Recent Reports on Application of Electrochemical Techniques for Corona Virus Diseases (COVID-19) Diagnosis: A Review

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Article info	Abstracts			
Keywords:	Coronavirus disease (COVID-19) belongs to the β -coronavirus genus and is			
Covid-19,	caused by Severe Acute Respiratory Syndrome Corona Virus-2 has spread out			
Polymerase Chain Reaction, Respiratory diseases, Electrochemical Biosensor,	the world since the end of 2019 and has resulted in a pandemic with never			
	known in socioeconomic consequences in the world. It can be transmitted			
	from an infected person to normal one either by droplet, contact, orborne,			
	fomite, fecal-oral, and bloodborne transmissions which exacerbate the rapid			
	spread of the virus. This review focuses on the current viewpoint to highlight			
	recent advances in the analysis of the novel coronaviruses by the			
	electrochemical methods for the diagnosis mechanisms of the COVID-19			
	pandemic and describe prospects for this technology. The development of low-			
	cost, easy-to-use, accurate, and rapid diagnostic electrochemical biosensors			
	with improved performance to perform accurate and widespread testing is			
	urgently needed in this stage to enable the infection control and suppress the			
	spread of the disease and also plays a major role in stopping the pandemic.			
	Electrochemical biosensors provide excellent diagnosis having better limit of			
	detection, and selectivity of electrochemical signal transducers with the			
	specificity of biomolecular recognition strategies.			

1. Introduction

The word Corona comes from the Latin word meaning "crown" [1]. The recent COVID-19 disease caused by SARS-CoV-2 coronavirus is spreading around the world and hence, accurate and easy to operate, cheap portable sensors are crucially important for the clinical diagnosis of COVID-19. It is a highly contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is declared by WHO as a global "public health emergency of international concern" on 30th January 2020, based on the report related to the epidemic caused by the 2019 novel coronavirus pandemic, that was started in a Wuhan seafood market, Hubei province according to the reported elsewhere [2, 3]. The world health organization assigned the name of the pandemic, which has spread so rapidly throughout the world, as coronavirus disease 2019 (COVID-19) and on the other hand, depending to their severe cases and effects international committee of the taxonomy of

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viruses named this novel coronavirus (COVID-19) severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) SARS-CoV and MERS-CoV originated in bats, and it appears to be so for SARS-CoV-2 as well [4].

These Coronaviruses are categorized into four genera, such as alpha-CoV, beta-CoV, delta-CoV, and gamma-CoV. While alpha and beta-viruses infect mammals, delta, and gamma viruses can infect only birds and these viruses are detected in a very wide selection of animal species, including humans. The virus that causes the COVID-19 disease belongs to the β -virus genus [5].

From the beginning of the twenty-first century onwards to these days, three groups of coronaviruses have crossed the species barrier: the severe acute respiratory syndrome SARS-CoV, and Middle-East respiratory syndrome (MERS-CoV)[6], and SARS-CoV-2 [7] coronaviruses. Compared with the previous coronaviruses that caused large-scale epidemics such as the Middle East Respiratory Syndrome (MERS) and severe acute respiratory Syndrome (MERS), the transmission rate for SARS-CoV-2 is much higher, with an average of two to three people becoming infected for every already infected person [8].

Physically the coronavirus has approximately 125 nm in size consisting of an envelope of 85 nm diameter, while the spikes are 20 nm long. The virus is a single-stranded RNA with a size ranging from 26,000 to 37,000 bases and is the largest known genome among RNA viruses [9]. The most abundant structural protein found in the virus is the membrane protein that has two different conformations that can promote the binding to nucleocapsid. The mechanism of infection can be understood as: the attachment to host receptors takes place with spike proteins; the genomic binding to the replication-transcription complex is abetted by nucleoplasid proteins, and finally, the membrane protein and envelopes protein provide the shape to virion particles, and the release of particles [10].

