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REVIEW

A short review on nanotechnology interventions against COVID-19

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Abstract
The COVID-19 has affected all major aspects of the society in a global perspective. The role of nanotechnology is much sought after in fighting this pandemic. Advanced materials based on nanotechnology are the basis of several technologies starting from masks and personal protection equipment to specific diagnostic tools that could diminish the impact of COVID-19. Development of nanotechnology-based products is therefore an absolute necessity for fight against COVID-19. We examine the fundamental concepts related to virology, histopathologic findings and how nanotechnology can help in fighting the disease. In this review we discuss the state of the art and ongoing nanotechnology-based strategies like antiviral coatings, 3D printing and therapeutics to fight against this deadly disease. The importance of using nanoparticles in point of care tests and biosensors is also highlighted.

Keywords COVID-19 · 3D printing · Nanotechnology · Antiviral coatings · COVID-19 testing

1 Introduction

The World Health Organization declared coronavirus disease 2019 or COVID-19 a pandemic on March 11, 2020. The impact of COVID-19 on the world as a whole is huge with economies collapsing with deep geopolitical and social impacts. The disease was first observed in December 2019 in Wuhan, Hubei City, when locals complained of several respiratory issues with pneumonia-like symptoms. In the first week of January, the new virus was found to have more than 70% similarity with SARS virus [1]. The cases started increasing exponentially in the Hubei province and to other areas suggesting that human to human transmission was indeed happening. The transmission occurs through the droplets as a result of coughing and sneezing from both symptomatic as well as asymptomatic patients. The infection occurs as a result of the direct inhalation or by the indirect transmission after being in contact with the surfaces contaminated by the virus. The virus remains active on the surfaces for a prolonged time but can be destroyed immediately with the use of common disinfectants. There are studies that reports on the transmission of these virion particles via aerosols and can stay active in air for more than 3 h [2]. It becomes very much necessary to stop the propagation of these viruses in the air by filtration techniques using nanofilters. There is an immediate global response requirement against this pandemic, and nanotechnology can contribute in providing solutions as the SARS CoV-2 has a core shell construction in the nanometre regime[3].

Viruses are produced by a self-assembly process having a core shell nanostructure and are metastable in nature. In the SARS CoV-2, RNA material is complexed with a protein shell [4]. The name coronavirus comes from the fact that it has a protruding spike-like protein structure which encapsulates the lipid bilayer membrane [5]. It is these spike-like corona structures that interacts and attaches with the host cell. The virus structure itself is very complex and requires sufficient structural integrity to perform their infectious functions. The genomic coil is elastically strained, and the protein encapsulation should be sufficiently strong and tough to sustain the fluctuating pressures encountered [6]. Even though stringent requirements are present, the structural integrity can be

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compromised by heating, UV irradiation, using acids, alcohols and are very effective in containing the virus transmission. The particles that are released as airborne materials contain insoluble proteins, enzymes and cell debris in addition to the virion particles. The flying or the final settled droplets will have the virion particles in varying concentration depending on the patient condition but will always be surrounded by other materials. When first-line precautionary measures are developed, it is imperative to account for these non-infectious components as these might serve as a protective covering for the virions. The present knowledge is that the virus gets easily attached on smooth surfaces like stainless steel and glass compared to surface that has perforations like textile and paper [7, 8].

