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A mini review of electrochemical genosensor based biosensor diagnostic system for infectious diseases

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Abstract

The quest for alternative methods is driven by the need to provide expertise in real time in biological fields such as medicine, pathogenic bacteria and viruses identification, food protection, and quality control. Polymerase Chain Reaction (PCR) and Enzyme Linked Immunosorbent Assay (ELISA) are examples of traditional methods that have some limitations and lengthy procedures. Biosensors are the most appealing option because they provide easy, dependable, fast, and selective detection systems compared to conventional methods. This review provides an overview of electrochemical genosensor based biosensor diagnostic system for infectious diseases detection as well as their applications, demonstrating their utility as a fast and responsive tool for detecting pathogenic bacteria, viruses, GMOs, and human diseases.

Keywords :
Electrochemical sensor; infectious diseases; DNA probe; nanoparticles; nucleic acid complementation

1 Introduction

The development and application of electrochemical genosensors is progressing at a rapid rate, and the description and classification of electrochemical genosensors cannot definitively address all information and nuances. The signal transduction mode or the biological specificity conferring mechanism may also be used to classify biosensors. In electrochemical genosensors, the bioreceptor may be a probe with a short series of oligonucleotides, as in electrochemical DNA-based genosensors, or an aptamer, a synthetic oligonucleotides sequence, as in electrochemical Aptamer-based genosensors that are immobilized at the transducer surface (Nor Azizah Parmin, Hashim, and Gopinath 2018; Uda et al. 2018). Genosensors based on electrochemical DNA may be paired with nanoparticles or nanocomposites such as gold nanoparticles (AuNP) (Azizah et al. 2016) and quantum dots (CQD) (Ma, Li, and Zhang 2018) to enhance both oligonucleotide hybridization sensitivity and sequence immobilization on the transducer surface. Genosensor based on DNA specific detection become the most promising method for infectious disease detection.

DNA can be successfully isolated from different biological sources like blood (Madhad and Sentheil 2014), saliva (Durdiakov et al. 2012; Lazarevic et al. 2013; Quinque et al. 2006) and swab tissue (Baay et al. 2011; Ghittoni et al. 2010; Verdon, Mitchell, and van Oorschot 2014; Yang et al. 2014). Conventionally, DNA analysis by using human samples was a lengthy process consumes several days or weeks. DNA extraction from biological samples, quantification of DNA extract, amplification by using Polymerase Chain Reaction (PCR), separation of amplified products by using gel electrophoresis, analysis of data for confirmation basically using DNA sequencing and result reporting are the routine analysis for DNA (Yang et al. 2014). All these analyses require at least 8 to 11 hours or more depends on skilled personnel like molecular biologist to complete the process under laboratory conditions.

Some DNA extraction methods become the most important thing in molecular biology and for the analysis on DNA biosensor. Purification of viral DNA with minimal elution volumes is required for higher sensitive detection for viruses. In the present study, the virus Human Papillomavirus (HPV) is targeted and analysed on the Interdigitated Electrodes (IDE) sensor (T. Lakshmipriya et al. 2016; S. Nadzirah et al. 2020; N.A. Parmin et al. 2019). Preparation of HPV DNA from the free viral particles is needed, especially for Specimen Transport Medium (STM) swab, typically used for sample collection system in Pap smear by Obstetrics and Gynaecology doctors. Direct swab method has used in the clinical laboratories and forensic laboratories (Gangano et al. 2013; Holland and Wendt 2015) and also for commercial sample processing equipment. Swab lysis in liquid lysate form is highly suitable for the microfluidic system (Brun et al. 2012; Kim et al. 2009; Yang et al. 2014).

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2 Electrochemical biosensor

Biosensors are a significant analytical instrument that alternate to conventional cellular and biological assays. It has arisen for viral detection that use organs, tissues, cells, and invasive methods. For many years, electrochemical biosensors have been used in a number of fields including medical and environmental. This type of biosensor analyzes any changes in dielectric properties and charge distribution on the electrode surface caused by the interaction of analyte and biorecognition factor. Electrochemical biosensors are graded as amperometric, potentiometric, voltammetric, and impedimetric based on the method of transduction. In molecular biology, the transduction was defined as the mechanism by which a virus or viral vector introduces foreign DNA into a cell.

An electrode transducer converts a chemical reaction into an electrical signal, which is used in electrochemical biosensors. Electrochemical biosensor was said to be highly sensitive transducers because they have ultra-low sensitivity (parts per trillion or sub-pico or femto molar ranges), linear efficiency, low power consumption, and good resolution. These sensors have the potential to be used as point-of-care (POC) and point-of-need detection systems. When evaluating a patient's care reaction, such testing helps medical staff to make fast decisions depending on the patient's condition. It is important to provide a wide understanding of the most recent novel methods and the problems that come with infectious disease electrochemical diagnostics. This kind of technology assist the researchers in developing the best possible solution of biorecognition elements that effectively overcome the difficulties that electrochemical transducers were facing.

3 Genosensor

A new type of affinity biosensor is created by combining nucleic acid layers with electrochemical or optical transducers as a DNA biosensor or well known as genosensor for low-molecular-weight molecules. Biological substance in various combinations in conjunction with various forms of transducers are a fascinating research subject to explore nowadays. A genosensor, also known as a gene-based or DNA biosensor, measures specific binding processes at the sensor surface, such as the formation of DNA–DNA and DNA–RNA hybrids. It also measures the interactions between proteins or ligand molecules and DNA. The following measures are involved in the design of a genosensor: i. The sensor surface is changed to provide an active layer for the DNA probe to bind to. ii. The probe molecule immobilization on the surface, preferably with a balanced density and packing orientation. iii. DNA hybridization at the sensor–liquid (aqueous form) interface to detect target gene sequences, preferably with controlled packing density and orientation of molecules on the surface.

