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Carbon nanotubes in COVID-19: A critical review and prospects

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ABSTRACT

The rapid spread of Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) around the world has ravaged both global health and economy. This unprecedented situation has thus garnered attention globally. This further necessitated the deployment of an effective strategy for rapid and patient-compliant identification and isolation of patients tested positive for SARS-CoV-2. Following this, several companies and institutions across the globe are striving hard to develop real-time methods, like biosensors for the detection of various viral components including antibodies, antigens, ribonucleic acid (RNA), or the whole virus. This article attempts to review the various, mechanisms, advantages and limitations of the common biosensors currently being employed for detection. Additionally, it also summarizes recent advancements in various walks of fighting COVID-19, including its prevention, diagnosis and treatment.

1. Introduction

The COVID-19 outbreak came to light in December 2019, when the Chinese Center for Disease Control and Prevention (CDC) reported a new coronavirus strain, which had great potential for transmission between humans [1].

Subsequently, the etiological agent of COVID-19 was confirmed to be the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), a recently discovered strain of the coronaviridae family that phylogenetically resembles the zoonotic SARS-CoV that previously emerged in 2002 [2]. Global molecular assay statistics state that as of February 1, 2021, there were more than 100 million subjects from over 210 countries confirmed to be infected from SARS-CoV-2 infection. Furthermore, over 2 million patients have succumbed to death from the infection, thereby posing a great peril to human physical and mental health, considerably affecting the quality of life (QoL) of people across the globe [1].

The SARS-CoV-2 infection has been shown to spread quickly through respiratory droplets that are produced during sneezing and coughing. Subsequently, the virus anchors to the host receptors, following which it invades the cells via endocytosis or membrane fusion. The primary structural proteins that make up the coronavirus consist of the envelope (E), membrane (M), spike (S) proteins, and nucleocapsid (N). The ACE2 receptors, predominantly expressed in the pulmonary epithelium, facilitate the binding of the S protein to host cells. Successively, the two-step protease cleavage marks the activation of the S protein, which brings about irreversible conformational changes that eventually facilitate the combination of the host and viral cell membranes with the release of viral contents into the host cell. After the viral RNA reaches the nucleus, it replicates and generates negative-strand RNA from a single-strand positive RNA template using RNA polymerase. This negative-strand RNA also helps make new positive-strand RNAs that serve as blueprints for synthesizing new viral proteins. Concurrently, while the viral mRNA is employed in the biosynthesis of new viral proteins, new viral particles are created and released into the other cells [3,4] (Figs. 1–3, Tables 1 and 2).

Growing bodies of evidence have suggested the mode of transmission of SARS-CoV-2 through several routes, which is primarily attributed to the expression of human angiotensin-converting enzyme-2 (hACE2) in a multitude of cell types, including alveolar, endothelial, vascular, hepatic, and gastrointestinal cells. Furthermore, as the hACE2 gene is imperative in routine functions, the entire human race is prone to SARS-CoV-2 infection [5].

2. Diagnosis of SARS-CoV-2

The diagnosis of the COVID-19 infection is primarily carried out by identification of the SARS-CoV-2 viral genetic material [6,7]. The

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generally preferred targets for gene-based analysis of the SARS-CoV-2 include the testing for spike (S) glycoprotein, envelope (E) protein gene, nucleocapsid (N) protein gene, non-structural RNA-dependent RNA polymerase gene, and the open reading frame of the 1a / bc ORF1 a/b genes. However, in the molecular testing methods, the E and ORF1a/b genes are the most commonly employed genes for detecting SARS-CoV-2 infections [8].

The current testing regimen is broadly classified into two types; viz. serological and molecular testing. However, nucleic acid amplification tests (NAAT) like real-time reverse-transcription-based polymerase chain reaction (RT-PCR) are considered to be the gold standard for the diagnosis of a multitude of samples from nasopharyngeal swabs to bronchoalveolar lavage [6,7]. Although geographies with profound community-level transmission and limited laboratory resources, RT-PCR for detecting SARS-CoV-2 is deemed adequate [7].