2 Antiviral polymer coatings

The materials that can kill the viruses upon contact are becoming although more cardinal in the present COVID-19 situation. Biocidal agents can be easily grafted onto the polymer surface or can be embedded inside, which can be later released as per requirement. Hsu et al. prepared a N,N-dodecyl methyl-polyethylenimine coating that can disinfect influenza virus. They found that the hydrophobic polycation coating could disinfect different strains of the virus, with viral RNA remaining in the solution. The researchers also found that DTAB was also effective in inactivating the virus which could be due to the presence of hydrophobic quaternary ammonium salt moiety [9]. In another study, many alkylated PEIs were covalently attached to glass surfaces and were complexed with different strains of influenza virus to check for their antiviral properties. The most potent was immobilized N, N hexyl methyl PEI and N,N dodecyl methyl PEI showing outstanding antiviral properties. These structure activity relationship studies were assessed quantitatively by measuring the protein affinity, roughness and quaternary ammonium group density. The study found that the antiviral activity of these materials depended on only one property, the surface density of quaternary ammonium groups [10]. In another study by Wong et al., N,N dodecyl methyl-polyethylenimine was layered with polyacrylic acid, and the bactericidal and the virucidal properties were analysed for the layer by layer surface. The study showed that the lbl films having thickness of 10 nm could kill both *E. coli* and *S. aureus* and a strain of A/WSN (H1N1) influenza virus. The films also had the added advantage of being non-toxic to the mammalian cell lines [11]. Bai et al. prepared electrospun nanofibres of chitosan which was functionalized with a quaternary amine to obtain (N-(2-hydroxypropyl)-3-trimethylammonium)propyl] chitosan chloride (HTCC). The electrospinning ability was improved by the addition of graphene which could remove around 95% of porcine parvovirus from solution. The HTCC and graphene showed high positive charge and hydrophobicity which further enhanced the virus removal properties [12]. Silver ions of very low concentration were encapsulated in a polylactide film, and its antiviral properties are measured against a *feline calicivirus* (FCV). The material showed good antiviral property in vitro by measuring its efficacy on food samples [13]. In a recent study, a sputter coating of silver nanocluster/silicate composite was used to show its antiviral activity against SARS-CoV-2 on a mask material. The virus activity was determined by the formation of cytopathic effect and staining using Gram's crystal violet solution. The biggest advantage of this coating is that it can be applied on many surfaces like glass, metallic and polymer surfaces [14]. Kim et al. prepared a surface coating of a spike like (3-(trimethoxysilyl) propyldimethyl octadecyl ammonium chloride (Si-QAC) and was applied on personal protection equipment to check for its antiviral properties. As shown in Fig. 1, these spike-like materials apply mechanical pressure on the cell membranes, through its sharp spikes making the virus adhere on the surface. The strains of different influenza virus were used for its analysis. The authors claim that the Si-QAC adheres to the personal protection equipment by a covalent bonding [15].

3 Role of 3D printing against COVID-19

Nanotechnology and 3D printing are two areas in which research and progress have been most plentiful in the past few years. They are both on their way to revolutionizing a wide range of fields, from medicine to production, from the global economy to space exploration [16]. These two methods are two advancing revolutions linked and intertwined. Nanotechnology is the manipulation of matter with at least one dimension sized from 1 to 100 nm. Just like 3D printing, nanotechnology has an extremely wide range of possible applications: surface science, organic chemistry, molecular biology, semiconductor physics, microfabrication, molecular engineering, nanomedicine, nanoelectronics, biomaterials, energy production, consumer products, etc. Nanotechnology can also be used to enhance the materials that are 3D printed. For example, research has been carried out into using a carbon-based filament for FDM 3D printing, in order to make it electrically conductible. Carbon nanotubes can also be used to reinforce plastic objects that were 3D printed using FDM: the plastic filament is coated in a carbon nanotube ink.

The arrival of coronavirus (COVID-19) as a global pandemic has created an exceptional global demand for medical equipments. Starting as an innovation with limited practical value, 3D printing have now uses and acceptances in different industries, say healthcare, engineering, car production and military manufacturing [17]. 3D printing is now commonly used to produce different equipments like face shields, masks and even ventilator components that are very much required in

the hospital environment. In 3D printing, products are manufactured from digital CAD files by layer by layer techniques [18, 19]. Due to its capability of outstanding customization, it is highly preferred in the medical fields. The advantage of this technique is that it can adapt to any changes as per the patient circumstance [20]. Many softwares are available nowadays to conceptualize medical parts rapidly, which can later be easily 3D printed in short time and cost. The digital flexibility and rapid prototyping of 3D printing authorize a swift mobilization of the machinery and hence a quick response to difficulties [20]. The broad spectrum of 3D printing applications in the fight against COVID-19 includes personal protective equipment, face shields, masks and even ventilator components [21].

3.1 3D printing for personal protective equipment (PPE)

During the COVID-19 pandemic, the usage of personal protective equipment (PPE) has significantly increased. Due to an increased necessity from standard suppliers and the partial ability to produce PPE through organized means, there is an increase in propagation of three-dimensional (3D) printing methods. Most of the investigators using 3D printing to produce face-wear prototypes are public members who employ stereolithography techniques and desktop fused deposition modeling (FDM) [22]. The hurried availability and invention of these prototypes have produced opportunities to fill the need in areas with limited PPE. Even though 3D printing has many advantages, a set of limitations and dangers of using 3D printing for PPE fabrication has also been highlighted [22]. Even the mechanical blockade of particles can be simulated to a degree, the reproduction of electrostatic properties of approved filter media with 3D printed materials boons a considerable challenge. Thermoplastic filaments for FDM printing also vary extremely in properties like porosity, environmental stability and material composition [23]. Many FDM filaments hold ambient moisture, which could pose a paradoxically increased risk for virus transmission during use or reuse[24].

