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Opinion

Opinion in Recent Nanomaterial-Based Electrochemical Platforms for Infectious Disease

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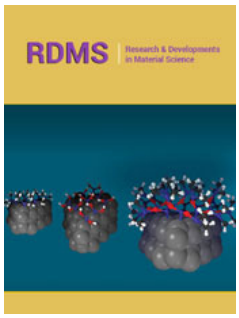
ISSN: 2576-8840



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Submission: January 19, 2024
Published: January 29, 2024

Volume 19 - Issue 5

How to cite this article: Sakda Jampasa and Orawon Chailapakul*. Opinion in Recent Nanomaterial-Based Electrochemical Platforms for Infectious Disease. Res Dev Material Sci. 19(5). RDMS. 000975. 2024. DOI: 10.31031/RDMS.2024.19.000975

Opinion

Numerous sensors have been established to explore vital disease-associated biomarkers in medical applications purposely for diagnostic, control, treatment, and prevention [1,2]. Infectious diseases caused by harmful pathogens such as bacteria, viruses, fungi, and parasites have received the most concern among others and need to be properly enumerated due to their symptom severity and rapid spread, for instance at the beginning of coronavirus disease (COVID-19) that caused at least million deaths worldwide [3]. Detecting biomarkers specific to disease onset has been proven to be the most effective way to reduce mortality and efficiently constrain disease outbreaks [4]. However, existing limitations of conventional methods (Polymerase Chain Reaction (PCR), Enzyme-Linked Immunoassay (ELISA), High Performance Liquid Chromatography (HPLC), Ultraviolet-Visible Spectroscopy (UV-vis)) such as their challenging instrument, lengthy analysis time, unaffordable price, low sensitivity, and specificity immensely hinder their practical outreach, Particularly at The Point-Of-Care Test (POCT), resulting in less effective disease control [5,6]. This suggests that alternative platforms with upgraded properties, affordability, multifunctionality, and minute size for infectious disease are highly sought after.

Electrochemical Sensors (ECs) have gained enormous interest for diagnosing infectious disease due to their exceptional characteristics that correspond to "ASSURED" standard criteria set by the World Health Organization (WHO) [7]. ECs are able to be flexibly integrated into diverse evaluation platforms including wearable and microfluidic devices, elastic materials, and fabrics, further facilitate their deployments [8]. In general, sensitive, and selective electrochemical measurements are typically influenced by two key components: modifiers and recognition elements. Nanomaterials (polymers, carbon-based materials, carbon composites, and crystal nanofiber, and metallic particles), classified by their size ranging from nanometers to hundreds of micrometers, have been broadly implemented as modifiers for fabrication of electrochemical sensors to improve their catalytic and conductive properties [9,10]. Because of their high surface area, presence of specific functional groups, biocompatibility, and inertness, they have been abundantly utilized in numerous clinical applications, exhibiting superior analytical performance from their distinct features [9]. Biorecognition elements, which can either be antibodies, aptamers, small molecules, DNAs and their analogues, Peptide Nucleic Acids (PNAs), or Molecularly Imprinted Polymers (MIP) are crucial components in addition to electrode modifiers which impact selectivity and sensitivity of electrochemical sensors deliberately developed to diagnose diseases [11]. Different capture elements offer different advantages and disadvantages; thus, their suitability may need to be taken into account.

Recent nanomaterial-based platforms integrated with various device designs to enable simultaneous and rapid detection have been demonstrated to diagnose tuberculosis (TB) [12],

leptospirosis [13,14], sepsis [15], Human Immunodeficiency Virus (HIV) [16], Hepatitis C Virus (HCV) [16], Hepatitis B Virus (HBV) [17,18], and COVID-19 [19]. Pornprom et al. [12] described a paper-based electrochemical biosensor using gold/carboxyl graphene nanocomposite (AuPs/GCOOH)-modified electrode for detecting a specific biomarker indicating the onset of TB infection. AuPs and GCOOH were applied to enhance electrode's conductivity and surface area, and as functional material to serve numerous active sites for anchoring antibody on the electrode surface, achieving superior performance in terms of sensitivity (limit of detection (LOD) = 10pg/mL) and specificity. Another recent sepsis biosensor is Jesadabundit et al. [15] dendritic copper nanostructures (CuNSs) combined with 4-aminobenzoic acid (4-AB, the diazonium salt) as antibody linker modified on a screen-printed graphene electrode for the early detection of the sepsis biomarker interleukin-6 (IL-6). CuNSs were exploited to improve electrode surface area (1.2 times), elevate active sites for antibody confinement, and enrich electrocatalytic property of ruthenium redox species, consequently resulting in a 0.02pg/mL of LOD. In addition to these detection schemes, integrated electrochemical sensor microfluidic devices have been introduced to detect both single and multiple analytes simultaneously [16,20]. For example, Naorungroj et al. [19] presented a G-quadruplex DNAzyme-based electrochemical sensor integrated with a sequential flow controllable microfluidic device for the detection of COVID-19. This combined platform allows sequential sample and reagent delivery as well as the DNA target hybridization and enzymatic reaction to be operated in a precisely controlled fashion. Chittuam et al. [16] proposed an electrochemical capillary-driven microfluidic DNA sensor for HIV and HCV coinfection analysis via the specific interaction between PNA probes and the DNA target. Chitosan polymers carrying plethora of amine groups were drop-casted on graphene electrode to anchor PNA probes. This device design eliminates a tedious process, enables automated sequential delivery, and retains high detection sensitivity, as it integrates the advantages of both static and flow-based electrochemical detection systems into a single device.

