Improvement of COVID-19 Diagnostic Tools: Nanobiosensors Challenges and Perspectives

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Abstract

To date, no vaccine or specific drug has been developed to treat CoV-2 infection, also early diagnosis is critical in dealing with the CoV-2 pandemic. Existing tests have some limitations including long analysis time, poor performance, insufficient sensitivity, and less than optimal portability. The development of biosensor technology promises development of fast and highly sensitive tests, and is suitable for on-site testing, which can make testing for CoV-2 much easier. However, the practical application of such a biosensor in a pandemic remains to be achieved. This review can serve as a guide for the development of modern nanomaterial techniques capable of applying biosensors to meet today's demand

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for inexpensive, rapid, and early diagnosis of COV-2 infection and fungal post-COVID infection. Further efforts will be needed to track and avoid further pandemic outbreaks of viral infectious diseases.

Keywords

Nanobiosensors · SARS-CoV-2 · Virus detection · Biosensors · Fungi associated COVID

23.1 Introduction

Diagnosis of viruses aims to identify agents which most likely responsible for the disease. For doctors, ideal virus identification methods in an infected patient should be specific, sensitive, and rapid, as once patient has recovered or died diagnosis has less practical value. From another side epidemiologic researches may have thousands of samples which require use of low cost, and high throughput virus modalities. Virus has its own detection challenges due to their simple biology, small size, and also obligates intracellular life cycle. Since 1940, there have been three general approaches on detecting virus: Analysis the response of viruses on the host organism, especially antibody serology, detection of a virus's molecular fingerprints, including viral nucleic acid and protein, and direct recognition of whole viral particle (Payne 2017). The traditional viral diagnostic techniques, especially culture, are expensive, slow, and often the diagnostic choice to make decision when no therapeutic agents are available (Storch 2000). Besides, there is high risk for human to expose to viruses in environment matrix. Additionally, detection of viral pathogen needs identification of the presence and/or quantity of virus (Julian and Schwab 2012).

The current episode of the extreme intense respiratory condition SARS-CoV-2 has given disease transmission experts around the world challenge: the capacity to dependably foresee the spread of this novel profoundly infectious Covid 19 and, in result, apply fitting isolate measures to forestall the transmission of the disease. In result, there is a critical need for symptomatic apparatuses capable not exclusively to dependably distinguish tainted individuals (Li et al. 2020). Moreover, an irreplaceable objective for the control of the COVID-19 pandemic is the limit with respect to mass populace screening, a condition that requests quick and cost-efficient measure draws near. Accordingly, various Point-of-Care (POC) quick and moderately affordable tests for SARS-CoV-2 have been as of late created (Sheridan 2020).

Currently, the real-time reverse-transcriptase polymerase chain reaction (RT-PCR) procedure is the most widely recognized and solid research facility testing technique for subjective/quantitative SARS-CoV-2 identification followed by serum infection balance examine (SVNA) for the assurance of neutralizer balance and compound connected immunoassays (ELISA) for the location of antibodies against SARS-CoV-2 (Chowell et al. 2015; Kang et al. 2017; Huang et al. 2020; Cesewski and Johnson 2020). Besides that, the significant restrictions of these research facility

based symptomatic tests are the obtrusive idea of the tests that regularly require prepared individual for nasopharyngeal example assortment, alongside the prerequisite of exceptionally complex machines, cross-reactivity with other infections, and longer span of testing. Therefore, there is an urgent need to find simple, inexpensive appropriate method for viral detection (Tahamtan and Ardebili 2020).

Biosensors are extremely precise, sensitive, and specific systems for calculating very low analytical sample concentrations. A biosensor is an analytical instrument composed of biological components, such as micro-organisms, organelles, receptors, enzymes, nucleic acids, etc., and an electric parameter transducer that transforms these signals. A high degree of specialty based on unique binding sites is essential for biosensor components. Various medical and therapeutic uses are planned to be used for biosensors, such as: (1) quick diagnosis and treatment of diseases such as cancer or diabetes; (2) pathogens detection; (3) measurement of the drugs, and the metabolites thereof; (4) new medicines development; (5) drug evaluation; and (6) evaluation of analyte and early detection of diseases by means of quick testing of biological samples (Pashazadeh et al. 2017; Hasanzadeh et al. 2016, 2017).

Recently, biomedical nanomaterials attract attention because of materials, their numerous exceptional optical, electronic, attractive, and mechanical properties. Until now, nanoparticles, such as metal, metal oxide, quantum spots, carbon nanotubes, graphene nanotubes, and polymeric nanomaterials have been utilized in viral identification, typically formed on their surface with biomolecules got from infections (DNA, RNA, antibodies, etc.) (Kang et al. 2017; Suo et al. 2020).

