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Nanomaterials Based Electrochemical Biosensors for the Detection of COVID-19

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Mini Review

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Abstract

The world is currently facing a global pandemic associated with the coronavirus (COVID-19), severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), for which virulence and infectious dose data are still emerging. The recent outbreak of potential infectious viral disease is caused by newly discovered coronavirus, which belongs to the single-stranded positive strand RNA virus. SARS-CoV-2 is dangerous threat to public health, economics and global disciples. Therefore, it is important to detect and isolate treat individuals at the early stages of the disease to control its spread. Since SARS-CoV-2 is new and due to lack of any approved drug or vaccine, there is urgent need for a highly sensitive and selective diagnostic tools to indentify infected people. Recently, various analytical methods are reported for the detection of several kinds of viral diseases based on various sensing principles. Of all the analytical tools available, electrochemical biosensors have achieved a high sensitivity, selectivity, rapid and portable analysis through the integration of advanced nanomaterials in the device fabrication. The present article explored the use of nanomaterials in the development of electrochemical biosensor for the detection of SARS-CoV-2 in various biological samples.

Keywords: Coronavirus; COVID-19; Electrochemical Biosensor; Nanomaterials; Viruses; Diagnosis; Pandemic

Abbreviations: RNA: Ribonucleic Acid; DNA: Deoxyribonucleic Acid; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; AP: Alkaline Phosphate; IC: Indigo Carmine; SPCEs: Screen-Printed Carbon Electrodes.

Introduction

Virus is a submicroscopic structure consisting of genetic material that can replicate through the hosts [1]. The genetic materials in the virus cannot replicate without the host cell, but remain as crystalline for long period until they come in contact with host cells [2]. The genetic material such as Ribonucleic acid (RNA) or Deoxyribonucleic acid (DNA) is encapsulated by a layer of protein. Upon the entrance of viral genome into the host cell, the replication and protein machinery is hijacked to make more virus particles is called virions [1]. The virions are capable to infect new cells once they release from the host cell. Currently world is facing such type of potential viral outbreak, which is pandemic, associated with the coronavirus (COVID-19), severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Virulence and infectious dose data of SARS-CoV-2 is still emerging worldwide. The need of the hour is to control the spread of SARS-CoV-2 worldwide. For this, it is important to detect and isolate treat individuals at the early stages of the SARS-CoV-2 disease. In view of this, the mini review summarizes the electrochemical biosensing detection technologies for SARS-CoV-2.

Electrochemical Biosensors for the Detection of SARS-Cov-2

Electrochemical biosensors measure the electrochemical changes that occur on the surface of transducer that is

the surface interaction or reaction with the SARS-COV-2. Based on electrical changes, change in current is measured at constant voltage (amperometric method), change in voltage is measured (potentiometric technique) and change in impedance is measured (impedimetric tool), different electrochemical techniques are being utilized for the fabrication of biosensing device for the detection of SARS-COV-2. The cost effectiveness, sensitivity, selectivity, biocompatibility and easy to operate are the advantages of electrochemical biosensors [3]. Recently, various nanomaterials have been used in the development of SARS-COV-2 biosensors in order to improve the sensitivity and selectivity of the biosensing devices. In this context, Mahari, et al. fabricated an electrochemical biosensor through the use of fluorine doped tin oxide electrode modified with gold nanoparticles (FTO/AuNPs) and immobilized with SARS-CoV-2 monoclonal antibody (SARS-CoV-2Ab) for the selective detection of SARS-CoV-2 in spiked saliva samples [4]. The output response of the proposed biosensing device is change in the electrical conductivity upon the binding of SARS-CoV-2. In the device fabrication, AuNPs acted as a bridge between SARS-CoV-2Ab and FTO substrate and utilized to improve the electrochemical signal. Under optimized conditions, the developed immunosensor able to detect SARS-CoV-2 in the concentration range of 1fM to 1μM. Analytical utility of the proposed device established in determining SARS-CoV-2 in spiked saliva samples with detection limit of 90fM [4]. Yet in an another work, Paredes et al. designed a biosensor using self-assembled monolayer, thiolated oligonucleotide, onto gold nanoparticles modified screen printed carbon electrodes for the detection of SARS-CoV-2 [5]. The fabricated biosensor is indicated as genosensor. The genosensor response was found to be linear in the range of 2.5 to 50 p mol/L with limit of detection of 2.5pmol/L [5].