The transmission mode of the virus of the novel coronavirus is either: droplet, contact, airborne, fomite, fecal-oral, or bloodborne transmissions which exacerbate the rapid spread of the virus. Thus, rapid diagnostic testing for SARS-CoV-2 at a large scale is crucial for virus detection, surveillance, and swift management of outbreaks [11, 12]. The symptoms of the disease when it infects the breathing system mainly include fever, dry cough, and fatigue [13]. Due to the effect of and degree of spread of the pandemic, there are several methodologies to detect it.

2. Diagnosis and treatment of coronavirus infections Respiratory virus infections have been detected/analyzed by a combination of several techniques such as enzyme immune assay, direct fluorescence antibody, staining, cell culture, and also nucleic acid amplification tests, reverse transcriptase-polymerase chain reaction, and immunoblotting [14]. The COVID-19 infectious disease eradication is an enormous challenge in healthcare systems, primarily due to the challenges associated with the spread of COVID-19 viral infections as well as the potential capability of the virus to survive through mutations [15]. Due to the rapid and widespread and also deadly effect of the novel coronavirus, some approved specific vaccine treatments have been licensed for COVID-19, yet prevention measures (e.g., blocking the transmission routes such as the mouth and nose by a napkin, frequent washing of hands, and hand disinfection after presence in public places) are important strategies to combat Coronavirus diseases.

In recent times, various coronavirus diseases diagnostic assays have been emerged in the world, namely: protein microarray [16], enzyme-linked immunosorbent assay (ELISA) [17], reverse transcription loop-mediated

isothermal amplification (RT-LAMP) [18], immunofluorescence [19], and viral flow cytometry (FCM) [18] for fast and accurate diagnosis of coronavirus infections. Despite that, the determination of the genome sequences of coronaviruses, e.g., COVID-19, leads to the recognition of reverse transcriptionpolymerase chain reaction (RT-PCR) assays as a standard and highly sensitive technique for clinical diagnosis of COVID-19 but the development of facile and quick assays is still a vital necessity [20]. Recently based on the severity of the case, the diagnostic tests for

3. Electrochemical biosensors

Some techniques such as nucleic acid amplification technique have been modified by multiplex polymerase chain reaction, (PCR) with fixed microarrays for clinical diagnosis. But they have their drawbacks such as these methods require expensive chemical compounds and instruments, time-taking sample preparation, and trained personnel. To overcome these disadvantages, techniques such as interferometry [22], surface plasmon resonance [23], and field-effect transistor [24] have been explored for the detection of viruses. The emergence of the electrochemical methods being as best technique in the past decade has seen explored for the detection and quantification of viruses. Electroanalytical methods are versatile and powerful analytical tools, which can provide high sensitivity, low detection limits, and low cost, associated with the use of inexpensive instrumentation which presents as an additional advantage to relatively low operator training requirements. [25].

Electrochemical biosensors for the analysis of viral diseases including the the current novel Covid-19 diagnosis provide an alternative and reliable means to clinical diagnosis it the diseases and are considered useful in clinical diagnostic methods and point-of-care testing (POCT) procedures [26]. As can been concluded

COVID-19 can be classified into two broad categories, those are molecular diagnostic tests, antibody or serology tests, and tests for management of COVID-19 [21].

This review processes mainly focused on the current viewpoint to highlight recent advances in electrochemical sensing of the COVID-19 pandemic and describe prospects for this technology. The application of different electrochemical analysis techniques for the current diagnostic method of Covid-19 of patients' samples had been reviewed.

that iosensors are advantageous for point-of-care and field detection applications as they are economical, portable, and easily operable techniques, which have emerged as valuable alternative solutions to conventional diagnostics, with rapid turnaround, pointof-care deployment, and low cost [27]. Ordinarily, conventional biosensors composed of three distinct components as a principle: a part that recognizes the analyte or biological identification part, a signal transducer, and an amplifier or a part that is known as the reader device [28].

Coronavirus diagnosis involved fast techniques for detection and control of the diseases in a very short period and rapid detection of the virus provides both accurate and targeted therapy. Nowadays electrochemical biosensors have emerged as a powerful tool to complement ELISA methods of analysis of diseases such as the virus including the current novel coronavirus [29]. Biosensors have been reported for testing and virus detection has been using specific transducers as a better choice to the traditional assays. They are closely linked within a microsystem of the Physico-chemical transducers or transducers of different types such as piezoelectric, electrical, optical, and electrochemical techniques [30].