It is significant that the use of nanomaterials in the production of biosensor has diminished the size of biosensor, making them more appropriate for in-field detection (Suo et al. 2020). In this review, we discuss nano-based sensor as effective method for viral detection including Sars-CoV-2 and the fungal infection as post-covid symptoms.

23.2 Biosensors for Viral Detection

Compound or organic receptors and transducers form the sensors. The receptor directly links with an objective analyte, and the transducer transforms into a quantitative sign over the recognition period (Ozer et al. 2020). Biosensors are analytical instruments in which organic particles, such as compounds, antibodies, or nucleic acids, paired with a transducer and an identifier that identifies the associated analyte and gives a computerized yield (Fig. 23.1). In light of innovation brought about, there are four kinds of biosensors via, optical biosensors, electrochemical biosensors, piezoelectric biosensors, and thermal biosensors (Saylan et al. 2019).

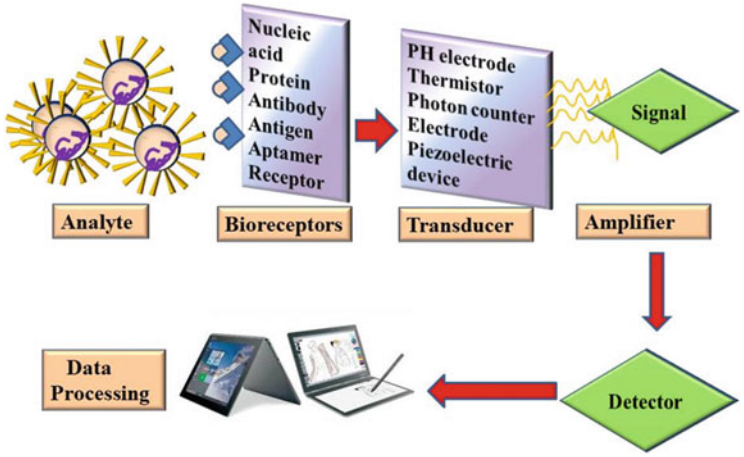

Fig. 23.1 Graphic diagram of biosensor for detection of viruses

23.3 Nanomaterials Based Sensor

Recent nanoscience and nanotechnology advances, together with the possibility of small-scale electrodes, allow nanoscale sensors, leading to a new range of diagnostic biosensors known as nanobiosensors. In this consequence, we should note that the arrangement of the nanomaterials and biological materials is essential to design hybrid nanostructured analytical instruments (Pinheiro et al. 2011; Gerrard 2013; Bellan et al. 2011). Due to the extremely large surface to volume ratios of nanosize devices, the surface interaction between the sensors and the analyte become extremely powerful (Nguyen et al. 2009). Nanoscale materials therefore exhibit specific characteristics, functionality, and effects. Nanotechnology currently focuses on removing the drawbacks of existing virus detection methods in order to reduce costs and time usage (Krishna et al. 2018). In addition, nanomaterial use in the biosensors' construction led to improved performance and sensitivity (Krishna et al. 2018) (Fig. 23.2). Due to the electrical and mechanical characteristics of nanomaterials for biomedical applications, many nanomaterials, such as nanorods, nanotubes, nanowires, thin films, and nanoparticles, have been studied for biomedical purposes. We will investigate the use of various nanomaterials for the manufacture of pathogenic viruses' biosensor such as quantum dots, carbon nanotubes, and metallic nanoparticles.

23.3.1 Magnetic Biosensors

Magnetic nanoparticles have provided significant interest to biosensing methods because they provide unrivaled benefits over other techniques. The development of

Fig. 23.2 Different nanomaterials that used as biosensor for viral detection

magnetic nanoparticles, for example, is cost-effective, mechanically and chemically stable, and biocompatible. Moreover, biological samples have practically no magnetic history and thus extremely sensitive experiments can be conducted without extra processing. However, optical methods are often influenced inside the sample by dispersion, absorption, and/or autofluorescence (Haun et al. 2010). A number of methods for sensing biomolecules with magnetic labels have been developed. These include magnetic sensors such as SQUID, and Hall sensors that sense magnetic particles directly (Kotitz et al. 1997; Chemla et al. 2000; Li et al. 2006; Osterfeld et al. 2008; Wang et al. 2005; Aytur et al. 2006). Another approach which has been considerably effective is a process that uses magnetic nanoparticles to speed up the relaxation rate of neighboring water molecules, which is based on magnetic resonance (MRI/NMR). This device is similar to magnetic resonance visualization used to see into the human body and is considered magnetic resonance diagnostic (DMR). DMR experiments use affinity molecule-conjugated magnetic nanoparticles to bind molecular goals and adjust the relaxation rate of protons using either of two separate types of proceedings. Firstly, it is important to tag large objects, such as whole cells, and then wash away unbound nanoparticle sensors. Secondly, the uses of the magnetic resonance switching phenomenon, where molecular targets are used to

