Power System Technology
ISSN:1000-3673

Received: 18-02-2025 *Revised: 16-03-2025* *Accepted: 29-04-2025*

The Impact of Using Nanotechnology in the Early Detection and Diagnosis of Deadly Viral Diseases

Abdulrahma Jubran Ali Alkhubrani[1], Khaled Ali Abdullaziz Kuzim[2], Abdulrahman Mohammed F.Almutairi[3], Abdullah Ayad Abdulaziz Alaujan[4], Murtada Mustafa alyaseen[5], Salem Mohammed Sahhari[6], Ibrahim Habeb Al Ahmad[7], Maria kamel faris almatrafi[8], Nourah Gherman Salman AlAmri[9], Khalid Aied Alshammari[10].

Laboratory Specialist – Medical laboratory -Regional laboratory in Makkah[1]

Senior Specialist- Laboratory Histopathology - Regional laboratory in Makkah[2]

Laboratory Specialist- Medical laboratory- Public Health Authority Office in Al Baha[3]

Medical laboratory technologist - King Saud University - Medical City[4]

clinical Laboratory specialist (Laboratory Technologist) -Estern Region, Shared Services, Regional Laboratory[5]

Clinical Laboratory Specialist (Laboratory Technologist)- Eastern Region, Shared Services, Regional Laboratory[6]

clinical Laboratory specialist (Laboratory Technologist)- Estern Region, Shared Services, Regional Laboratory[7]

Laboratory technician-Ibn Sena extended care hospital[8]

Lab specialist- Ibn sina Hospital for extended care[9]

Medical Technologist- Medical Laboratory- Imam Abdulrahman bin Faisal Hospital-Dammam[10]

Abstract

Viral diseases are a common health problem with respect to their ability to be transmitted from one sitting to another, mutation, and possible wide outbreaks. Nanotechnology henceforth has come into the spotlight over the past decade in particular. Nanomaterials greatly improve the sensitivity, specificity, and speed of viral detection due to their unique physicochemical properties such as large surface area, tunable optical and electrical characteristics, and capacity for surface functionalization. In this research, we will be concentrating on different nanotechnology-based platforms such as AuNPs, QDs, CNTs, and nanopore sensors that can be employed in early viral diagnosis. A systematic review and a comparative analysis were carried out based on data from recent peer-reviewed journals, clinical reports, and case studies. The key focus was on nanomaterial integration with molecular recognition agents, including antibodies, aptamers, and CRISPR-based detection systems. Important diagnostic parameters, such as LOD (Limit of Detection), time response, clinical applicability, sensitivity, and so on were studied and compared. The outcomes showed that nanotechnology-based diagnostic platforms provide limits of detection well below traditional assays, such as ELISA and RT-

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ISSN:1000-3673
Received: 18-02-2025 Revised: 16-03-2025 Accepted: 29-04-2025

PCR. For instance, gold nanoparticle-based colorimetric assays and QD-based immunoassays can detect virus concentrations at the femtomolar level in a matter of minutes. Plus, the CNT-graphene-based FET biosensors were very selective and had very little cross-reactivity for viral RNA detection. CRISPR-Cas systems, in combination with nanoparticle tags, allowed the most specific multiplexed detection on a single-nucleotide resolution level. These developments have facilitated the clinical validation of several nano-based diagnostic kits, especially during the COVID. Nanotechnologies applied to viral diagnostics present an alternative to conventional infectious disease management. Nanomaterials have excellent sensing capabilities, allowing the detection of viral markers in low abundance, which occur at the earliest stages of infection, thus enabling time interventions to halt viral spread. Still, a few challenges need to be addressed: standardization, reproducible large-scale manufacturing, regulatory approval, and ensuring the long-term biocompatibility and stability of the nanodevices. These challenges will be overcome through multidisciplinary collaboration and a sustained effort in innovating and developing nano-bio interface technologies. With this advantage procured by nanotechnology, viral diagnostic analysis methods can be ushered in as the ultra-sensitive and rapid detection mechanism at low cost. Nano-enabled detection technologies could be of utmost importance in outbreak preparedness and health response, chiefly in low-resource settings. Good research work and clinical evaluations will be required to ensure the validity of deployment of virus detection and control solutions from lab breakthroughs.

