was formed and it was capable to block the flow current through the interface. Meanwhile, as the Aβ (1-40) was adsorbed on the Pt/PPD/mAβA the lower Rct value was produced which is 1.52 MΩ with the lowest chi square ($\chi 2$) obtained was 0.06. The lowest value of $\chi 2$ obtained represent the most fitted of equivalent circuit onto the system. A simple, sensitive and fast electrochemical immunosensor for Alzheimer's disease biomarkers is presented. The changes signal from impedance generated due to the detection of Aβ 1-40 peptide was demonstrated to be practicable in the development of a direct, one-step amyloid beta biosensor. The reagent less detection process based on the inherent adsorption of Aβ (1-40) peptide was simplified for the sensor utilization.

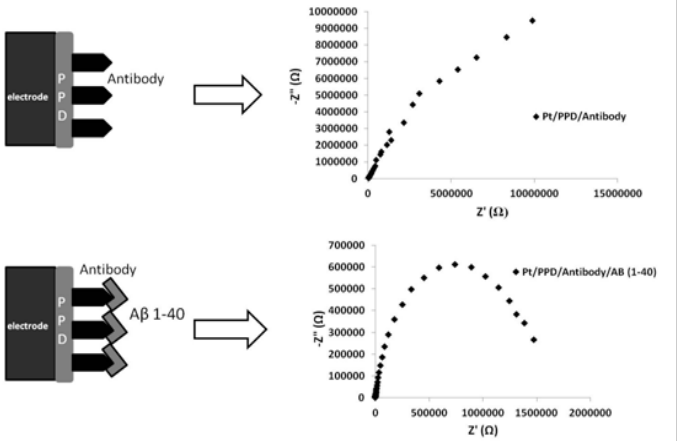

Figure 1 Nyquist response of Pt/PPD/ mAβA microelectrode corresponding to the (A) absence and, (B) presence of Aβ (1-40).

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Conflict of interests

There is no conflict of interest.

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