Table 23.1 DMR biosensing methods for viruses

Viruses	Magnetic nanoparticles sensors	References
Herpes simplex virus	Anti-gpD (HSV-1)-CLIO; Anti-HSV1-CLIO	Perez et al. (2003)
Adenovirus-5	Anti-Adenovirus-5-CLIO	Perez et al. (2003)
Influenza viruses	Magnetic nanoparticles with H5N1 viral antibodies	Chou et al. (2011)
SARS-CoV-2	Giant magnetoresistive (GMR) biosensor and magnetic nanoparticles	Aminul Islam and Ziaul Ahsan (2020)

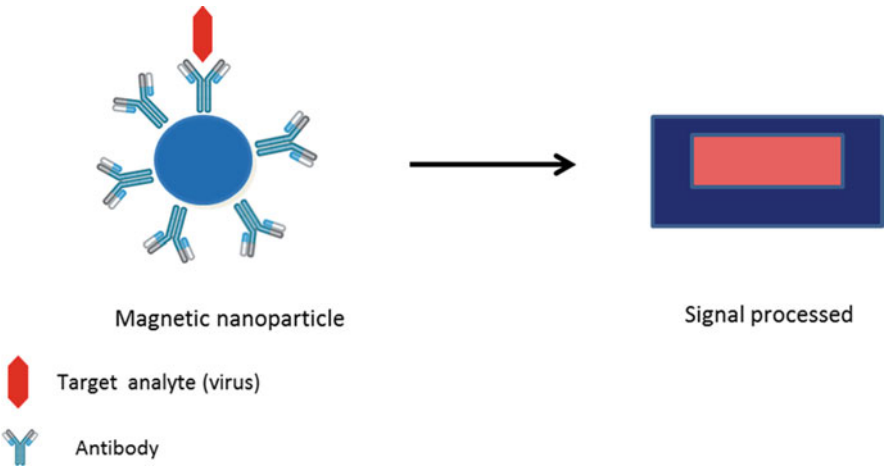

Fig. 23.3 Graphic diagram of magnetic nanoparticle for detection of viruses

assemble magnetic nanoparticles in clusters and thus affecting a corresponding shift in the change of bulk relaxation (Fig. 23.1) (Perez et al. 2002; Josephson et al. 2001). Magnetic nanoparticles (MNPs) are functionalized with antibodies or DNA/RNA probes that can precisely bind to target analytes. The target analyte concentration is then translated into the magnetic signal produced by the magnetic nanoparticles (Wu et al. 2020; Storch 2000). A wide range of high sensitivity and unique molecular targets viral pathogens were identified successfully by DMR as shown in Table 23.1.

Antibody-conjugated MRSw sensor is used to detect viruses. This is exciting matter since these targets are of the same or even greater order than magnetic nanoparticles. For example, identification of adenovirus-5 and herpes simplex virus1 by polyclonal antibody conjugated cross linked iron oxide nanoparticles in serum (Fig. 23.3) (Perez et al. 2003). Also, Chou et al. (2011) fabricated magnetic nanoparticles with H5N1 viral antibodies, which show high specific binding to H5N1 viruses.

Recent literature studied the detection of viral genome like +ssRNA, and S (spike)—protein containing into SARS-CoV-2 by magnetic nanoparticles.

Attachments of viruses with magnetic nanoparticles are necessary to detect the viral genome mechanism by magnetic biosensors. As supramolecular architecture with special building blocks, viruses and nanoparticles are attached. These supramolecular assemblies with the optimum virus ratios change pure magnetic nanoparticles optical and magnetic properties (Aminul Islam and Ziaul Ahsan 2020). These supermolecular structures are very vulnerable to the virus, enabling magnanimous nanosensors to be built to distinguish targets like nucleic acid (DNA, RNA) and proteins, particularly SARS-CoV-2, and thus finally to rapidly identify SARS-CoV-2 protein (+ssRNA) (Wang et al. 2002; Schotter et al. 2004).