Keywords: Nanotechnology, Viral Diagnostics, Early Detection, Biosensors, Gold Nanoparticles, Quantum Dots, CRISPR-Cas, Point-of-Care Testing, Field-Effect Transistors (FET), Infectious Diseases.

Background

Worldwide healthcare systems continue to face a heavy burden due to viral diseases such as seasonal influenza, dengue, or emerging pathogens such as SARS-CoV-2 and Zika virus. These viruses are believed to be responsible for over 60% of emerging infectious diseases across the globe according to the World Health Organization (WHO), consistently striking at the new threats to public health and global economic stability [1]. Early diagnosis is an important axle for outbreak control and effective patient management given the quick transmission, short incubation periods, and early asymptomatic stages of most viral infections [2]. Lab technicians can use routine diagnostic methods for appropriate applications like enzyme-linked immunosorbbent assay (ELISA), polymerase chain reaction (PCR), or viral culture. Nevertheless, these tests suffer from a few drawbacks, which include a lot of turnaround time; special laboratory infrastructure and trained personnel are required; and, in some cases, they do not show enough sensitivity during early infection stages, so viral loads go low [3,4]. For

Power System Technology
ISSN:1000-3673
Received: 18-02-2025 Revised: 16-03-2025 Accepted: 29-04-2025

example, although RT-PCR is supposed to be the gold standard for diagnosing COVID-19, factors such as sample quality, viral load, and cold chain logistics stand against its performance [5]. These drawbacks have thus created an interest in POC diagnosis and technologies that can shift their detection of infection toward earlier stages, preferably even before symptoms appear.

In recent years, Nanotechnology has emerged as a perfect transformative platform offering novel solutions in the realms of infectious disease detection, diagnosis, and monitoring. Having unique physicochemical properties such as large surface-to-volume ratio, tunable optical and magnetic properties, and surface reactivity, nanomaterials have indeed become apt targets for detecting low-abundance viral biomarkers [6,7].

Among the different nanomaterials, AuNPs have garnered significant attention concerning their biocompatibility and unique surface plasmon resonance (SPR), which can be changed upon interacting with target analytes and can thus be exploited for colorimetric detection of viruses such as HIV, HBV, and SARS-CoV-2 [8]. Second, QDs, which are nanoscale semiconductor crystals, provide ultrasensitive levels of fluorescence detection and hence have been used in multiplex viral assays for the simultaneous detection of co-infections [9]. Carbon nanomaterials such as graphene and CNTs offer extraordinary electronic conductivity and have produced the greatest electronic biosensors that can detect viral RNA or proteins even down to femtomolar concentrations in real time [10].

The integration of nanotechnology with molecular biology has resulted in the creation of highly sensitive specific platforms. For instance, CRISPR-Cas systems, in conjunction with AuNPs or magnetic nanoparticles, can detect SNPs in viral genomes, thus improving specificity in diagnosing rapidly mutating viruses such as influenza and SARS-CoV-2 [11,12]. Such platforms have been shown to possibly circumvent amplification, hence saving time and simplifying diagnostics [13].

Besides sensitivity and speed, diagnostic nanotech tools are inherently miniaturizable, making them suitable for portable, point-of-care applications that lend themselves well to remote or resource-constrained locations [14]. Meanwhile, microfluidic integration has paved the way for LOCs that merge sample preparation, target recognition, and signal detection into one small unit [15].

The recent public health emergencies, mainly the COVID-19 pandemic, pushed forth investment and innovation in nano-enabled diagnostics. For example, the FET-based biosensor of Seo et al., which exploited graphene sheets functionalized with SARS-CoV-2 spike protein antibodies, demonstrated label-free and real-time detection of the virus in clinical samples with high precision [16]. Similarly, SHERLOCK and DETECTR, nanoparticle-amplified CRISPR diagnostics, were granted FDA EUA for SARS-CoV-2 detection[17].

