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REGULAR ARTICLE

Evaluating Next-Generation Nanobiosensors for Detecting Dangerous Biological Markers in Diseases

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The emergence of a novel human coronavirus in 2019 and its swift global transmission led to a pandemic that heightened morbidity and highlighted the limitations of existing diagnostic approaches, which are often labor-intensive, slow, and non-portable. In contrast, biosensors (BS) offer a promising alternative by enabling rapid, cost-effective, accurate, selective, and sensitive detection of numerous illnesses. Their ability to quickly identify a wide spectrum of viruses allows timely medical intervention. Recent progress in nano-technology has further enhanced diagnostic capabilities through the development of advanced nanobiosensors (NBS), compact and intelligent devices that have transformed viral detection due to their portability, robustness, and affordability. This review provides an in-depth assessment of the biosensor technologies employed for virus identification, with particular emphasis on the role of NBS in detecting COVID-19. It also explores the challenges and future prospects associated with designing ultrahigh-sensitivity NBS before establishing them as the next-generation gold standard in diagnostics. Overall, these innovations hold substantial potential to advance medical diagnosis and improve treatment evaluation.

Keywords: Biosensing technologies, Nanoscale innovations, Critical diseases, Advanced nanobiosensor systems.

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1. INTRODUCTION

Nanotechnology combined with biosensing has provided a revolutionary platform in the contemporary healthcare system, and a new generation of exceptionally accurate diagnostic potentials. Over the past few years, ultra-sensitive nanobiosensors (NBS) have received considerable attention because of its extraordinary ability to detect minute biological agents which can be used to realize the early detection of life threatening diseases. This combination of nanoscience and biosensing has enormous potential in further development of disease detecting, treatment options and general patient treatment outcomes [1].

NBS constitute an advanced combination of nanoscale technology and biological sensing processes, which forms a platform, which has surmounted the constraints of the traditional diagnostic procedures. The miniature systems are able to detect biomolecules in extremely low quantities and the difference in the physico chemical characteristics of nanomaterials is used to bring about high sensitivity [2]. Their critical operation is normally based on the interaction mechanisms of such nanomaterials with biological agents which creates very specific and measurable responses which can be well utilized in diagnostic studies [3].

The NBS that are ultrasensitive are unique in the sense that they are highly sensitive to detect disease related biomarkers. These sensors are able to detect and amplify even the smallest biological signal by utilizing the special characteristics of nano materials like graphene, carbon nanotubes, metal nanoparticles and the list is not limited to these materials. The amazing sensitivity ensures that severe health ailments can be detected at a very early age before a clinicians has time to intervene when treatment is optimum and eventually enhance patient outcomes [4].

One of the greatest strengths of these NBS is that they can identify life threatening diseases at an early stage, which is usually a determining factor of whether a person will survive or not [5]. Their high level of sensing could transform the world in terms of dealing with an array of health issues, such as infections, cancer, and the neurological diseases [6]. Ultrasensitive NBS can be used to change the paradigm of medical diagnosis and treatment of diseases by identifying the relevant biomarkers in the early stages of disease occurrence, to orient medical care toward more proactive, personalized, and timely in-interventions [7].

Moreover, the ultrasensitive NBS provide much more than the high-quality diagnostic accuracy they are exceptionally versatile. They are useful in a wide range of clinical settings because their ability to interact with a wide range of biological samples such as saliva, blood, and urine. Since a good number of these tests are not invasive, the diagnostic process is simpler, more comfortable, and with reduced stress, which patients undergo. Not only has this patient friendly approach enhanced cooperation but it has also contributed to a more patient-centered model of healthcare [8-10].

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2. PREVALENCE OF SERIOUS AND POTE TIALLY FATAL ILLNESSES

Over the past few years, there has been an increase in the number of life-threatening diseases which has led to recurring endemics, outbreaks and epidemics among the population of different parts of the world. These vicious pathogens enter into host cells and make use of receptor ligand interactions to cause disease. A variety of famous viruses, including hepatitis B (HBV), hepatitis C (HCV) [11-12], and HIV, still continue to become a significant threat to global health. Equally, other types of viruses such as Zika (ZKV), influenza, respiratory syncytial virus, astroviruses, rotavirus, and West Nile virus cause extensive harm to the organ infected rendering them to be a serious health hazard that can result in serious illness or even death [1]. Table 1 gives an overview of the various viruses that have been observed over the years in the world. At present, the world is aware of three very fierce coronaviruses namely, SARSCoV 1, MERSCoV and the most recently developed COVID19 which cause severe respiratory diseases worldwide. The previous versions of influenza are considered to have been introduced by birds and then transmitted to horses and thence to people causing the catastrophic pandemic of 1918. This epidemic has led to almost 50 million fatalities in the period of only two years. Subsequently, the Asian flu, the Hong Kong flu pandemics of 1950s and 1970s each caused over 2 million deaths, and represent more tragic stages in the history of influenza pandemic on the planet [13].