However, in most cases, serological tests like the chemiluminescence immunosorbent assay (CLIA) and the enzyme-linked immunosorbent assay (ELISA) may be recommended to detect the humoral response mediated by IgA, IgG, and IgM that is characteristic of viral proteins. Additionally, the evidence of prior immune response to the virus is attributed to the cytotoxicity demonstrated by the Natural-Killer (NK) cells and the CD8+ lymphocytes [6].

Ponti et al. opine that there is an interplay of several biochemical, hematological and inflammatory indicators that exert their influence in the COVID-19 infections. They also reported that the major hematological indicators in COVID-19 include the absolute and relative (ratios) counts of the circulating neutrophils and lymphocytes in the blood [9]. Several studies also reported clinical incidences of lymphopenia in progressing and more severe cases of COVID-19 infections in patient populations [10]. Of the numerous biomarkers in the progression of

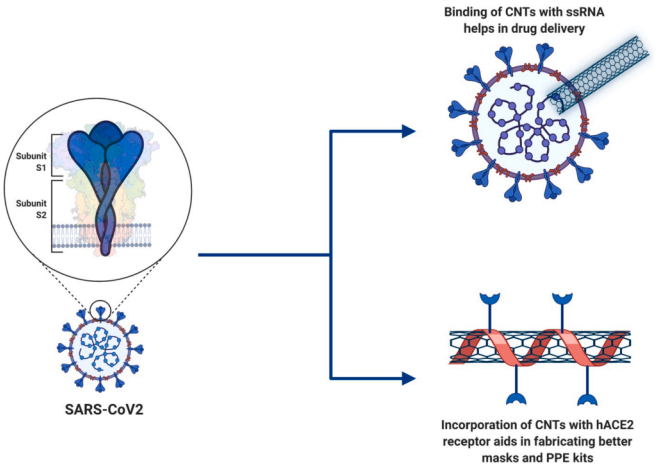

Fig. 2. Models of using CNTs for the prevention and treatment of SARS-CoV-2 infection.

COVID-19 infection, the most conspicuous ones include creatine kinase, D-dimer, and troponin. The evidence presented by Tersalvi et al. and Yao et al. underscores the direct relation of D-dimer levels with the severity of the COVID-19 conditions [11,12]. However, Garg et al. state that the severity of the SARS-CoV-2 infection can be analyzed by measuring the elevated levels of inflammatory biomarkers like C-reactive protein (CRP), ferritin (FT), interleukin-6 (IL-6), and procalcitonin (PCT) [13].

Nevertheless, there has not been a commercially available test kit that facilitates the evaluation of specific immune responses while