Advanced technologies such as Near Field Communication (NFC), a wireless and short-range communication technology for data transmission between devices, have emerged as a vital instrument to engineer electrochemical sensors to diagnose infectious diseases. NFC is mostly furnished with smartphones to permit its broad applicability. Jampasa et al. introduced a resistance-based lateral flow immunosensor diagnosis device (R-LFI) that integrates NFC with smartphone to diagnose leptospirosis. Like a strip test device, a specific monoclonal antibody against the pathogen was coated on nitrocellulose membrane and subsequently assembled with other components. This gathered device was sandwiched among two electrodes to detect resistive response and inserted in a strip cassette. The innovative platform can dismiss such a tedious and time-consuming step from preparation and detection process, such as multiple washing steps and additional labeling requirement, offering simplicity. Furthermore, an innovative wireless electrochemical card sensor for field-deployable diagnostics of HBV surface antigen (HBsAg) was recently developed [17]. This platform used chitosan polymers to immobilize the anti-HBsAg monoclonal antibody onto a screen-printed graphene surface. The presence of HBsAg resulted in a decline in the current response measured by using NFC combined with smartphone-based amperometric detection system. The proposed sensors demonstrated desirable properties for rapid and onsite detection. Overall content of the recent nanomaterials-based electrochemical biosensors for infectious disease detection is summarized in Figure 1.

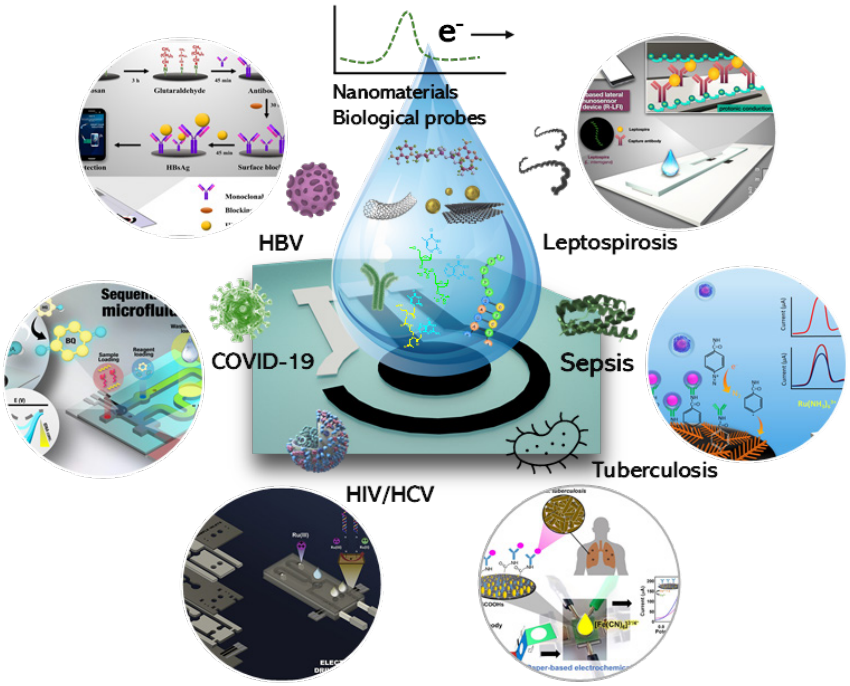

Figure 1: Illustration of recent and various nanomaterial-based electrochemical platforms and their sensing applications for infectious disease analysis.

In conclusion, nanomaterials modified electrochemical platforms make tremendous progress in infectious disease diagnosis. Nanomaterials are mostly utilized to (I) improve active surface area and conductive property of the modified sensor and (II) enhance catalytic property of redox species of interest and (III) provide plethora of functioning groups to create biorecognizable layers, therefore achieving superior performance. With flexible and portable designed platforms, rapid, sensitive, selective, and simultaneous multiplex detection of infectious diseases can be achieved, particularly at POCT. However, novel materials and alternative platforms that meet desirable expectations are still in great demand. Future hybrid electrochemical sensors using greener methods, multiplexed detection, and applications of artificial intelligence machines will also be possible. Connecting the sciences and arts of nanomaterial design and synthesis with the electrochemical properties of materials allows for the improvement of electrochemical sensors for better disease diagnosis and ultimately good health and wellness.

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