The giant magnetoresistive (GMR) biosensor along with magnetic nanoparticles is a potent device for rapid biomolecule detection. The basic concept of GMR-based immunoassay is magnetization alternation with electrical transition. As a consequence, when the spin collision increases, the electrical resistance decreases, which eventually increases the magnetization of the interface between the magnetic nanoparticles and proteins, and thus, through proper calibration of the uninfected body, the magnetic signal may be the measurement parameters of the detector in its operation. In the overall debate, detecting respiratory viral pathogens such as SARS-CoV-2, magnetic nanoparticles play a crucial role in GMR biosensing technology. The GMR biosensor-based platform is more responsive, time-consuming, and low cost than other traditional testing systems (Wang et al. 2015; Schotter et al. 2004; Krishna et al. 2016; Nabaei et al. 2018).

23.3.2 Gold Biosensors

Gold nanostructures were used particularly to produce biosensors for virus detection in terms of optical signal amplifiers, current amplifier, and light diffusion (Draz and Shafiee 2018). They have excellent optical/electric characteristics, fantastic biocompatibility, catalytic properties, and relatively easy production processes (Bollella et al. 2017). Qiu et al. (2020) have developed a novel plasmone-based double-function biosensing platform for sensing SARS-CoV-2. In the course of auto-assembly, the Au-Film was first prepared by magnetron sputtering using a two-dimensional gold nanoisland (AuNIs) chip [2D-AuNIs]. On the BK7 glass surface, the au-film was formed by magnetron sputtering. Furthermore, 2D-AuNI were worked with the complementary DNA receptors and were enabled by a nucleic acid hybridization to detect SARS-CoV-2 sensitively (Fig. 23.4). In order to improve laser beam sensing properties, the plasmonic resonances of the plasmonic photothermal and localized surface plasmon resonance were permitted to drop at two different wavelengths. The in situ enhancement in plasmonic photothermal was furthermore reported to significantly improve the kinetic hybridization and thus the specific detection of nucleic acid. With present COVID-19 detection methods, there are several false positives or false negatives registered. The plasmonic photothermal heating inhibits the falsified binding of non-compatible sequences and thus prevents the erroneous diagnosis (Qiu et al. 2020).

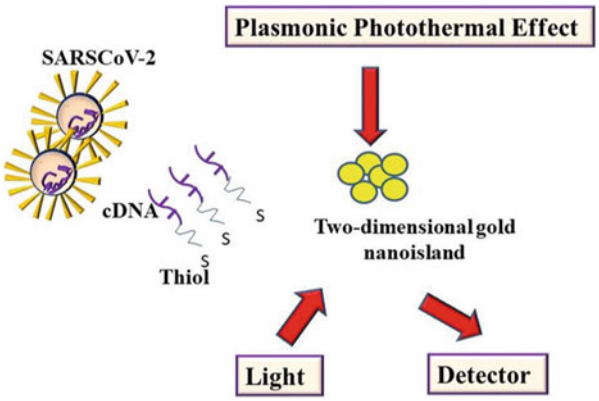

Fig. 23.4 Schematic diagram of two-dimensional gold nanoisland-plasmonic photothermal enhanced localized surface plasmon resonance DNA sensor. (Antiochia 2020)

23.3.3 Graphene-Based Biosensors

A graph sheet is the sensing region for the biosensor based on field effect transistor (FET), which is transmitted to a substratum SiO_2/Si and subsequently modified by the spike antibody SARS-CoV-2, which is disseminated correctly to the graphene sheet surface by casting. The system allowed detection at levels of 1 fg/mL in the phosphate buffer of a SARS-CoV-2 antigen spike protein, which is much smaller than the ELISA and PCR-methods shown (Qiu et al. 2020; Chu et al. 2020). Moreover, there was no substantial response to MERS-CoV spike protein from this sensor, ensuring that the antigen protein was highly selective and unique for the Spike SARS-CoV-2. Without sample preparation or preprocessing, this nanobiosensor permitted the discrimination between patient and normal samples with detection limits lower than those recorded with other current methods as denoted in Fig. 23.5 (Seo et al. 2020). In another recently published study, *Vibrio parahaemolyticus* can be translated for COVID-19 detection using a portable electrochemical biosensor based on graphene for highly sensitive point-of-care diagnostic tests. Detection was achieved with a loop-mediated isothermal amplification (LAMP) (SPE). The interaction between a graphene-based screen-printed electrode and amplicons leads to a change from the interplay of the redox sensor with ds-DNA in cathodic current (Kampeera et al. 2019).