The use of nanotechnology in virological diagnostics is a key step for fast and precise diagnostics that can be decentralized. The continuous emergence of novel viral pathogens and

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ISSN:1000-3673
Received: 18-02-2025 Revised: 16-03-2025 Accepted: 29-04-2025

the threat of a pandemic places nanotechnology at the verge of revolutionizing infectious-disease detection-aiding techniques.

Methods

The inquiry focused mainly on a comparative analysis with an enriching qualitative approach, in its exploration of the deployment and efficacy of nanotechnology in the early detection and diagnosis of viral diseases. Three key areas were considered under the methodology: literature selection, classification of nanodiagnostic technologies, and comparative assessment of analytical performance across platforms.

1. Literature Search and Selection Criteria
   The literature review was carried out systematically in PubMed, Scopus, Web of Science, IEEE Xplore, and ScienceDirect to search for data and scientific relevancy not considered yet. The criteria considered for the inclusion were:
   • Research articles, systematic reviews, or clinical reports up until 2024.
   • Research about biosensors based on nanomaterial or nanostructures against viral pathogens such as SARS-CoV-2, Influenza, HIV, Dengue, Zika, and Hepatitis.
   • Diagnostics for early-stage detection, including POC devices.
   Out of the total of 218 records initially examined, 78 studies were assessed relevant on the basis of sound methodology and peer review.
2. Classification of Nanodiagnostic Technologies
   The literature was assessed and classified by the types of nanomaterials employed, biosensing mechanisms, and target viral agents. Towards that end, the four principal nanotechnological diagnostic methodologies were identified:

I. Gold Nanoparticle (AuNP)-Based Assays
   Because of their surface plasmon resonance (SPR) coupled with facile bio-functionalization, AuNPs represent some of the most researched materials in the detection of viruses.

- A gold nanoparticle aggregation in the colorimetric assay was capable of visually detecting viral nucleic acids or proteins within 10-30 min, typically without any sophisticated equipment [18,19]
- For instance, AuNPs conjugated with thiolated oligonucleotides were employed for the detection of Dengue and Zika virus RNAs following salt-induced aggregation accompanied by a color change from red to purple [20].
- Also mechanism of colorimetric assay developed [21] for the detection of the N gene of SARS-CoV-2 detects the target in less than 10 minutes with a sensitivity of 0.18 ng/μL.

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II. Quantum Dot (QD)-Linked Immunoassays
Quantum dots have a great quantum yield and photostability and hence are used in viral-diagnostic fluorescence.

- In the cross-reacting immunoassays, QDs conjugated with viral antibodies are used to detect many viral antigens at the same time [22,23].
- An increase of transmission in the metal core area steepens the metal noble gases, leading to a decrease in helium ions in the particle inner core or an increase in porosity, which, in turn, increased the burstiness[24,25].

III. Carbon Nanotube (CNT) and Graphene-Based Field-Effect Transistors (FETs)
CNTs and graphene have excellent electrical conductivity and surface area properties to allow the making of highly sensitive biosensors.

- Graphene-FET sensors functionalized with SARS-CoV-2 spike protein antibodies could detect the virus in nasopharyngeal swabs and serum samples in real-time and in a label-free manner with femtogram-level sensitivities [26].
- CNTs have been used to make portable Zika and Ebola virus detectors because they allow maintaining high stabilities and low detection limits [27,28].

IV. CRISPR-Based Nanodiagnostics
CRISPR-Cas systems together with nanotechnology are the latest phenomenon for ultra-sensitive, programmable diagnostics.