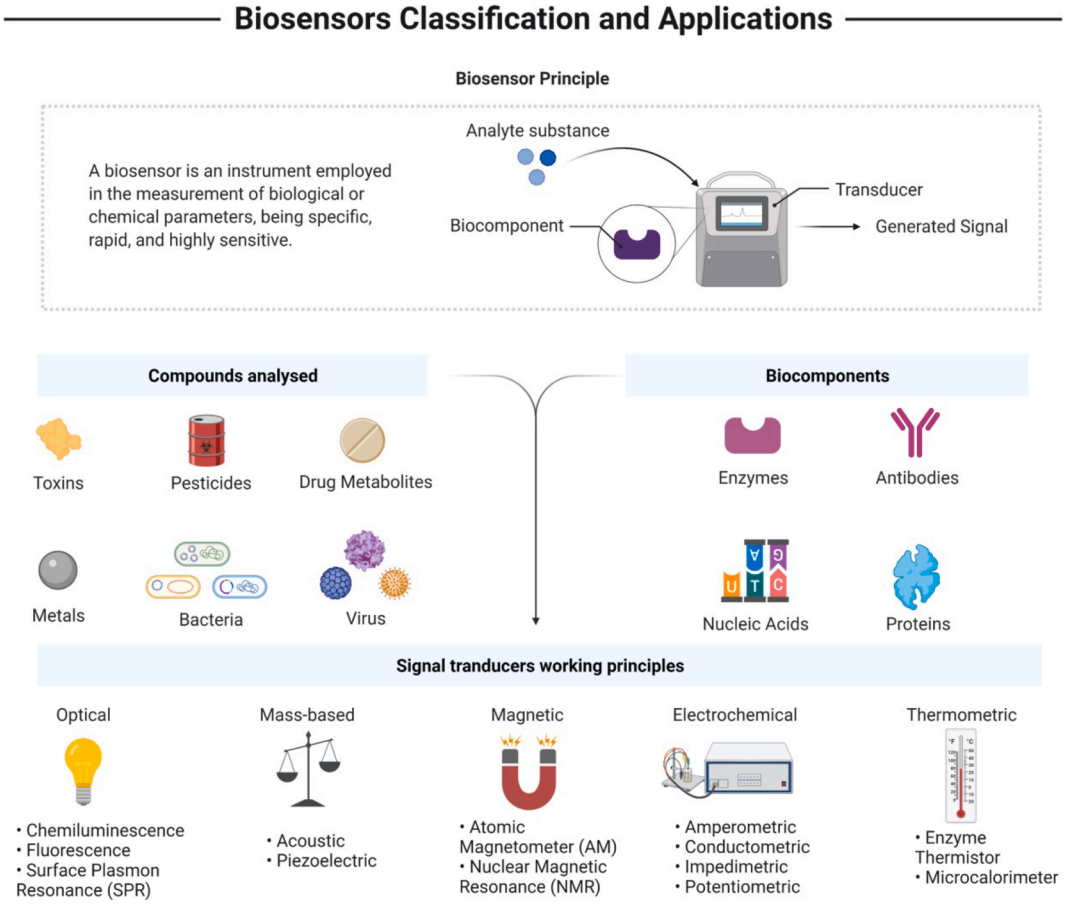

Fig. 1. Classification and applications of various biosensors.

eliciting a robust cellular response. Although antibodies targeted against the receptor-binding domain (RBD) of the S protein are highly specific for the SARS-CoV-2, their role against other proteins in the pathogenesis of COVID-19 still needs to be elucidated and studied further [6].

Furthermore, the factors such as the individual, test technique, and the data collection strategy can profoundly affect the test sensitivity, which may further introduce inconsistencies and errors between the tests. Additionally, a negative test report in a typical clinical setting does not rule out the possibility of COVID-19 infection, reiterating the need for additional laboratory and serological studies [6,7]. In addition, the entire scientific community across the globe is working relentlessly to find a viable and economical diagnostic option for early diagnosis of the COVID-19 for people across the globe.

With the rapid community-level spread of the SARS-CoV-2 and associated morbidity and mortality statistics have produced a great demand for rapid, highly selective, and sensitive detection methods to ensure early diagnosis and to avail treatment, primarily in cases where there are limited prevention and mitigation strategies in place [24].

Most diagnostic toolkits that employ antigen-based or human blood serum-based lateral-flow immunoassays usually suffer from low sensitivity issues. In addition, the performance is improved by advanced digital systems, but at the cost of speed and the requirement for massive equipment [25].

Furthermore, the gold standard currently employed for detecting COVID-19 is the commonly utilized quantitative real-time polymerase chain reaction (qRT-PCR). Nevertheless, this method is arduous, cumbersome, require skilled labor, and might be of limited utility in distant and resource-constrained surroundings. Moreover, this method may also produce specific individual false-positive results. It could fail to meet the newer challenges (like rapid viral mutation) or the need for mass-producing methods for quicker and more direct detection of viral particles or proteins. In contrast, most biosensors work by detecting the viral internal genetic material or the viral surface proteins.

Therefore, these shortcomings limit its utility while impeding the ability to produce accurate data on the infectivity and extent of COVID-19 infection in the community or population [24].

In addition, the pandemic has strained the testing resources, further prompting the development of rapid point-of-care assays along with the deployment of isothermal DNA amplification. Several emerging technologies like CRISPR gene-editing tools also prove advantageous due to their ease of utility in lateral-flow assays. They complemented with their high sensitivity and high specificity of molecular diagnostics. Furthermore, DNA sequencing and sample pooling methodologies are required to maximize the capabilities of available biosensors and to expedite mass testing [25].