A new biosensor has been developed, by Mavrikou, et al., through the use of engineered biorecognition element (mammalian cells bearing the human chimeric spike S1 antibody) for the detection of S1 spike protein expressed on the surface of the SARS-CoV-2 [6]. In the present work, the binding of the protein to the antibodies results in a selective detection and considerable change in the cellular bioelectric properties measured by bioelectric recognition assay. The device showed actual availability of SARS-CoV-2 *via* change in the membrane potential and other electric properties of the cells in a high sensitive, speed and reproducible mode. The biosensor provided detection limit of 1 fg/mL and linear response range was between 10 fg and 1 μg/mL. The biosensor was also configured as ready to use platform, including a portable read out device operated through tablet/smart phone. The demonstrated biosensor was potentially applied for the mass screening of SARS-CoV-2 surface antigens without prior sample processing [6].

The detection of genomic DNA of SARS-CoV-2 was done by Costa-Garcia and group [7]. In the report, they have made use of strong thiol-gold interaction to immobilize SH-DNA probes on a sputtered gold film. Upon hybridization with the biotinylated 30-mer SARS-CoV-2 sequence, conjugation with alkaline phosphate (AP) - labelled streptavidin occurred, thus promoting the conversion of the enzymatic substrate 3-Indoxy phosphate (3-IP) into the electroactive indigo carmine (IC). The voltammetric signal was then measured and correlated to the presence and amount of the target analyte. The selectivity of the developed biosensor was assessed by using a 3-base mismatch DNA target as the negative control. Due to the nature of the SARS-CoV-2 virus to undergo potential mutation in order to adapt to the environment, the same group showed that the developed biosensor was also able to distinguish among the complementary target and sequences carrying one and two base mismatches respectively [7]. Yet in an another report, Diaz-Gonzalez et al. have used the same approach for the immobilization of the biotinylated probe through electrostatic interactions on screen-printed carbon electrodes (SPCEs) modified with positively charged polylysine [8].

Mark et al. has developed a commercial electrochemical biosensor, ePlex® SARS-CoV-2, for the qualitative detection of SARS-419 CoV-2 in nasopharyngeal swab specimens. The detection process involves the extraction of viral RNA from the swab samples and reverse-transcribed to complementary DNA (cDNA) before PCR amplification. Next, a complementary ferrocene-labelled signaling probe was combined with the amplified target DNA to form a target DNA/signaling probe complex. Upon hybridization with the specific capture probes immobilized onto the surfaces of the gold electrode microarray, the electrochemical signal from the ferrocene label was correlated to the presence of the target DNA. This study showed the clinical performance of the ePlex® SARS-CoV-2 test to be comparable to the approved RT-PCR, with less susceptibility to contamination and reduction in sample preparation time required [9].

Conclusion

The pandemic of corona virus has motivated many researchers to make efforts towards the development of an advanced detection technology with high degree of efficiency and cable of responding to the present demand for early diagnosis to manage the spread of virus. Since there is no vaccine for the treatment of SARS-CoV-2, therefore management of this pandemic is only possible through its monitoring, prevention and early stage detection. However, this virus is novel and complex and hence it is necessary to invent rapid, sensitive and low cost technology for the early diagnosis. The biosensors have shown their potential role towards the diagnosis of viral infections and hence may

perhaps fulfil the current demand for early stage diagnosis. A number of biosensing electrochemical methods reported including impedimetric, amperometric and potentiometric have been discussed. The reported methods could be used to detect the SARS-CoV-2 within short period of time and they could offer alternative approach to PCR based testing for SARS-CoV-2 infection.

Future Perspectives

Compared with the traditional analytical method, polymerase chain reaction, biosensors have number of advantages, including ease to achieve selectivity and selectivity, smaller size and high accuracy for the viral detection. Though the reported biosensors having advantages has many advantages, but still they also suffer from some limitations: (1) biological complexity of samples, (2) preparation and screening of suitable antigen antibody for the fabrication of biosensors and (3) miniaturization of the devices. In future research, the application of electrochemical sensors and biosensors by the application of various stable nanomaterials could be studied in detail, modification of electrode substrates with biocompatible nanomaterials (quantum dots and carbon nanomaterials) could be utilized to achieve selectivity. The affinity of sensor to specific biological targets could be explored to generate sensitive response.

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