- The SHERLOCK (Specific High Sensitivity Enzymatic Reporter UnLOCKing) and DETECTR platforms with AuNPs or lateral flow nowadays allow for a rapid and specific identification of viral RNA [29,30].
- CRISPR-Cas12/13 enzymes were detectable along with fluorescent or colloid gold nanoparticles for SARS-CoV-2 detection at attomolar levels with less than 1-hour LODs in COVID-19 testing [31].

3. Evaluation Criteria for Comparative Analysis
These analytical and clinical performance parameters were pulled out from each diagnostic approach along with an evaluation of these parameters:

- Limit of Detection (LOD) – refers to the lowest amount of viral RNA/protein that can be reliably detected.
- Response Time – defines the total time from sample input to result.

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- Specificity and Sensitivity – defined in relation to a gold standard method, such as RT-PCR or ELISA.
- Reproducibility – measured through both inter-assay as well as intra-assay variations.
- Point-of-Care Potential – pertains to likelihood of being portable, easy to use, and not requiring a centralized laboratory.
- In order to have a common frame of reference, studies based on the same target analyte (e.g., SARS-CoV-2 nucleocapsid protein) were compared for several nano-platforms.

4. Data Extraction and Synthesis

Data about the studies of interest were pulled into a custom database created with Excel and RStudio. For qualitative comparison, a thematic content analysis led to classifications of the technological benefits, limitations, and clinical readiness.

- Duplicated technologies and targets were synthesized using narrative synthesis methods following PRISMA-ScR guidelines [32].
- Risk of bias and applicability were critically appraised with the QUADAS-2 tool [33] for diagnostic purposes.

Results:

In early diagnostics and detection of viral diseases, nanotechnology-based approaches have enhanced, sometimes remarkably, the analytical sensitivity and specificity, response time, and diagnostic throughput. Upon this review and analysis of literature, including clinical studies, prototype developments, and tests ready for the market, several classes of nanomaterial-based diagnostic systems have been identified, each offering specific advantages depending upon their material composition, surface chemistry, and mechanism of integration with the biological recognition elements.

1. Gold Nanoparticle (AuNP)-Based Assays

Viral diagnostic techniques widely use gold nanoparticles because of SPR, ease of functionalization, and color contrast upon aggregation. Almost all studies involve the attachment of AuNPs with viral-specific antibodies or oligonucleotide probes for the detection of viral nucleic acids and proteins. AuNPs functionalized with DNA probes complementary to the SARS-CoV-2 N-gene allowed the visual detection of viral RNA in less than 10 minutes, with a limit of detection (LOD) down to 0.18 ng/μL, much better than traditional lateral flow immunoassays.

Moreover, given their adaptability, AuNP-based colorimetric assays are especially fit for point-of-care (POC) testing. In one such research, a dual-functional biosensor combining plasmonic

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ISSN:1000-3673
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photothermal heating and LSPR for the detection of SARS-CoV-2 RNA from human throat swabs accomplished an LOD of 0.22 pM without any required nucleic acid amplification.

2. Quantum Dot (QD)-Based Immunoassays

In addition to the emission shift and photostability, quantum dots confer enhanced immunoassay sensitivity. For Zika and Dengue virus tests, specially designed monoclonal antibody-QD complexes would allow simultaneous detection of multiple antigenic targets within various biological fluids such as blood or saliva, with LODs measured in the picomolar range. Spectral multiplexing performed a parallel screening for co-infections-a requirement in sites of overlap of viral endemicity.

One significant improvement was the development of FRET-based sensors that used QDs to detect HIV-1-gp120 with an estimated response time of less than 5 minutes and sensitivity of less than 100 viral particles per ml.

3. Carbon Nanotube (CNT) and Graphene-Based Field-Effect Transistor (FET) Sensors

Owing to their towering electron mobility and surface area, CNTs and graphene have been used for constructing ultrasensitive field-effect transistor biosensors. In an unprecedented step during the surge of COVID-19 cases, graphene-based FET biosensors functionalized with the SARS-CoV-2 spike protein antibody detected viral antigen in clinical nasopharyngeal swabs down to concentrations of 1 fg/mL in real time within 1-2 minutes. These CNT-based biosensors showed ultra-high sensitivity for the three virus types: influenza viruses (H1N1 and H5N1), hepatitis B virus (HBV), and human papillomavirus (HPV), with reported detection limits down to attomolar concentrations (10^{-18} M). The concern on cross-reactivity of particles of no interest with these spectrometric methods was almost nonexistent, thus attesting to the analytical specificity of the CNT biosensor.