Table 1
Different types of biosensors and their respective recognition elements for the detection of SARS-CoV-2

Types of biosensors	Recognition Element	References
Piezoelectric immunosensor	Spike protein S1	[14–16]
Thermal Biosensor	RNA-dependent RNA polymerase	[17,18]
Optical Biosensors (Plasmon-enhanced fluorescence)	Fluorescently labeled antibodies attached to AuNPs	[19]
Field-effect transistor biosensors (BIO-FETs)	SpAb-PBASE/Graphene-FET	[20]
Plasmonic photothermal (PPT) and localized surface plasmon resonance (LSPR)	SARS-CoV-2 Nucleic acid	[21]
Colorimetric biosensors	RNA sequence of SARS-CoV-2	[22]
Surface-enhanced Raman scattering biosensors (SERS)	Spike protein receptor-binding domain (RBD) by the ACE-2 protein	[23]

3. Introduction to nanobiosensors

With the evidence of recent pandemics and viral outbreaks, the viruses are considered a great peril to the health and well-being of humans, owing to the ravage that they cause on both health and the global economy alike. Additionally, their higher prevalence of these outbreaks can be attributed to the current improper detection tools employed for the detection of these infectious agents. Therefore, this demands a detection or diagnostic tool that is robust, rapid, selective, and accurate in its biosensing properties. The biosensors can be defined as analytical instruments that can assess very low concentrations of an analyte in biological samples (like the human serum, blood, tears, saliva, etc.) [26]. Compared to conventional qualitative and quantitative test kits, these biosensors are highly accurate, specific, and sensitive to the directed target. Generally, these biosensors comprise a biological element like a microorganism, cell organelle, cellular receptor, enzyme,

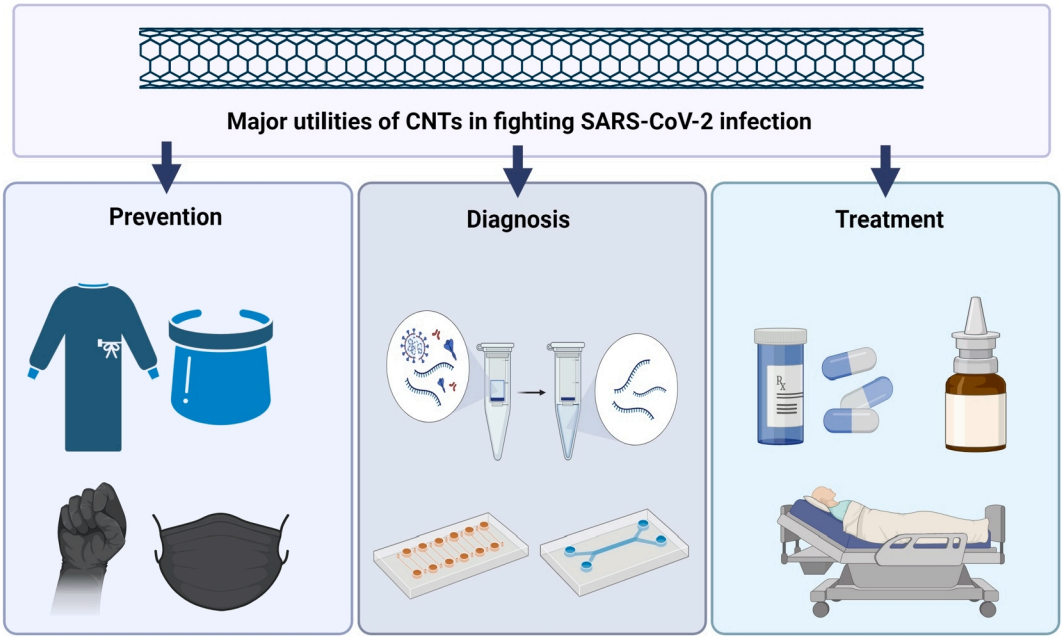

Fig. 3. Future prospects of CNTs in the prevention, diagnosis and treatment of SARS-CoV-2 infection.

Table 2
Various detection techniques with their characteristics and limitations.