Table 1 – Viruses discovered across different periods

Year	Virus Name	Location
2016	Zika Virus (ZKV)	Brazil and other parts of the world
2015-2016	Asian Zika Virus strain	Western Hemisphere
1998	Nipah Virus	Malaysia
2001- 2007	Nipah Virus	Bangladesh
2001- 2007	Nipah Virus	India (Kerala)

3. SERIOUS AND LIFE-COMPROMISING DISEASES

In December 2019, in Wuhan, China, physicians spotted an abrupt increase in unexplained cases of pneumonia. These had never been reported before and this made the World Health Organization (WHO) to define the disease as coronavirus disease 2019 (COVID19). The WHO made an official declaration that it was a global pandemic on March 13, 2020. The COVID19 causing virus is a new pathogen that is approximately 80 percent related in genetic composition to SARSCoV, the virus known in China in 2002, and 50 percent to MERS CoV. The new virus was categorized as a part of the COVID19 group because of its close resemblance to the SARSCoV. The pandemic of COVID19 has led to critical health issues and extensive socioeco-nomic impacts due in large part to its capability to be transmitted easily on the person-to-person basis even when individuals have no symptoms [14].

3.1 Observed Clinical Indicators

The WHO claims that individuals of any age group can be infected with COVID19. The virus is primarily transmitted by direct or indirect contact with a diseased individual. Infectious particles can be transferred by minute droplets emitted by coughing or sneezing or by contact with contaminated surfaces. Viral RNA has been even found in feces in certain studies which indicates that the fecal oral route of transmission is also possible [15].

3.2 Virus Biology and Pathogenesis

Coronaviruses are spheric viruses which are large and surrounded by a protective envelope. Their genome is a single strand of positive sense RNA, usually of 27 to 32 kilobases in size. There are two major subfamilies (Coronavirinae and Torovirinae) of the Coronaviridae family. There are four different genera of the Coronavirinae subfamily, namely, Alphacoronavirus and Betacoronavirus, Gammacoronavirus and Deltacoronavirus. It is important to note that HCoV229E and NL63 are the members of Alphacoronavirus, whereas MERSCoV, HCoVOC43, SARSCoV, HCoVHKU1, and COVID19 become the representatives of Betacoronavirus. The COVID19 genome is divided into 10 open reading frames (ORFs), the first one occupying about two-thirds of the RNA genome, and produces two large polyproteins. The rest of ORFs encode the principal structural proteins of the virus such as the membrane protein (M), the envelope protein (E), nucle ocapsid protein (N), the spike glycoprotein (S) and all these comprise approximately a third of the genome. In addition to these, there are a number of ancillary proteins that have not been studied in detail and need not be directly related to the process of viral replication. Studies have revealed that COVID19 prevents entry to the host cell through the angiotensin converting enzyme 2 (ACE2) receptor, and the spike protein is important in this crucial interaction. Once inside the cell, the viral genome is released and translated into polyproteins, while replication and transcription of the RNA and capsid proteins occur in the cytoplasm. The other structural proteins are processed through the endoplasmic reticulum and Golgi apparatus, completing the assembly of new viral particles.

4. NANOBIOSENSORS: REVOLUTIONIZING RAPID DETECTION TECHNIQUES

The concept of bio sensors (BS) is not new as it was utilized almost four decades ago, though recent achievements in the nanoscience system and technology led to new perspectives in the sphere of the bio sensors development. Today the nanomaterials are being integrated to make nanobiosensors (NBS) that are able to detect nucleic acids such as DNA and RNA with high accuracy as well as selectively. As shown in Fig. 1, NBS are nothing more than biosensors whose transducers are fabricated using nanomaterials, which introduce special mechanical, electrical, catalytic, magnetic, biological, optical, and surface characteristics to the system. Although NBS operate in the same way as conventional biosensors, their nano size elements present signific-icant benefits such as reducing the time response, reuse, reduced energy usage and allow the inclusion of enzymes. Sensitivity is also increased by the use of nano-sized elements that permit smaller devices, which require less experimental space. Besides, the use of sophisticated manufacturing processes to NBS can decrease the costs of production hence decrease healthcare costs related to disease detection and monitoring.

4.1 Diverse Nanobiosensor Technologies

Within the recent years, bioreceptors have increased the use of various nanomaterials to increase their specificity and sensitivity. The following paragraphs demonstrate some of the most significant nanobiosensors that are currently being used.