3.2 3D antibacterial bio-cellulose swabs lattice structure for COVID-19 test

The nasopharyngeal swab is a serious component of the COVID-19 testing kit. Teams from USF Health Radiology and Northwell Health System established a 3D printed stopgap substitute [25]. 3D printed nasopharyngeal swabs deliver a cost-efficient and fast substitute to the standard NP swabs used for COVID-19 testing kits. As members of the Radiological Society of North America's 3D Printing Special Interest group, this project was introduced and advanced through collaborations established in the 3D SIG

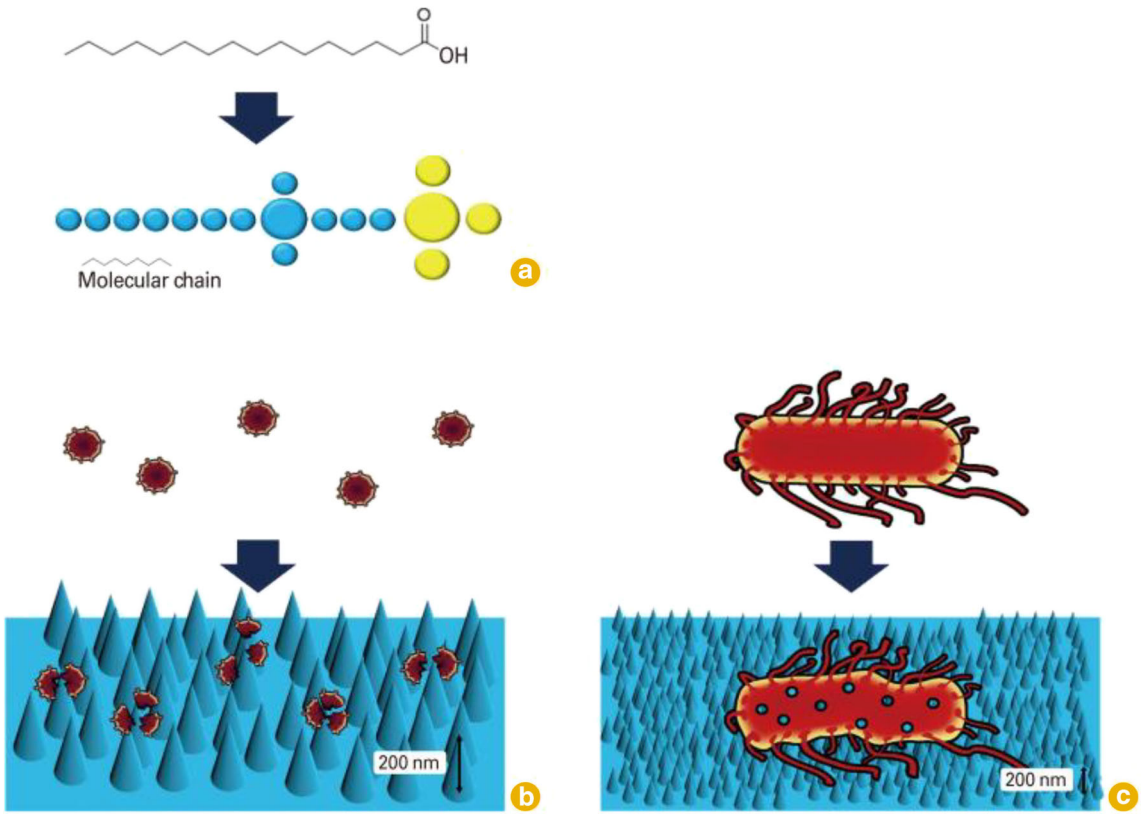

Fig. 1 Schematic diagram of the disinfectant used in the test (**a**), and the mechanism of action on a virus (**b**) and bacteria (**c**) [15]

[26]. Point of care or in hospital 3D printing is exceptionally positioned to understand the immediate needs of a hospital and act on them quickly; by functioning together between hospitals and industry through the pandemic, valuable time was saved to address the shortage needs in our respective hospitals. One swab design is shown in Fig. 2.