Detection Techniques	Time	Advantages	Disadvantages	References
Reverse transcription-polymerase chain reaction (RT-PCR)	Hours	Ease of setting up; very high sensitivity	Easily susceptible to contamination; skilled technicians required to operate; difficult for result quantification.	[30]
Field-effect transistors (FET)	Minutes	Simple; rapid and accurate results	Ion trapping in dielectric membranes can decrease the accuracy of detection; sensitivity could be further improved.	[31]
Reverse transcription loop-mediated isothermal amplification (RT-LAMP)	Minutes	Easier to use than RT-PCR; high specificity; portability	LAMP tests can only detect if the person is currently infected but can miss patients that have recovered; reasonably new technology, so the amount of data available is insufficient.	[32]
ELISA	Hours	Absence of hook the effect at higher analyte conc.; just a single incubation step; less expensive comparatively	Need to dilute the sample arises beyond a specific concentration; the response produced by the antigens and antibodies is identical and hence cannot be distinguished between	[26]

antibodies, nucleic acids, proteins, or any other such biological element that could potentially generate signals (like thermal, electrical, or optical signals). These signals are produced on the interaction of these biological elements with a tested element and a transducer, which further aids in converting these signals into a quantifiable electrical parameter [27]. These measurement methods usually encompass special features for identifying and measuring these target analytes, owing to the utilization of distinct biological components. Several biosensors are currently being developed for a plethora of clinical and pharmaceutical applications. These utilities range from the early diagnosis and treatment of chronic disorders like diabetes and cancer to acute diseases like pathogen infestation. However, their pharmaceutical applications include drug discovery, assessment, and measurement of drug metabolites and drug activity. A more recent application of the same also provides the assessment of drugs in various biological samples and the preliminary diagnosis of disease by rapid and real-time tests [26–29].

In recent years, several novel biosensors have been employed in the detection of RNA viruses. The most prominent ones include aptamer-based biosensors, antigen Au/Ag-based electrochemical biosensors, CRISPR-Cas9-based paper strips, nucleic acid-based biosensors, optical biosensors, and surface plasmon resonance biosensors, to name a few. These biosensors could be potential instruments in providing a rapid, more accurate, compact, and much promising diagnostic tool in the light of the World Health Organization's (WHO) test-test-test theme. Furthermore, the newer technologies like aptamer-based bio-nanogate, DhITACT-TR chip-based biosensors, graphene-field-effect transistor (FET) based-biosensors, nucleic acid hybridization, rapid-cum-portable RNA extraction preps, and surface plasmon-based [like quartz-crystal microbalance (QCM), surface-enhanced Raman scattering (SERS), and surface plasmon resonance (SPR) technologies] innovations could promote rapid, highly sensitive, and efficient solutions for better diagnosis and biosensing for COVID-19 or any further unprecedented outbreaks [24].

Although numerous biosensors have been developed and commercialized for regular use, they pose several downsides. These shortcomings have been studied to be eliminated by employing nanotechnology-based interventions that perform the real-time direct detection of specific molecular targets. Thus, various nanomaterials like carbon nanotubes (CNTs), quantum dots (QDs), gold (Au), and other metallic-nanoparticles are being complemented with several biosensors owing to their characteristic features (physical, chemical, mechanical, electrical, magnetic, etc.) to accentuate the biosensing capability [26].

4. Carbon nanotubes in protection and biosensing applications

At the outset, the specific properties of the carbon nanotubes (CNTs), like the chemical, electrical, mechanical, and thermal characteristics, open new horizons for scientific development in nearly all fields of science. In the field of biosensors, the clinical and pharmaceutical utility of the CNTs is significant, as they play an essential part in the development of biosensors, primarily for the detection of target molecules when present in trace quantities within biological fluids. This characteristic of CNTs is attributed to their higher surface area to volume ratio, low density, fine pore size, flexibility, high mechanical strength, and the ability to transmit the generated physical or chemical interactions. These CNTs are also resistant to most acids and bases, resistant to respiratory droplets, able to create reactive oxygen species (ROS), and biologically compatible with various drugs [33,34]. The CNTs also comprise covalent bonds (sp2 + sp3 hybrid phases), accounting for exceptional electrical conductivity. The single-walled carbon nanotubes (SWCNTs) and multi-wall carbon nanotubes (MWCNTs) are studied to be folded graphene sheets with lengths ranging from ~50–1000 nm and diameters of ~5–20 nm [35]. These factors thus deem SWCNTs as a favorable nanoparticle for detecting, filtering, and the inactivation of biological agents. Their use has been employed in diagnosis, viral protein detection, and drug delivery modalities for fighting viruses like influenza, SARS-CoV-1, SARS-CoV-2, and HIV [34].