23.3.4 Black Phosphorous Nanobiosensor

Infection with SARS-CoV-2 allows IgM, IgA, and IgG antibodies to form, like infections with other pathogens (Ma et al. 2020). A new research has shown that the electrochemical biosensor was formed with an aptamer-functionalized nanostructured black phosphorus. After poly-L-Lysine coating, the black phosphorus nanosheets are functionalized with anti-antibody-aptamers. Compared to the lower graphene oxide biosensors, biosensors on the black phosphorus nanostructure

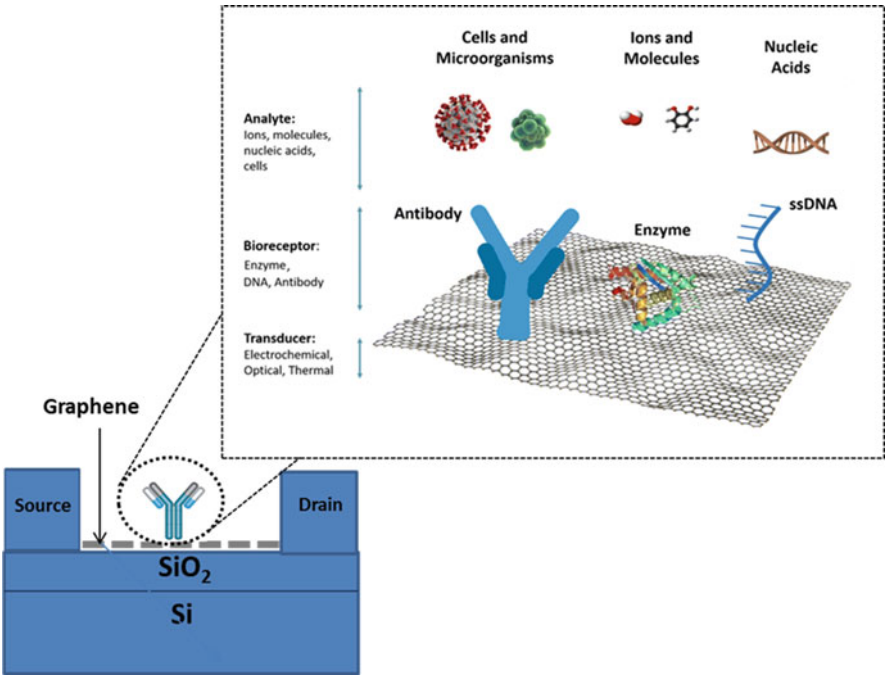

Fig. 23.5 Graphic diagram of graphene-based biosensors

base demonstrate higher sensitivity and specificity to detect, respectively, down to pg and ng level (Kumar et al. 2016).

23.3.5 Carbon Nanotubes Sensor

Carbon nanotubes have offered a wide range of scientific research according to particular characteristics and activities, such as thermal, electrical, chemical, and mechanical behavior. In the field of biosensors, the biomedical usefulness of these carbon-based nanomaterials is of particular interest. In the preparation of biosensors that can detect target molecules in trace quantities, carbon nanotubes play a significant role (Yang et al. 2015). In order to generate a modified AuNP-containing carbon nanotube electrode, Oh et al. (2009) and Duc Chinh et al. (2019) used electrochemical impedances to deposit AuNPs on single in situ wall carbohybrid nanotubes (SWCNTs). The DNA of hepatitis B and papilloma virus were restrained on SWCNTs/Au and catched by DNA probe as shown in Fig. 23.6 (Duc Chinh et al. 2019; Oh et al. 2009). Also, carbon nanotubes/Pt/Cr sensor used for detecting the DNA of influenza type A and catched by using DNA probe (Gopinath et al. 2018). The new generation of carbon nanotube biosensors showed great sensitivity because of their high surface area, simple preparation, and a good retention for nanoparticle (Oh et al. 2009).

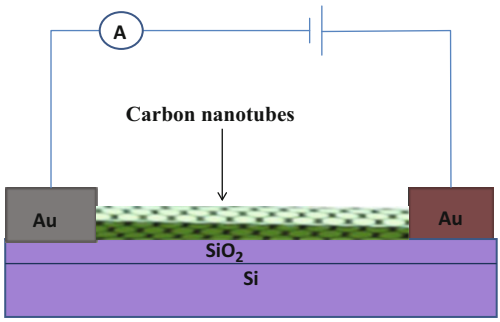

Fig. 23.6 Graphic diagram of carbon nanotubes based biosensors

23.3.6 Silica Nano-Based Sensor

The visible benefits of silica nanoparticles concern their ability to design special, biologically compliant nanolayer structures. It promotes the use of bio- and immunosensors in various forms. Chen et al. (2010) have studied the identification of Epstein-Barr virus-derived latent membrane protein 1 (LMP-1) using a multi-layered structure to improve the detection sensitivity. With silica nanospheres and QDs of CdTe/QDs on gold layer, a biosensor was designed to amplify the signals with a limit of LMP-1 detection of 1 pg/mL and 0.001–10 ng/mL of linear range.