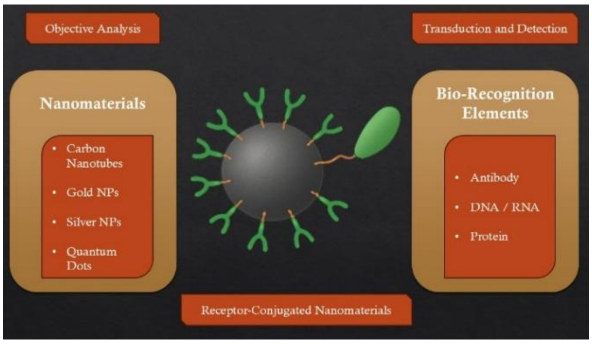

Fig. 1 – Diagrammatic representation of a nanobiosensor

4.1.1. Carbonaceous Nanomaterials Carbon Based Nanotubes

Spherical geometry Carbon nanoparticles have been considered in medical applications because of their biocompatibility, non-immunogenicity and homogeneous surface chemistry, though there has been limited practical application of these in biomedical applications. Carbon nanotubes (CNTs) have since 1991 received considerable interest in nanobiosensors (NBS) research due to the high mechanical strength, high electrical conductivity, chemical stability, high surface area, and fast heterogeneous electron conduction. These properties of CNTs render them especially useful in adsorbing nucleic acids or biomolecules and incorporating them with functional structures to allow fast, label free bioelectronic detection. Recent developments involve the development of CNT based electrodes that have been improved with gold nanoparticles (AuNPs) in detecting life threatening diseases. In such systems, single walled CNTs (SWCNTs) with AuNPs make use of variations in electrical resistance permitting viral nucleic acids to be immobilized with probe DNA. This type of innovations offers an effective starting point to medical diagnostics at an early stage.

Graphene-Enhanced Nanobiosensors

Graphene is a nanomaterial that is a highly researched carbon material with excellent physical characteristics. Nanobiosensors (NBS) prepared using graphene oxide (GO) are usually synthesized by reduction processes. The chemically reduced GO sheets, which are functionalized graphene sheets, improve the performance of NBS because it has great surface to volume ratio and transfer of electrons. Graphene has been utilized especially in electrochemical detection of small biomolecules despite the fact some of its optical qualities are yet to be explored. Similar to carbon nanotubes, graphite coated with metallic nanoparticles still enhance the accuracy of detection of viruses than the traditional method and optical biosensing has been used to identify specific viruses.

4.1.2. Metallic Nanostructure Biosensors

Silver Nanoclusters

Silver nanoparticle (AgNPs) products are some of the most popular metallic nanoparticles mostly used in biological detection. Their distinctive physicochemical characteristics, high adsorption potential, and excellent electrical conductivity render them perfect in the application of electrochemical (EC) as well as surface plasmon resonance (SPR) biosensor. An example of this is a label free fluorescent system which is constructed using DNA stabilized silver nanoclusters to concomitantly detect two distinct sequences of HIV DNA. AgNPs have also been used in another study to allow real time detection of influenza viruses to the single virus level, which shows the great potential of AgNPs in sensitive and fast viral testing.

Gold Nanoclusters

The use of gold nanoparticles (AuNPs) in bio-sensing is highly appreciated because of its ready preparation, large surface area, adsorption capacity, and conjugation of biomolecules. Their properties render them especially useful in the electrochemical (EC) and optical nanobiosensor modalities in the detection of life-threatening diseases. AuNPs serve as electroactive tags and catalytic labels of viruses in EC based assays. As a case in point, colloidal gold nanoparticles have been used in the development of a lateral-flow immunochromatographic test to detect herpes simplex virus type 2. Likewise, unconventional physicochemical and optical characteristics of gold nanoparticles have been utilized to develop sensitive assays to detect and quantify hepatitis C virus (HCV), which can be seen to demonstrate their applicability in the state-of-the-art viral diagnostics.

4.1.3. Electrospinning-Based Nanofibers

Electrospinning is a common nanotechnology procedure in which an electric field drives a charged polymer solution to an oppositely charged collector to form ultra-thin fibers. High surface area, increased sensitivity, and superior permeability have made these electrospun nanofibers to have wide applications in drug delivery, biosensing and in tissue engineering scaffolds. Nanobiosensors (NBS) draw on a wide range of sensing principles, as these include: electrical resistance change, electrical current change, optical and photoelectric effects and vibrational frequency change. As an illustration the DNA hybridization could be detected with an unbelievable accuracy through an electrochemical plat form constructed of electrospun semiconducting manganese oxide. The biosensor can detect dengue primers of consensus zeptomolar concentration, and the sensitivity value is even higher with a range of 130 1030 M, which demonstrates the incredible potential of the electrospun nanofibers in ultrasensitive biosensing.