Electrochemical biosensors are favorable for their lowcost assembly rapid detection, and quantitative readout. These platforms further allow for multiplexing, miniaturization, and automation [31]. Compared with other optical ones, electrochemical detectors are recently more advanced interest due to the exploitation of novel materials and advances in instrumentation technologies for sensitive, rapid, and selective identification, detection, and quantification of viruses [29]. This electrochemical technique offers an excellent capability to discriminate small changes from the recognition event on the electraoactive surface of th electrode, thus enabling label-free detection with no need for a single antibody for COVID-19 analysis. Technically, such binding events between biomolecules affect the ability of the redox indicator (usually $[Fe(CN)_6]^{3-/4-}$ couple) to reach the electrode surface and consequently its redox conversion.

4. Electrochemical sensor in covid-19 diagnosis

Electrochemical biosensors have been successfully applied for the detection of coronavirus diseases due to their unique characteristic such as: they combine the selectivity of electrochemical signal transducers with the specificity of biomolecular recognition strategies. Among them, paper-based sensors and other related assays have evolved rapidly due to the conversion of paper-based microfluidics, functional paper coatings, and other new electrical and optical readout techniques. Nanomaterials have gained substantial attraction as key components in paper-based sensors, as they can be coated or printed relatively easily on paper to locally control the device functionality [32, 33]. The devices like electrochemical paper-based analytical device for the diagnosis of COVID-19 sometimes consists of three parts (working ePAD, counter ePAD, and closing ePAD), and they have their own functions [33]. Those COVID-19 ePAD is intended for the qualitative screening of total SARS-CoV-2 antibodies against the viral protein.

Yakoh A. et al. [33] had been successfully studied the SARS-COV-2 by detecting the immunoglobin with square wave voltammetry-based ePAD. According to their report, both IgM and IgG were seized by SP RBD and illustrate similar performance as shown in Figure (Figure 3A and B) and IgM test result revealed a higher sensitivity than IgG testing (Figure 3C), which could be ascribed to a larger IgM antibody size. IgM is the largest immunoglobulin, with pentamer units and ten antigenbinding sites (~900 kDa) as described somewhere else [34]. This electrochemical immunosensor exhibited a sensitive response to the presence of SARS-CoV-2 antibodies, where the ΔI proportionally increased with logarithmic concentrations of SARS-CoV-2 IgG and IgM in the range from 1 to 1000 ng/mL ($R^2 > 0.99$). From this logarithmic response, the limit of detection (LOD) values of SARS-CoV-2 IgG and IgM were 0.96 and 0.14 ng/mL, respectively according to the report.

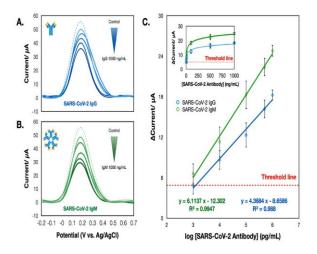


Figure 3: SWV responses of the COVID-19 ePAD tested with different concentrations of SARS-CoV-2 IgG (A) and SARS-CoV-2 IgM (B) in the presence of 5 mM $[Fe(CN)6]^{3-/4-}$. (C) A linear relationship between ΔI vs log[conc] of SARS-CoV-2 IgG and IgM and its corresponding relationship between ΔI and concentration of SARS-CoV-2 IgG and IgM.

Generally, one can easily estimate the redox current response based on the limit of detection (LOD) and starting point of the calibration plot from the curve (~ 1 ng/mL) as the cutoff threshold for additional experiments furtherly. From the reported result, the reproducibility evaluated in terms of the percentage relative standard deviation (RSD) from different ePADs for triplicate experiment (n=3) was 4.2% and 3.3% for IgG (1000 ng/mL) and IgM (1000 ng/mL) respectively.