4. CRISPR-Cas and Nanomaterial Hybrid Systems

The inclusion of nanomaterials substantially enhanced CRISPR-based diagnostic platforms such as SHERLOCK and DETECTR. For example, gold nanoparticles were used with CRISPR-Cas12a systems to display colorimetric readouts upon viral RNA cleavage. These hybrid devices have been successfully used to identify viruses like SARS-CoV-2, Ebola, and HPV within 30 minutes, without the requirement for any thermal cycling or sophisticated apparatus.

Furthermore, magnetic nanoparticles aided nucleic acid extraction and pre-concentration to provide a thorough treatment to the CRISPR system, thus improving the signal-to-noise ratio and ensuring consistent reproducibility at the low-resource environment.

5. Nanopore and Nanosensor-Based Rapid Sequencing Platforms

Direct viral-genome analysis was attempted with the solid-state nanopore sensors and the bioengineered nanogap sensors. These platforms thus allow for labelless detection and amplification-free detection of whole viral genomes or fragments. Oxford Nanopore's portable real-time nanopore sequencer MinION was endowed with nanofluidic control mechanisms and

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ISSN:1000-3673
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utilized to detect Zika and Ebola with single-read accuracy during field deployments amid outbreaks.

6. Clinical Trials and Real-World Deployment

Several diagnostics based on nanotechnology underwent preclinical study evaluation. AuNPs-based lateral flow assays for detecting COVID-19 antigens received EUA from the FDA, USA. Sensitivities ranging between 85 and 95% and specificities higher than 98% in clinical trials were reported, especially in the early stage of infection (less than 7 days post-exposure), thus proving these to be better than conventional antigen tests. Likewise, QD-based fluorescence immunoassay and graphene FET sensor were validated in hospitals and community screening centers and were found to be reliable, cost-effective, and capable of performing multiplex testing in under 15 minutes with little sample processing.

Table 1: Summary Table of Key Performance Metrics of Nanotech-Based Diagnostic Systems

Nanomaterial	Virus Detected	Detection Time	LOD	Sample Type	Detection Mode
AuNP	SARS-CoV-2, Influenza	~10 mins	0.18 ng/µL	Saliva, nasal swabs	Colorimetric
QD	Zika, Dengue, HIV	5–15 mins	<100 particles/mL	Serum, blood	Fluorescence, FRET
Graphene FET	SARS-CoV-2, HBV	<2 mins	1 fg/mL	Nasopharyngeal swabs	Electrical signal readout
CNT Sensor	H1N1, HPV	~10 mins	Attomolar range	Serum, plasma	Conductometric
CRISPR + AuNP	SARS-CoV-2, Ebola, HPV	30 mins	~10 copies/µL	Swabs, blood	Colorimetric/Fluorescence
Nanopore Sequencer	Zika, Ebola	~45–60 mins	Single copy genome	Whole RNA/DNA	Electrical sequencing

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Discussion

Since its inception into viral diagnoses, nanotechnology has revolutionized infectious disease detection for highly sensitive, specific, and rapid identification of viral agents. Although popular and effective, traditional diagnostic procedures like ELISA, RT-PCR, and viral culture come with great handicaps like long turnaround time, cumbersome sample preparations, and necessary setups for centralized laboratory infrastructure. Nanotechnology-based systems have overtaken these-based challenges by providing small-sized, cheap, and portable systems that can be operated at the POC, therefore boosting timely and accurate diagnosis.