The CNTs functionalized with antibodies have been created to detect a plentitude of viral proteins. Recent studies have also claimed the utility of a specific RNA lyase-coupled acidified CNTs with a photothermal conversion effect as a probable inhibitor for SARS-CoV-2 [34]. Yang et al. demonstrated the acid-sensitivity of coronaviruses towards acidic and higher temperature environments (above 56 °C for more than 30 min). Thus, CNTs fabricated by acidizing followed by conjugating a special RNA lyase to exploit the capacity of photothermal conversion may prove to be a potential toolkit in the illumination and inhibition of SARS-CoV-2 [36].

Further studies by Yeh et al. fabricated a size-adjustable micromachine on the multi-walled carbon nanotubes (MWCNTs) for the label-free detection of the detection and quantification of the avian influenzas virus [37]. This intratubular spacing between the MWCNTs was tailored between 17 nm to 325 nm for allowing size-based viral entrapment [34]. A study conducted by Wasik et al. manufactured and demonstrated the utility of a chemiresistive biosensor in the detection of dengue virus based on a heparin-functionalized SWCNT network [38]. Additionally, as the SARS-CoV-2 spike (S)-protein experiences a conformational shift around its receptor-binding domain on interaction with heparin [39], which directs the utility of these heparin-functionalized CNTs in developing potent SARS-CoV-2 therapies.

Furthermore, the CNT-based filters were stated to be practical in removing pathogens. A study conducted by Vecitis et al. has demonstrated the utility of MWCNT as an anodic filter for the inactivation and

removal of the bacteria (*E. coli*) and virus (bacteriophage MS2) [40]. Moreover, Németh et al. have inspected the removal of the MS2 bacteriophages from contaminated water using the inorganic nanoparticle-conjugated MWCNT hybrid membranes. These studies unraveled that the Cu2O nanoparticle-coated MWCNT was highly efficient and removed the bacteria and viruses with ≥99.99% efficiency [41]. Another study by Viswanathan et al. demonstrated the extrapolation of the MWCNTs as aerosol filters. The filtration quality of the MWCNT-coated cellulose fiber filters outperformed that of the cellulose filters [42]. In a clinical setting, this salient feature could be employed in a multitude of ways, including limiting the virus transmission and bio-aerosol sampling to characterize the community-wide transmission [34].

In addition, the SWCNTs have been studied for manufacturing fabrics with breathable protective layers. Bui et al. created a composite material with the vertically SWCNTs implanted in the parylene-N polymer. This SWCNT-polymer composite is an ultra-breathable and protective membrane due to a better water flow rate in the nanotube cores. Additionally, their distinct inner diameters and by size exclusion principle, the SWCNTs provide a significant level of defense from bio-threats [43]. Moreover, the nanoparticles could be coated as a layer on the protective garments to trap the pathogenic microbes. Thus, the CNTs can be coated on personal protective equipment (PPEs) to decrease the spread of the SARS-CoV-2 infection [34]. A UV irradiation has reportedly inactivated the coronaviruses at 254 nm and thermal treatment at 56 °C for 30 mins, which facilitates achieving a state of photodynamic hyperthermia. However, owing to the exceptional nIR-absorption behavior and photothermal conversion efficiency of the CNTs, they experience a rapid increment in temperatures greater than 51 °C, which aids in achieving the state of photodynamic hyperthermia. These outstanding features could have profound applicability in both sterilizations of the infected protective equipment and PPEs functionalized with CNTs, as well as several theranostic applications [34].

Additionally, Lee et al. have developed a CNT face mask filter that demonstrates strong uniform hydrophobicity, high durability, high thermal conductivity while exhibiting excellent barrier and antiviral effects against the COVID-19 virus. Their exceptional barrier and filter functions can be attributed to the uniformity, strength, and durability of the CNTs. They also investigated that the pore size of the CNT network is smaller than the average size of a SARS-CoV-2, thereby filtering it without impeding the breathability that was found equivalent to a conventional polypropylene filter. The simplistic processability, feasibility, and light-weight of the aerosol-synthesized CNT filters underscore its practicality, especially in fighting against the COVID-19 pandemic [44].