Furthermore Yakoh et al. [33] investigated the comparative performance characteristics of their developed COVID-19 ePAD with other techniques like ELISA method practically by collecting real serum samples from clinical formulations and those samples were tested with the prepared ePAD. In their study report, the researchers had collected total of 17 clinical serum samples and those samples were tested with both the ELISA and ePAD systems comparatively

The ELISA result confirmed that from total of 17 serum samples tested, 7 of these sera were confirmed to be infected with SARSCoV-2 according to the result obtained by a commercial ELISA test kit (the gold standard method for protein detection). In addition to that, 9 clinical serum samples tested to be negative by the ELISA test kit correspondingly tested to be negative by the COVID-19 ePAD and confirmed, whereas one tested negative control sample was positive by COVID-19 ePAD as can be seen in table 1 indicating the effectiveness of the electrochemical methods.

Table 1: Comparison between the Electrochemical (ePAD) and ELISA techniques

		Commercial ELISA Techniques			
		+	-	Total	
COVID-19 ePAD	+	7	1	8	
	-	0	9	9	
	Total	7	10	17	

One can concluded from the result that the positive result is most likely due to the possible SARSCoV-2 IgM present in the sample, which cannot be detected by ELISA or the effectiveness of the electrochemical method. similarly, the COVID-19 ePAD can capture all of the immunoglobulins present in the sample (IgG, IgM, and IgA); thus, it is clear that the COVID-19 ePAD may result in a more sensitive response.

Electrochemical nanotechnology has emerged as an analytical methodology for the detection of viral infections in electrochemical sensing. An interesting feature of NPs including high surface area, conductivity, and catalytic properties have led to their use in (i) surface immobilization of biomolecules, (ii) enrichment of electron transfer, (iii) effective catalysis, and (iv) labeling biomolecules [35]. The electrochemical immunosensors are composed of an electrode surface immobilization with recognition element (i.e., antibody or antigen) and gained promising attention as a reliable and efficient sensing platform for detection of viral infections [36].

Bhaskar S. et al. [37] have been reported their developed a Co-metal functionalized TNT-based amperometric electrochemical sensor for an alternative means of sensing material for electrochemical detection of SARS-CoV-2 infection through the detection of the receptorbinding domain (RBD) of spike glycoprotein . They have determined the potential of Co-functionalized TiO₂ nanotubes (Co-TNTs) for the electrochemical detection of S-RBD protein of SARS-CoV-2. Firstly, they prepared/ synthesized TNTs by a simple, cost-effective, one-step electrochemical anodization route, and they carried out Co functionalization by using the incipient wetting method and the schematic of the whole sensing set up along with the detection methodology is shown in figure 4.

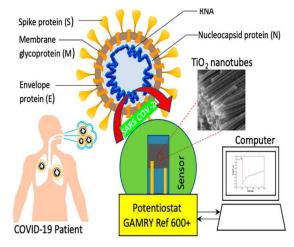


Figure 4. Schematic of Co-functionalized TiO₂ nanotube (Co-TNT)-based sensing platform for the detection of COVID-19

They carried out the electrochemical sensing of S-RBD protein by using a custom-built Co-TNT packaged printed circuit board setup by applying constant potential amperometric techniques. The technique uses response current to determine the concentration of the analyte in the electrolyte solution between the electrodes. The S-RBD protein in the elution buffer (20 mM sodium phosphate, 500 mM NaCl, 8 M urea, 200 mM imidazole, pH 4.0) was transferred onto the surface of Co-TNT using a micropipette [38].

Bhaskar S. et al. [37] also have been determined the electrochemical ability of the synthesized Co-TNT to sense the S-RBD protein of SARS-CoV-2 by performing an amperometry experiment at the above bias voltage of -0.8 V. The bias voltage was determined by conducting the cyclic voltammetry experiments in the voltage window -2 to +2 V.