In DNA biosensors based on electrochemical hybridization transduction, the high specificity of hybridization reactions is combined with the excellent sensitivity and portability of electrochemical transducers. The ultimate aim of all research studies involving genosensor is to build DNA biosensors in order to lay the groundwork for a potential DNA microarray device. Electrochemical genosensors based on various materials and transducers, in terms of chip-based technology, have recently been developed in response to clinical demand for promising results. Biosensors based on nucleic acids (genosensors) are being designed to overcome the limitations of traditional methods. The reverse transcription polymerase chain reaction (RT-PCR) is a tool for amplification of nucleic acids and become the gold standard of the molecular diagnostic studies. There are some drawbacks of RT-PCR. The probability of false-negative and false-positive results with the RT-PCR test is high. Inadequate of viral RNA for RT-PCR at the time of detection will result in false-negative results.

For infectious diseases, genosensors have evolved into a responsive and reliable technology. Electrochemical genosensors have attracted a lot of attention among genosensors because of their fast response, sensitivity, and cost-effectiveness, as well as their ideal for point-of-care (POC) research due to their compatibility with microfabrication technology and easy operating mode.

4 Infectious disease cause by pathogenic virus

Pathogens were classified as microorganisms that cause infectious disease. Pathogenic virus can damage the cells by entering the body and cause problems. During vaccination, pathogens are introduced into the body in weakened form, allowing the body to produce enough white blood cells to protect against the pathogens and prevent disease. Antibiotics are useful in the fight against bacteria that are not resistant to antibiotics, but not against viruses. Early, fast, and accurate identification of infectious virus is directly linked to the efficient management of the spread of disease and the enhancement of patient outcomes are two issues that need to be discussed. The identification of unique nucleic acid sequences of the target virus is the most common method for diagnosing and assessing viral infections (Kelley 2017). Infectious diseases spread directly from one person to another in some cases, but not all. Several viruses, including HIV, Human Papillomavirus (HPV) (N.A. Parmin et al. 2019), dengue virus (Nuzaihan et al. 2016), and hepatitis virus, have been detected using electrochemical genosensors. Dengue viral RNA can be identified at levels of 103 to 106 copies per milliliter in biological samples (blood, saliva, or urine) (Hue et al. 2011), a special DNA capture probe is modified and sandwiched with a digoxigenin-labeled detector probe (HPV-16 and HPV-18) to detect DNA sequences from high-risk human papillomavirus (hrHPV) strains (Bartosik et al. 2016). HPV also can be detected by using electrochemical genosensor due to easy to handle compared to molecular methods (Azizah et al. 2015; N.A. Parmin et al. 2019).

5 Infectious disease cause by pathogenic bacteria

Infectious diseases spread directly from one person to another in some cases, but not all. Bacterial detection and identification are primarily based on microbiological and biochemical recognition of various microorganisms techniques, which can take anywhere and the results will take anywhere from 3 to 7 days to appear (Bifulco, Ingianni, and Pompei 2013). Electrochemical genosensor was developed based on an oligonucleotide probe derived from the Escherichia coli O157:H7 genome's 16s rRNA coding region (Sh. Nadzirah et al. 2015; Rajapaksha et al. 2017). A life-threatening infection can be caused by as little in a milliliter of blood as 1 to 10 colony-forming units (cfus) of bacteria [28]. When used as a target, ribosomal RNA should have a copy number of 103 or 104, which corresponds to detecting a subfemtomolar RNA concentration in a sample with an overwhelming abundance of non-target RNA. Direct detection methods for bacterial infection face a significant challenge as a result, and molecular-level analysis is normally performed after bacterial culture enrichment (Kelley 2017). The pathogens that cause urinary tract infections (UTIs) such as Staphylococcus saprophyticus, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, and Pseudomonas aeruginosa. Urine that contains more than 105 cfu mL-1 is considered positive for UTIs (Karaba et al. 2021).

6 DNA structures at electrodes

The electrochemical behavior of deoxyribonucleic acid (DNA) and its reactions with different types of ligands and complemen-

tary or partially complementary nucleic acid sequences are both influenced by the surface state of DNA immobilized at electrodes. Since they directly associate with the presence of an active infection, DNA and RNA sequences are ideal candidates for infectious disease surveillance (Kelley 2017). Gold-standard techniques include microscopy, plating and culturing methods, nucleic acid-based approaches, and immunological assays were used for diagnosing bacterial and viral infections, The most popular approach for determining virus-specific antigens is to use Enzyme Linked Immunosorbent Assay (ELISA), which have been granted regulatory approval and are commercially available. However, they are time-consuming and multi-stage, have low sensitivity, can produce false negative results, and highly dependent on operator skills (Karaba et al. 2021; Uda et al. 2018).

The identification of nucleic acids can be more precise and sensitive than immunological methods (Nor Azizah Parmin, Hashim, and Gopinath 2017). Since they associate with the existence of an asymptomatic microorganism, these special DNA and RNA sequences are ideal targets for infectious disease study. Electrochemical biosensors combined with low-cost field-portable and programmable battery-operated instrumentation open up exciting new possibilities for non-experts to perform easy and cost-effective analytical strategies (Thangavel Lakshmipriya et al. 2016).

7 Conclusion and future perspectives

The rapid development and the use of biosensors can never be limited. The use of nanoparticles, nanocomplexes, and nanostructures has increased, allowing progress in electrochemical genosensors for pathogenic bacteria, virus detection, plant breeding, food safety, and quality control. Electrochemical genosensors are still the most appealing choice for developing a functional and a portable device is used to provide easy, accurate, fast, and selective detection systems.

Declaration of competing interest

The authors declare no known competing interests that could have influenced the work reported in this paper.

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