Furthermore, owing to the powerful oxidizing nature of hydrogen peroxide (H2O2), several living beings produce it for a multitude of reasons, including cellular signaling, self-defense mechanism, or killing of pathogens. This has also extrapolated the utility of H2O2 in the cleaning and the disinfection of microbial pathogens. According to the density functional theory (DFT), the adsorption energy of a single H2O2 molecule onto the pristine SWCNT estimates to 0.25 eV, implying its modest interaction. Thus, for developing a filter with a long shelf life in a clinical setting, it is imperative to ensure the retainability of the H2O2 and the virus on the CNT filter. Thus, due to their catalytic activity, the transition metal atom-conjugated SWCNTs aid in eliminating the virus and improve the association between the target molecule and the biosensing material [34].

From a biosensing perspective, Zhang et al. investigated the molecular mechanics simulations to examine the molecular interactions between the carbon nanoparticles (CNPs) and an RNA fragment of the SARS-CoV-2. Their study unraveled that the interaction affinity between the CNPs and the SARS-CoV-2 RNA fragment increased in the order of fullerenes < graphene < CNTs. Additionally, these quantitative structure-activity relationships (QSAR) models on their interaction energies of the nanoparticles with the RNA fragment demonstrated robustness and high goodness-of-fit [45]. These observations were further researched for it's practical applications in different studies, which have been explored by various researchers.

Firstly, Pinals et al. demonstrated the utility of single-walled carbon nanotubes (SWCNTs) in the quantitative and qualitative analysis of a multitude of biological analytes. Furthermore, the SWCNTs inherently possess near-infrared (nIR) fluorescence. They could be functionalized with a plethora of sensing moieties or functional groups, facilitating the production of stable biological sensors with quick readouts of the alterations in the fluorescence readings. In contrast to the other traditional methods, these SWCNTs do not photobleach, thereby allowing for long-term applications. In addition, the biomolecules absorb and scatter the SWCNT nIR emission to a small extent, resulting in a readout that could pass through optically occluded patient samples, eradicating the want for sample purification and processing substantially limiting the amount of conventional testing modalities. Moreover, SWCNTs are also easy to incorporate into portable form factors after immobilization on hydrogels or papers and subsequent detection of the SWCNT nIR signal by a Raspberry Pi system, which is a form factor similar to the smartphone [46].

Concurrently, Thanihaichelvan et al. demonstrated a CNT field-effect transistor (FET)-based biosensor for the selective detection of SARS-CoV-2. The sensors were made by immobilizing the reverse sequence of the RNA-dependent RNA polymerase gene of the SARS-CoV-2 onto the CNT channel on a flexible Kapton substrate. They were then evaluated for synthetic positive and control targets. The biosensor responded selectively to the positive target sequence, with a limit of detection (LOD) of 10 fM, demonstrating its potential utility in SARS-CoV-2 diagnostic kits [47].

However, the biosensors fabricated by Shao et al. detected the existence of SARS-CoV-2 in nasopharyngeal samples, by employing a high-purity semiconducting SWCNT-based field-effect transistor (FET) embellished with specialized binding chemistry. The biosensors were then conjugated with the anti-SARS-CoV-2 spike (S)-protein antibody (SAb) and anti-nucleocapsid protein antibody. This has facilitated the SWCNT-FET sensors to recognize the Spike (S)-Antigen (SAg) and the Nucleocapsid (N)-antigen (NAg) in the calibration samples, with a LOD of 0.55 fg/mL for Sag and 0.016 fg/mL for Nag. Moreover, the Sab-functionalized FET sensors also demonstrated decent sensing performance in demarcating the negative clinical samples from positive ones, validating its utility as an economical COVID-19 antigen diagnostic device with high analytical specificity and sensitivity [48].

Additionally, Baloch et al. examined the affinity of SWCNTs with the B-domain of the S1 subunit of the S-protein based on Lennard-Jones potentials. The adsorption of the SWCNTs on the B domain surface triggered an alteration in the inner hydrogen bonds, solvent-accessible surface, and the tertiary structure, which aids in preventing the ACE2 from interacting with the S-protein. Additionally, a reduction in the mean square displacement of the B-domain was observed post the SWCNT adsorption, owing to the enhancement of its hydrophobic-hydrophilic characteristics. The interaction of the SWCNTs on the B-domain was measured using the 2-acetamido-2-deoxy-β-d-glucopyranose group, which elucidated the modification in the affinity of the S1 subunit, proving as a potential barrier for viral replication. Thus, these SWCNT-based interactions can be used for drug-delivery systems, following adequate in vitro and in vivo investigations [49].