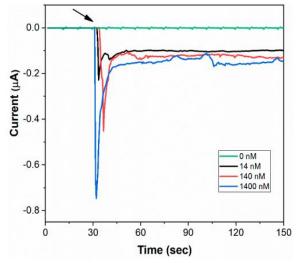
Their reported data depicted that cobalt functionalized TNTs can selectively detect the S-RBD protein of SARS-CoV-2 using the amperometry electrochemical technique in ~30 s. The amperometry curves obtained at various concentrations of protein are shown in Figure 5. The sensor was exposed to protein 30 s after the beginning of the experiment (marked by an arrow). The sensor response current increases sharply and rapidly as the sensor was exposed to the protein. At a protein concentration of 1400 nM, the peak sensor current output was found to be ~0.74 μ A. The peak current decreases to ~0.45 µA at a protein concentration of 140 nM and further decreases to ~0.23 µA at a protein concentration of 14 nM. The sensor detection time was ~30 s over the concentration range of 14 to 1400 nM [37]. The report shows all S-RBD proteins were reported to underdo electrochemical oxidation under application of potential [29,32].

The electrochemical oxidation process involves deprotonation, where the -OH functional group in the protein is converted to -O-. They envisaged that the complex formation occurs between the Co^{+2} ion in Co-TNT and the -O- radical in the protein [39].

As can be seen from the figure, the relationship between sensor response and protein concentration was found to be linear with the limit of detection as low as 0.7 nM levels. Importantly, their sensor detected SARS-COV-2 S-RBD protein in a very short time (~30 s), confirming its implication in developing a rapid diagnostic assay. This report indicates that response of current on different concentration of protein leads variation of response times upon increasing the concentration beyond 1400 nM and under 14 nM. Beyond the concentration of 1400 nM the activity of the sensor may be decreased due to the formation complex between cobalt ion and deprotonated side of the protein. Leila et al. in their report of "a nanoscale Geno-sensor for early detection of COVID-19 by voltammetric determination of RNA-dependent RNA polymerase (RdRP) sequence of SARS CoV-2 virus for the detection of SARS-CoV-2 RdRP" [40] have been successfully studied the voltammetric response of COVID-19 based on a signal off strategy by the DPV technique in the potential range from 0 to 0.8 V (vs. Ag/AgCl).

Figure 5. Amperometry response curves of Co-TNT sensor, at a bias voltage of -0.8 V, upon exposure to SARS-CoV-2 S-RBD protein of conc. 0 (background), 14, 140, and 1400 nM.

They prepared the sensor chitosan/SIDQs @PAMAM modified CPE-HT18C6 and incubated with different concentrations of the target sequence, and the peak current of silver was measured as a redox probe. The addition of targets with different concentrations on the modified electrode surface-induced different decreases in the peak current of the Ag probe. Their report reveals that the addition of a target with different concentrations



on the modified electrode surface-induced different decreases in the peak current of the Ag probe. The oxidation peak current of silver decreased by adding more increments of SARS-CoV-2 RdRP sequence to the solution and the genosensor exhibited a good linear response to target in the concentration range of 1.0-8.0 nM and also the LOD and LOQ were 0.3 pM and 1.0 pM respectively as shown in figure 6 [40].

On the other hands, Yakoh et al. [33] studied the performance of the electrochemical sensor for detecting the SARS-CoV-2 spike protein was evaluated by the square wave voltammetric technique. According to the square wave voltammogram presented in figure 7A, it can be clearly seen that the sensor also exhibited a sensitive response to the presence of the SARS-CoV-2 spike protein, where the current response proportionally decreased to the concentration of the SARS-CoV-2 SP RBD. From the figure 7B, the observed linear dynamic response toward spike protein sensing was constructed in range of 1–1000 ng/mL with an LOD of 0.11 ng/mL.