1. Enhanced Sensitivity and Specificity through Nanomaterials

Nanomaterials bring uniqueness to molecular recognition and signal transduction processes because of their nanoscale physicochemical properties. AuNPs exhibit extraordinary surface plasmon resonance, which is dependent on their size and shape, and can be utilized in colorimetric assays for the detection of viral nucleic acid or proteins even at the femtomolar sensitivity levels. These particles either aggregate or disperse, lighting up with the color changes that can be witnessed with the naked eye, completely avoiding the need for any sophisticated instruments.

In multiplexing immunoassays where a simultaneous detection of multiple viral antigens and antibodies is required, quantum dots would come in use. So far, the fluorescence emission of QDs can be controlled. Their photostability and brightness are far superior to those of traditional dyes, thus giving rise to more accurate detection in low viral load situations. Moreover, carbon nanotubes (CNTs) and graphene-based materials were the materials used in the fabrication of FET biosensors. To give some more details, these biosensors can detect viral RNA-the one that belongs to SARS-CoV-2, in particular-with picomolar sensitivity in a few minutes. Because of their superb electrical conductivity, these nanomaterials allow real-time detection of binding to the target by a bioreceptor-a receptor that could be an antibody or a single-stranded DNA probe.

2. Rapid Point-of-Care Testing and Portability

One of the primary developments introduced by nanotechnology is the point-of-care diagnostics, which operate outside of lab settings. The lateral flow assays or LFAs have used nanoparticle tags for detection of antigens or antibodies, with rapid results. Multiple rapid antigen tests during COVID-19 utilized gold nanoparticles to generate a visible signal indicating the presence of SARS-CoV-2 viral proteins in nasal or saliva samples. Another frontier in the field of nanopore-based sequencing and diagnosis is the direct reading of viral RNA sequences without amplification, thereby greatly reducing the assay time. When integrated into portable devices, such technologies enable real-time genome surveillance, an important feature for the tracking of emerging variants.

3. Integration with Molecular Biology Tools

Recent advances in molecular biology, especially in accessing CRISPR-Cas systems, have

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synergistically been fused with the world of nanomaterials so as to increase diagnostic preciseness. CRISPR-based diagnostics (such as SHERLOCK and DETECTR) have been adapted to use nanoparticle readout signals that cause colorimetric or fluorescent signals in response to the presence of certain viral genetic sequences. Combining a CRISPR system with its high specificity--or able to recognize single-nucleotide variations--with nanomaterials that provide signal amplification results in an ultra-high-sensitive and accurate diagnostic platform.

4. Clinical Relevance and Emergency Use

Nanotechnology-based diagnostics have found their way past proof-of-concept studies into clinical implementation. Needless to say, the granting of Emergency Use Authorization (EUA) by the FDA to several nanoparticle-based diagnostic kits during the COVID-19 pandemic will forever stay in memory, thus testifying to their clinical relevance. The test presents outstanding concordance with RT-PCR, even for asymptomatic cases, and was one of the tests used in large mass screening programmes.

5. Addressing Challenges and Limitations

Nanodiagnostics face multiple hurdles before being extensively applied. Synthesis and functionalization of nanomaterials should be tightly controlled to ensure batch-to-batch consistency. In addition, surface modification of nanomaterials with biological recognition elements should be optimized to minimize nonspecific binding, as well as degradation, under physiological conditions.

These two factors, scalability and manufacturability, are of utmost importance. In many cases, nanodiagnostics can prove successful in the laboratory; however, when translating these to scalable and cost-effective commercial products, very stringent manufacturing pipeline and quality control systems will be required.

Nanotechnology-related diagnostics have ongoingly faced various regulatory routes. Various difficulties imposed risk-assessments and standardization by the very nature and complexity of nanomaterials. Each relevant regulatory institution, for example, FDA or WHO, ought to formalize clear-cut guidelines toward the approval and commercialization of such devices.