Furthermore, Jeong et al. developed a modular technique using the "capture" ssDNA sequence-coupled CNTs for the high-yield extraction of ss-nucleic acids. These ssDNA-nanotube conjugates can be employed to isolate the SARS-CoV-2 from the liquid phase with minimal chemical reagents for the quantitative RT-PCR (RT-qPCR) detection. This nanotube-based extraction approach yields 100% of target SARS-CoV-2 RNA from the phosphate-buffered saline compared to the conventional commercial silica-column kit that yields only ~20%. These CNTs also facilitate the extraction of nucleic acids directly from the human saliva with nearly comparable efficacy as the commercially available DNA/

RNA extraction kits, obviating the necessity for additional purification of the biofluids. The use of CNTs in the extraction of viral nucleic acids allows for high-yield and high-sensitivity identification of the SARS-CoV-2 nucleic acids, relying less on chemicals that are subject to change by constraints in the supply chains [50].

In the context of alleviating the symptoms associated with COVID-19, the CNTs may demonstrate limitations due to the toxicity issues post their intranasal administration. On exposure to the lungs, the CNTs tend to activate the lower respiratory tract macrophages, which paves the way for pulmonary fibrosis and collagen creation in the lesions. These changes are brought about by the instantaneous internalization of the CNTs by the lung epithelial cells via attachment to the epidermal growth factor receptor (EGFR). However, these downsides of CNT administration could be brought about by the surface functionalization of these CNTs by conjugating biomolecules like polymers or proteins, which substantially decrease their cytotoxicity on the lung tissue. In addition, the functionalization of the CNTs by conjugating hyaluronic acid moieties considerably increases their interactions with the bronchial cells. It averts the inflammatory cascade, as the alveolar macrophages do not engulf them. Further shreds of evidence have also demonstrated that the surface functionalization of CNTs using cellular ligands significantly increases the uptake of these nanoparticles. This also aids in the release of the drugs at the intended tissue by means of endocytic absorption, but without incurring damages to the plasmatic membrane. Recent studies also increased the specificity of the SWCNTs to target only receptors on the lung tissue, post their functionalization with the anti-CTLA-4 antibodies. The CNTs conjugated with antiretroviral drugs were also found to be potent in inhibiting the reverse transcriptase enzyme activity in the lymphocytes of patients who tested positive with HIV. These insights may be of paramount importance in the diagnosis, treatment, and theranostics of SARS-CoV-2 infection, as the CNTs could facilitate the targeted and effective delivery of the drugs to the intended site of action. Although the CNTs could potentially lower the immune cell infiltration and subsequently the inflammatory cascade, but they may not be recommended for use in the treatment regimen [51].

5. Conclusion and outlook

With the global burden of SARS-CoV-2 infected patients increasing by the day, the urge for rapid and convenient testing methods has never been more. Compared to the conventional sensing methods, the nanomaterial-conjugated or nanomaterial-based biosensors offer a superior level of selectivity, sensitivity, reliability, robustness, reproducibility, and repeatability of the samples, all being economical in the first place, as it may be required for the mass populations. Additionally, with the increasing importance of nanotechnology-based biosensing platforms in clinical practice, the studies demonstrating the applicability and utility in diagnosing RNA viruses have increased substantially. Based on these conclusions, it can be made concrete that these nanotechnology-based biosensors will surely play an indispensable role in the efficient and convenient diagnosis of the SARS-CoV-2 infection. Additionally, their utility can also be extrapolated to detect various other respiratory and systemic RNA viruses, with sufficient calibration and modifications based on the biological fluid used for testing purposes. With further research and development, these biosensors could present a realistic view of the several nanomaterials and interface-based nanotechnological approaches for detecting SARS-CoV-2 in various biological fluids. These biomedical gadgets being both reliable and economically feasible, are projected to give rapid, convenient, and easy-to-use toolkits for masses across the globe. Additionally, clubbing it with interventions like the Internet of Things (IoT) and Artificial Intelligence (AI) can efficiently track, control, and forecast the spread of the COVID-19 pandemic and any other such unforeseen outbreaks.

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Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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