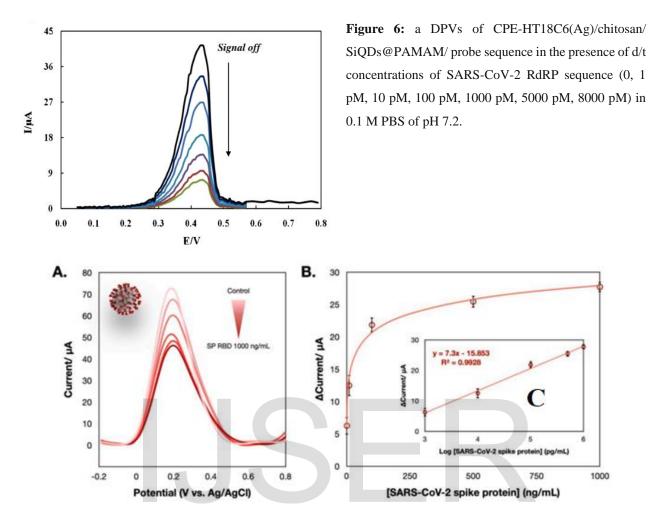


Figure 7: SWV responses of the COVID-19 e-PAD tested with different concentrations of SARS-CoV-2 spike protein in the presence of 5 mM [Fe(CN)6]3-/4 (B)The relationship between Δ current and concentration of SARS-CoV-2 spike protein (C) A linear relationship between Δ current vs log[conc] of SARS-CoV-2 spike protein.

From the given result, one can conclude that, the progressive development of the SARS-CoV-2 biosensor is achieved among limited sensors that are currently available.

In addition, electrochemical biosensors have greater capability to simultaneously identify multiple markers. These simultaneous determinations are an important need for the fast detection of multiple analytes present in a sample matrix. The biosensors can simultaneously identify and screen COVID-19 and other local infectious diseases, serving as an early warning system in resource-poor areas. More critically, these biosensors can be used for the label-free and nucleic acid amplification-free detection of DNA/RNA for the sensitive diagnosis of infection [41, 42]. We can conclude that the immobilized DNA probe selectively binds to the target sequence. These outcomes show the selectivity and specificity of the electrochemical genosensor toward the SARS-CoV-2 RdRP sequence [43].

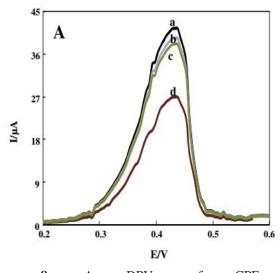


Figure8:ADPVsofCPE-HT18C6(Ag)/chitosan/SiQDs@PAMAM/probesequence in (a) PBS of pH 7.2, (b) E gene (50 pM), (c)SARS RdRP gene (50 pM), and (d) SARS-CoV-2RdRP gene (10 pM).

On the other hand, Shimaa and his co-workers [44] on their work of voltammetric-based immunosensor for the detection had reported the development of a labelfree voltammetric-based immunosensor for the determination of SARS-CoV-2 N antigen using gold nanoparticles-modified screen-printed carbon electrodes. They confirmed the analytical performance of the SARS-CoV-2 sensor by investigating by incubating the immunosensor with a different concentration range of the N protein ranging from 0.1 pg/mL to 100 ng/mL in PBS buffer pH 7.4. as can be seen in figure 9a, SWV results of the immunosensor at various concentrations of the N protein. From the figure 9, a gradual increase in the reduction peak current was seen after incubation of the immunosensor with an increased concentration of the protein likely due to the surface charge offered by the N protein as explained above. And the calibration of the plot of the SARS-COV-2 response against their logarithm of concentration was plotted as shown in figure 9b and a straight line was observed with a linear regression equation: $(i-i_0)/i$ % = 119.3 + 33.2 log C [ng/mL] and correlation coefficient of 0.998. They reported the performance characteristics of their developed sensor having the LOD was 0.4 ng/ml, the limit of quantification (LOQ) was 1.3 ng/ml and relative standard deviations (RSD%) of the experiments were ranging from 3.0 to 6.1%, implying very good reproducibility of the SARS-CoV-2 immunosensor [44]. These figures of merits of the sensor indicate that the sensor is highly sensitive and good performance for COVID-19 sensing. And their method is effective for diagnostic application of COVID-19.