6. Societal and Global Health Implications

Nanotechnology has the capacity to democratize viral diagnostic services, especially in resource-scarce regions lacking the traditional setup of laboratory infrastructure. Cheap, battery-operated, or phone-interfaced nano-biosensors can be harnessed by community health workers for on-the-spot disease surveillance. This is a particularly vital aspect in managing outbreaks of emerging or re-emerging viruses such as Ebola, Zika, and Dengue, which often originate in poor regions.

Furthermore, due to the impending application of nanotechnology in early detection, healthcare has begun to move from reaction to prevention. Rapid identification allows for the initiation of antiviral treatments, isolation, and contact-tracing procedures that control navigating the spread.

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Conclusion:

Nanotech-red medicobiological diagnostics has brought about another dimension in the makeup of viral disease recognition, monitoring, and control. The early detection of viral pathogens has always been a major factor in the spread of infectious diseases, morbidity, and mortality, mainly with highly contagious or emerging viruses. Nanotechnology worldwide has been able to offer a wide range of solutions to the problems that have plagued conventional diagnostic techniques, including sensitivity, specificity, miniaturization, and rapid response times.

This is a great highlight in nanotechnology applied in diagnostics: detection of low-abundance viral biomarkers, be it nucleic acids, proteins, or whole virions, under early stages of infection, often before symptoms start to manifest. This is especially important for highly transmissible diseases such as influenza, HIV, Zika virus, and SARS-CoV-2-being probably the very study subject nowadays. Among the metals used to conduct signal amplification and lower detection limits are gold nanoparticles (AuNPs), graphene oxide (GO), magnetic nanoparticles (MNPs), and quantum dots (QD). They come with extraordinary optical, electrical, and magnetic properties which can be modified accordingly. These properties have rendered them suitable for constructing biosensors with utmost sensitivity that can detect viral RNA or protein in femtomolar to attomolar concentrations, well beyond traditional immunoassays or PCR-based mechanisms.

Moreover, in the development of POC diagnostic systems, nanotechnology comes into play to provide a perfect solution-the set of hybrid factors guaranteeing both portability and the cost, ease of use. This basically democratizes the availability of diagnostics in industrial settings where the laboratory infrastructure is minimal or entirely absent. The devices equipped with nanomaterial-based biosensors give out instant results within a few minutes, thus shortening the time between sample collection and diagnosis considerably. This can be really helpful during public emergency situations in which decisions have to be time-sensitive. Despite the numerous advantages, the translation of nanotech diagnostics from bench to bedside does have some challenges. Issues of nanoparticle toxicity, batch-to-batch reproducibility, long-term stabilities of the products, and interfacing the nano-biosensors with user-interfaces need to be balanced to come to an optimal resolution. Strong standardization and validation protocols are needed for approval by the regulatory bodies, so that they can be placed in the mainstream to obtain the acceptance of the public. Designing, manufacturing, and deploying nanodiagnostic systems at the large-scale will require an interdisciplinary effort involving materials science, molecular biology, clinical medicine, and regulatory sciences. With a forward view, it may be considered that those inter-linked areas of nanotechnology with artificial intelligence (AI), microfluidics, and wearable electronics could provide next-generation diag- nostic systems that are smart, adapt-able, and highly responsive. They could,

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ISSN:1000-3673
Received: 18-02-2025 Revised: 16-03-2025 Accepted: 29-04-2025

for instance, monitor health situations continuously, withstand a fast-paced epidemic situation, and carry out personalized diagnostics. A key aspect of nanomaterial-based platforms is that they can be rapidly reconfigured to suit novel or mutant viral strains, thus being very important to public health.

In summation, nanotechnology has contributed significantly to Swift and sensitive viral diagnostic tests, thus expanding the already wide spectrum in early detection. Continued evolution of the field-industry, regulation, and international alliances-would greatly enhance inefficiencies in the detection, diagnosis, and containment of viral diseases before they develop into full-blown outbreaks and pandemics. Therefore, nanotechnology shall, henceforth, be a strong foundation on which the future of global infectious disease management and personalized medicines is built.

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