23.3.7 Silver Nano-Based Sensor

The fluorescence features of silver nanostructures provided high sensitivity for optical biosensors. Cao et al. (2015) prepared biosensors based upon fluorescence activity of the silver nanoclusters with the detection of target DNA sequence (HIV), (HBV), and (HTLV-I) genes. The fluorescence behavior of the silver nanoclusters is strong and bright before the conjugation of the hairpin probe with the target DNA viruses. However, the fluorescence of nanoclusters become weak and the structure of the hairpin probe is thus disorders after binding between the strand of the probe and the target DNA. High sensitivity and low LOD of 4.4, 6.8, and 8.5 nM for the detection of HIV, HBV, and HTLV-I were the advantages of this type of biosensor (Fig. 23.7).

23.3.8 Copper Nano-Based Sensor

New nanotechnology offers new ways to investigate the viral impact of copper nanoparticles. Copper nanoparticles can interact closely with the virus and identify it easily (Magdassi et al. 2010). In recent study, they used copper nanoclusters to create colorimetric biosensing technique. A naked eye may make it possible to identify the DNA hepatitis B virus. This method has significant potential compared to traditional methods. The high sensitivity and selectivity, correct diagnosis, and a

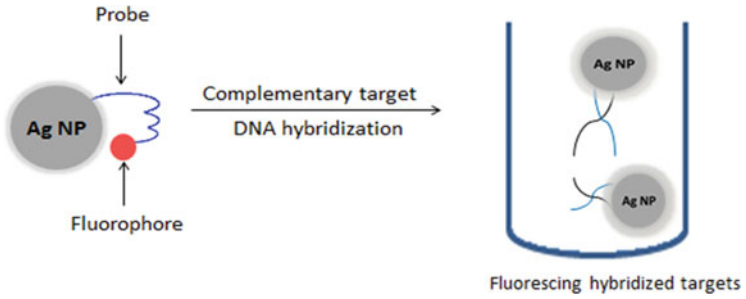

Fig. 23.7 Graphic diagram of silver nano-based sensor

cost-effective were beneficial. In short, this test is a very desirable one in DNA analysis candidate who does not need sophisticated and costly solvents (Mao et al. 2016).

23.3.9 Lanthanide-Doped Polystyrene NPs Enabled Biosensing

The lanthanides have a unique electronic configuration that allows lanthanide doped NPs to have many attractive optical properties, including a long luminescence life, a large and sharp emission band. Due to the long luminescence period, lanthanide doped NPs are often used for highly sensitive biosensor applications (Banerjee and Jaiswal 2018). Using lanthanide doped NPs, a lateral flow immunoassay (LFIA)-based biosensors have been described as a diagnostic point for the treatment of infectious agents (Chen et al. 2020). The LFIA developed is based on the principle of detection of antiCoV-2 IgG in human serum samples. This biosensor platform was made using lanthanide doped polystyrene nanoparticles (LNP) which were made by a mini emulsion polymerization process. In addition, surface modification of the LNP, which acts as a fluorescent probe, was carried out using murine anti-human IgG (MH-IgG) and rabbit IgG (R-IgG) antibodies after the EDC/NHS chemical reaction. The nitrocellulose membrane is used as a template to immobilize the recombinant nucleocapsid-phospho-protein from CoV-2, which is responsible for the specific IgG configuration. The resulting LIFA can detect anti-CoV-2 IgG in human serum in about 10 min. To confirm the clinical application of LIFA, the authors also compared the detection results of anti-CoV-2 IgG using the RT-PCR technique. The LIFA observations were the same as those obtained by the RT-PCR technique, except for one sample which showed the opposite result. Thus, the authors confirm that the developed LFIA does not provide precise quantitative results due to the lack of an anti-CoV-2 IgG standard but can be of great interest for the rapid diagnosis of a suspicious COVID-19 case (Ma et al. 2019).