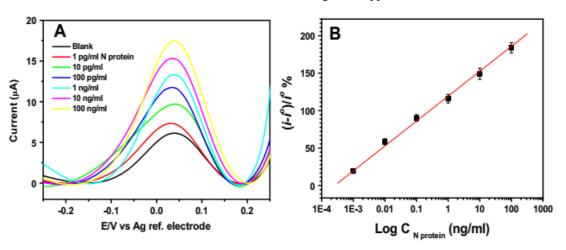


Figure 9: SWV of the N protein biosensor incubated in concentrations of the N protein solutions from 1 pg/mL to 100 ng/mL that was carried out in 5 mM ferro/ferricyanide redox couple in PBS buffer solution pH 7.4 (a) and Calibration

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plot of the biosensor's percentage of the change in the reduction peak current is plotted versus the protein concentration (b).

Shimaa and his co-workers investigated the application of the carbon-based immunosensor for real analysis of COVID-19 by analyzing nasopharyngeal swab samples that were collected from healthy and patient individuals. Firstly, they analyzed the samples with an RT-PCR kit which has a Ct cut-off value of 35. They observed that two samples exhibited low Ct values (21 and 24), indicating a high number of virus copies, and three samples showed high Ct values (33, 32, 31), implying a low number of virus copies and the healthy sample is PCR negative. They diluted the samples to 1:10 in BS buffer pH 7.4 and then incubated on the immunosensors for 15 min. Figure 10 shows the electrochemical immunosensor response obtained for the negative and five patient samples. It was observed that the negative sample showed a very minor response (below 5%), whereas the five patient samples showed a higher response. In addition, the two samples with the low Ct values showed higher immunosensor response compared with the three samples with the high Ct values. These initial results indicate the capability of their immunosensor to distinguish the positive and negative samples with a strong correlation between the biosensor response and the RT-PCR results [44].

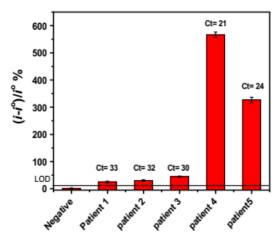


Figure 10: The response as the percentage change in the reduction current of the immunosensor response obtained for the negative and five patient samples with their corresponding Ct values.

In general, the electrochemical biosensor was developed for SARS-CoV-2 detection and it relies on the attachment of the anti-SARS-CoV-2 N antibody on gold nanoparticles modified carbon screen-printed electrodes. The detection was achieved in a label-free format via monitoring the change in the voltammetric reduction current upon binding of the immunosensor with the virus. The sensor exhibited very good sensitivity and limit of detection, likely due to the fast electron transfer rate and the high surface area of the gold nanoparticles. The immunosensor showed a very good degree of selectivity for SARS-CoV-2 against other potential interfering viruses such as HCoV, MERS-CoV, Flu A and Flu B. The sensing application of their immunosensor in clinical samples showed good agreement with the RT-PCR results. These show that the SARS-COV-2 immunosensor is considered a rapid, low-cost, selective and sensitive diagnostic method that has the capability to be integrated into a handheld potentiostat, and controlled via regular cell phone for point-of-care testing.

5. Conclusion

COVID-19 is an ongoing pandemic disease, and can lead to severe permanent respiratory problems and possible death, there is a critical need to provide various diagnostic strategies for early detection of the disease. This review summarizes the applicability, demand, and significance high of developing an electrochemical biosensor for COVID-19 POC application. diagnostics at The electrochemical biosensor development for application should successfully be adopted to facilitate diagnostics and bioinformatics-based big data analysis needed for timely decisions. These electrochemical platforms are especially attractive as point-of-care sensors to detect pathogenic virus because they are portable, fast, and easy to use. The refined speed and sensitivity of these platforms make them suitable for whole-cell detection. Moreover, nowadays, several virus detection methods are available for viral diseases, the use of which depend on specific properties of each virus or virus family, however, they are not much enough for COVID-19 detection, which requires further research for the development of more accurate tests. Hence, researchers should focus more on different approaches, in order to ultimately find a highly efficient and accurate method for the rapid and precise detection of viral diseases like COVID-19. In

this way, the devastating outcomes of the disease could be prevented.

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Competing interests

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Author contributions

Melaku Metto finding paper on the topic and revised the writing of the paper. Availability of data and material are not applicable for this mini-review paper.

Conflict of interests

The author declare that there is no conflict of interest regarding the publication of this paper.

And also consent for publication in your journal.

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