4.1.4. RT LAMP Mediated Nano-Biosensing Devices

One of the most accurate RT LAMP tests is designed that employs nanoparticles as a biosensor to identify COVID19. This assay increases viral nucleoprotein genes such as the F1ab region in a single step through the use of LAMP primer sets. This is then tested using the nanoparticle-based biosensor which possesses high sensitivity to detect as few as 12 copies per reaction. This sensitivity is also high which means that there are very few false positive results and the whole process can give the correct results within one hour.

4.1.5. FET-integrated biosensor systems

A biosensor that relies on the use of a field effect transistor (FET) has been developed to detect COVID19 in clinical specimen with a high level of accuracy. This sys-tem features a sensing material that is made of graphene on which specific antibodies are modified in order to develop a highly responsive detection platform. The FET biosensor could detect the SARS CoV2 spike protein in extremely low concentrations of 1.6×10^1 pfu/mL in culture media and 2.42×10^2 copies/mL in actual patient swabs when tested with nasopharyngeal swob samples collected on infected patients. The device has shown superior sensitivity and quick detection limits, and was able to detect very small quantities of viral material, and with no cross reaction with the MERS CoV antigen.

4.1.6. Challenges Associated with Nanobiosensors

In most instances, nanobiosensors have been shown to be very effective in the detection of the virus, but their clinical applications have a number of impediments. Advanced nanomaterials such as the carbon nanotubes are expensive to produce, thereby complicating their commercial production. They are also very sensitive and extremely small in size hence making it difficult to produce. In addition to this, their biological safety has not been fully comprehended as toxicity differs according to their physical and chemical characteristics. With adjustment of these properties, the adverse effects may be minimized, yet further research is required to learn the behavior of NBS within the actual biological setting, before they can be safely integrated into the mainstream of healthcare practice.

5. CONCLUSION

Nanobiosensors (NBS) are sensitive biosensors that can be used to detect very serious diseases, as they have the ability of interacting directly with biological targets, which provide a high degree of precision which can not be matched with the traditional method. The high-technology tools would allow detecting health hazards quickly and precisely, changing the diagnostic potential and providing a chance to intervene during severe conditions in time. This review has discussed the wide variety of biosensors available to measure life threatening illnesses as well as attended recent advances in nanotechnology which have resulted in the development of intelligent, miniaturized NBS. They are portable, durable, and cost effective and thus particularly useful in the diagnosis of different types of viruses including COVID19. The review has also assessed the role of these state-of-the-art NBS in the detection of the COVID19. Nevertheless, there are still certain problems, including signal jamming, stability, and the problem of scalability. Environmental conditions and complexity of biological systems can affect their performance. The further advances will rely in the enhancements of their accuracy, the reliability, and the breaks of such scalability barriers improvements that may have a significant impact on medical diagnostics and treatment study. This section outlines and agrees the important developments, focusing on methodological developments, reported performance, and knowledge gaps in current research.

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Оцінка нанобіосенсорів наступного покоління для виявлення небезпечних біологічних маркерів при захворюваннях

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Поява нового коронавірусу людини у 2019 році та його швидке поширення по всьому світу призвели до пандемії, яка підвищила захворюваність та висвітлила обмеження існуючих діагностичних підходів, які часто є трудомісткими, повільними та непортативними. Натомість біосенсори (БС) пропонують перспективну альтернативу, дозволяючи швидко, економічно ефективно, точно, вибірково та чутливо виявляти численні захворювання. Їхня здатність швидко ідентифікувати широкий спектр вірусів дозволяє своєчасне медичне втручання. Нещодавній прогрес у нанотехнологіях ще більше розширив діагностичні можливості завдяки розробці передових нанобіосенсорів (НБС), компактних та інтелектуальних пристроїв, які трансформували виявлення вірусів завдяки своїй портативності, надійності та доступності. Цей огляд надає поглиблену оцінку біосенсорних технологій, що використовуються для ідентифікації вірусів, з особливим акцентом на ролі НБС у виявленні COVID-19. У ньому також досліджуються проблеми та майбутні перспективи, пов'язані з розробкою надвисокочутливих НБС, перш ніж вони стануть золотим стандартом наступного покоління в діагностиці. Загалом, ці інновації мають значний потенціал для розвитку медичної діагностики та покращення оцінки лікування.

Ключові слова: Біосенсорні технології, Нанорозмірні інновації, Критичні захворювання, Передові нанобіосенсорні системи.