23.3.10 Nanowire Affinity-Based Biosensors

Nanowire (NW) is one-dimensional nanostructures in the form of wires that can consist of non-metallic and metallic elements with a nanometer and micrometer diameter. NW is strong and has high physical strength, which is directly due to the unique crystal structure and morphology of 1D, as well as its mechanical, electrical, magnetic optical and thermal properties. Silica NW has been extensively researched for biosensor applications due to its photonic, optical, and electronic properties with excellent biocompatibility for sensory applications (Ambhorkar et al. 2018; Patolsky et al. 2006). Due to their wide band, which extends the detection range from purely electrochemical or FET-based detection to simpler optical methods, NW silicon and indium oxides are primarily investigated as new biosensors for the detection of highly sensitive viruses (Kaushik et al. 2014; Arora et al. 2013).

23.4 Fungal Infections as Post-COVID Symptoms

People suffering from COVID-19 threat, such as those in an intensive care unit (ICU), are especially susceptible to fungal infections. Aspergillosis or invasive candidiasis (caused by white fungi) is the most frequent fungal infections in people with COVID-19 (Koehler et al. 2020a, b; Song et al. 2020). These fungal co-infections are becoming more common and have been linked to serious sickness and mortality. It is critical to be aware of the likelihood of fungal co-infection in order to decrease delays in detection and treatment and thereby assist prevent serious disease and death from these infections (Beer et al. 2020; Lansbury et al. 2020). Previously, researchers believed that aspergillosis only occurred in persons with extremely compromised immune systems. However, aspergillosis is increasingly being documented in people who do not have impaired immune systems but have severe viral respiratory infections, such as influenza. Several recent studies have described COVID-19-related pulmonary aspergillosis (Benedetti et al. 2020; Marr et al. 2021; Dellière et al. 2020; Koehler et al. 2020a, b; Verweij et al. 2020). In individuals with severe COVID-19, fungal infections that are resistant to antifungal therapy have also been reported. Early detection and monitoring for Candida infections and antifungal resistance infections (e.g., *Candida auris*, azole-resistant *Aspergillus*) are critical for minimizing COVID-19 mortality in individuals with severe COVID-19 fungal infections (Posteraro et al. 2020; Meijer et al. 2020).

23.4.1 Biosensors for Fungal Diagnosis

Current and future advances in biosensor technology, which employ a slide of approaches that have yet to be utilized in the framework of medical mycology, are anticipated to improve fungal diagnostic research greatly. Biosensor technologies are projected to play an increasingly essential part in the detection and monitoring of all infectious illnesses, with particular relevance in the initial identification of fungal

Table 23.2 Methods documented for fungal diagnosis based on nanomaterials

Fungi	Nanomaterials	Specimen	Limit of detection	References
Paracoccidioides brasiliensis	Gold nanoparticles	Fungal DNA	Greater than 4 mg mL	Martins et al. (2012)
Candida albicans	Carbon nanotubes	Fungal solutions	50 Colony Forming Unit/mL	Villamizar et al. (2009)
Candida spp.	Gold nanoparticles	Wastewater effluent	–	Naja et al. (2008)
Candida albicans	Peptide nuclei acids	Blood culture	100%	Rigby et al. (2002)
Aspergillus fumigatus				
C. glabrata	Gold nanowire	Fungal DNA	100 fM	Yoo et al. (2011)
C. krusei				
Cryptococcus neoformans				
Candida spp.	Nanoparticles	Whole blood	1 Colony Forming Unit/mL	Neely et al. (2013)

infection. Furthermore, biosensors provide continuous monitoring of analytes, which may aid in assessing therapy response. Recently, most fungal diagnostic approaches include invasive sample, are time demanding, and/or have limitations in terms of specificity or sensitivity (Hussain et al. 2020). As a result, creating new analytical methods that overcome these constraints is critical in establishing improved fungal infection control techniques. The development of nanotechnology has enabled the combining of numerous analytical approaches to develop new options in this arena. For example, spectrophotometric methods have been applied to diagnose *Paracoccidioides brasiliensis*, and currently an amalgamation of artificial intelligence and metabolomics was documented for paracoccidioidomycosis (Martins et al. 2012; De Oliveira et al. 2020). Fluorescence in situ hybridization approaches for aspergillosis and candidiasis have been published (Rickerts et al. 2011; Da Silva et al. 2015). MALDI-TOF analysis (matrix-assisted laser desorption/ionization time of flight) currently allows the exact and quick detection procedures for Candida and other yeast species, which are quickly being adapted for filamentous fungus (Lacroix et al. 2014). On primary patient samples, this methodology is also being examined for its value as a diagnostic approach. However, this is a costly approach that needs specialized technical expertise and equipment and cannot be easily deployed in field conditions. Recent studies have also concentrated on the synthesis of new nanomaterials for the building of analytical stages in order to increase sensitivity and specificity. Quantum dots, molecular beacons, DNA dendrimers, and other nanomaterials have been used in numerous techniques (Table 23.2).

Microfluidic-based approaches for fungal detection have lately emerged as an active research topic (Zhou et al. 2019). There have been published literatures based

on various detection methodologies. Using a real-time PCR-based microfluidic device, *Candida albicans* DNA was identified in human blood (Busser et al. 2020). Other reports documented approaches including the use of gold nanoparticles, peptide nucleic acid, gold-nanowire, and colloidal gold and silver (Rigby et al. 2002; Yoo et al. 2011; Naja et al. 2008; Neely et al. 2013). A polymerase free technique for *C. albicans* identification in clinical samples was just published (Chen et al. 2020). The suggested approach was based on single molecule tethering where the movement of the beads tethered by DNA probes provided the signal, and the suggested approach could detect 1 colony forming unit per milliliter in blood sample. A colorimetric approach for the diagnosis of *Aspergillus niger* spores was established based on interfaces between fungal spores and gold nanoparticles altered with a specific binding peptide that was recognized by phage display screening. These binding peptides can be identified 50 spores within 10 min (Lee et al. 2020).

Generally, for the manufacturing and development of fungal biosensors for clinical application, there are two important needs: first, unique biomarkers that would allow particular identification of the target organism, ideally from a variety of clinical specimens, must be identified. Secondly, the chosen biomarkers must be successfully immobilized on the sensing surface. Biomarkers must have features that can be quantified and utilized to determine if the circumstances are ordinary or pathogenic. They are cellular or molecular in origin and may be tested in tissue biopsies, or in cerebrospinal fluid, and blood, etc. A diverse range of fungal biomarkers have been investigated as potential candidates such as galactomannan, mannan, beta-glucan, and cryptococcal antigen (Huppler et al. 2017; Kauffman et al. 2011). These biomarkers, which have been identified and established into diagnostic investigations, might be studied for their possible adaption for detection via biosensor, which could then be reduced and put into a portable instrument. Other biomarkers, as siderophore, mycotoxins,, dendritic cell-associated lectin-2, offer promise but have not yet to be turned into diagnostic tools (Kong et al. 2019; Chauhan et al. 2016; Vendele et al. 2020).

23.5 Conclusion

The traditional virus detection methods have difficulties such as cost, high risk of contamination, and the viral load. However, biosensors offer highly precise sensitive and specific systems able to calculate very low viral concentrations. Nanomaterials have succeeded in integrating in biosensing applications to easily, sensitively, and reliably recognize influenza A, hepatitis B virus, papilloma virus, and SARS-CoV-2. Magnetic nanoparticles have provided significant interest to biosensing methods because they provide unrivaled benefits over other techniques. The development of magnetic nanoparticles, for example, is cost-effective, mechanically and chemically stable and biocompatible, and they are functionalized with antibodies or DNA/RNA probes that can precisely bind to target SARS-CoV-2, herpes simplex virus, adenovirus, and influenza viruses. Also, using of black phosphorus nano-based sensor

provides high sensitivity at ng levels for detection of SARS-CoV-2 antibodies. Other nano-based sensors like carbon, silica, silver, and copper nano-based sensors used to detect the viral DNA according to the particular characteristics. In brief, major challenges still need to be tackled, and tremendous efforts should be made to improve future nano-based sensor studies for virus detections because of their potential for early, precise diagnosis and avoiding further outbreaks of the pandemic. The protein constituents of coronaviruses that have been used for the attacking of these respiratory viruses and their replication were essential in nanobiosensors for human coronavirus detection.

Nowadays, fungal infections are becoming a growing health and economic problems. Especially, black or white fungi are the most frequent fungal infections in people with COVID-19. Accurate and timely identification of fungal infections is critical to supplement efforts in the development of therapeutic medicines, because late identification of fungal infections dramatically reduces the possibility of therapeutic treatments being successful. Traditional diagnostic techniques have already made tremendous progress in identifying and managing invasive fungal diseases. The problem is to determine the causal agent precisely and quickly since this typically directs the right antifungal therapy. Recent diagnosis will be progressively supplemented as nanotechnologies evolve, perhaps leading to the creation of less invasive and miniaturized detection systems. The next age of biosensors is now being created by immobilizing particular protein indicators onto gold nanoparticles. Photonic approaches can be used to identify biosensor interactions with particular targets on the surface of pathogenic fungus. These innovative approaches provide significant potential in addressing the issues connected with the quick identification of fungal infection in human medicine.

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