3.3 3D printed face masks

In this pandemic situation, face masks are really important, and there are several 3D printed solutions. The FDA, NIH 3D Print Exchange and the United States Veterans' Association are operational together in this concern, including raising a prototype N95 mask currently being tested [27]. By now, many face mask designs have been proposed and tested by researchers, physicians, individual users and commercial entities. The Copper 3D NanoHack mask establishes the boundaries of the community-generated strategies and the need for design improvements based on local testing and available technical base. It is printed with polylactic acid (PLA) filament and is intended to be hand assembled in the last stage into its final three-dimensional configuration after heating to a temperature of 55–60 °C through forced hot air or a hairdryer (Fig. 3) [28]. Critically, all seams must be manually sealed to ensure an airtight fit. The mask comprises a simple air intake port into which two reusable filters may be inserted, with a screw-in cover to hold the filters in place [27].

4 Nanotechnology approaches for diagnosing COVID-19

Nowadays, new nano-technological methods have emerged for detecting the novel coronavirus infection because of some existing problems associated with the current methods [28]. The nucleic acid testing method involves reverse transcription polymerase chain reaction (RT-PCR), and there are few difficulties associated with its diagnosis. That is, the RT-PCR method is useful for detecting the asymptomatic patients in which it also detects the presence of SARS-CoV-2 in the samples. Some of the healthcare centres such as non-urban places were unable to provide testing for high number of samples because of the lack of satisfactory PCR infrastructure. And finally, the unavailability of RT-PCR kits and reagents were unable to meet the greater demand [29–31]. The report given by WHO states about the urgent need for the diagnostic kits such as point of care and the protein and nucleic acid detection tests for SARS-CoV-2. There are numerous methodologies by which nanotechnological methods can help to improve and understand the demands in testing [32–34].

4.1 Nucleic acid testing

The nucleic acid amplification in the isothermal conditions aids in completely eliminating the usage of the sophisticated instruments which are required for RT-PCR detection. LAMP (loop-mediated isothermal amplification) is an isothermal nucleic acid amplification process which is a very rapid, highly specific and sensitive method [35, 36]. In a recent work by Zhao et al., magnetic nanoparticles were used in the RT-PCR diagnosis for the extraction of SARS-CoV-2 viral RNA. The used magnetic nanoparticles are functionalised with the poly (amino ester) in which the extracted RNA were absorbed on the surface. They were absorbed on the surface of the magnetic nanoparticle containing functionalised carboxyl groups. The absorption is due to the interaction of the carboxyl groups, and the RNA magnetic nanoparticle complex is used directly for the RT-PCR analysis (Fig. 4a). They have been used

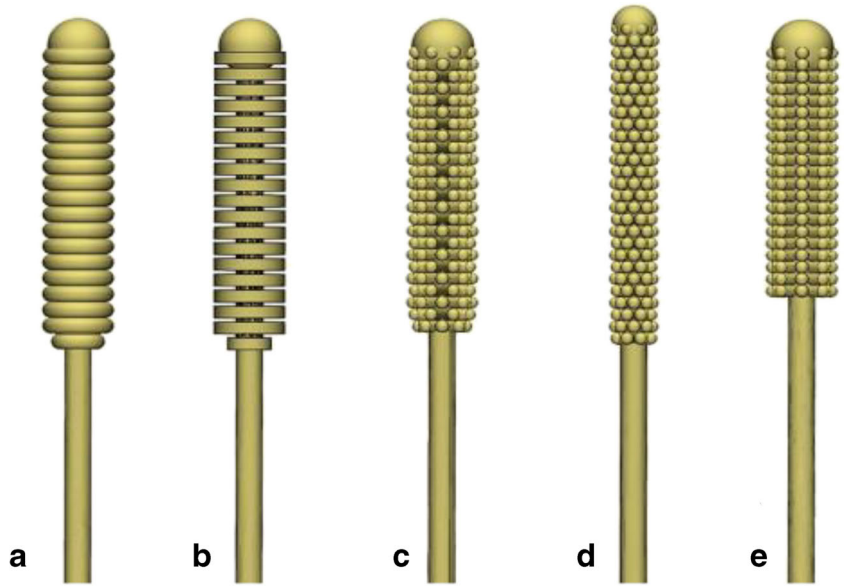

Fig. 2 Early alternate 3DP swab designs. Letter C is the current version in use [25]

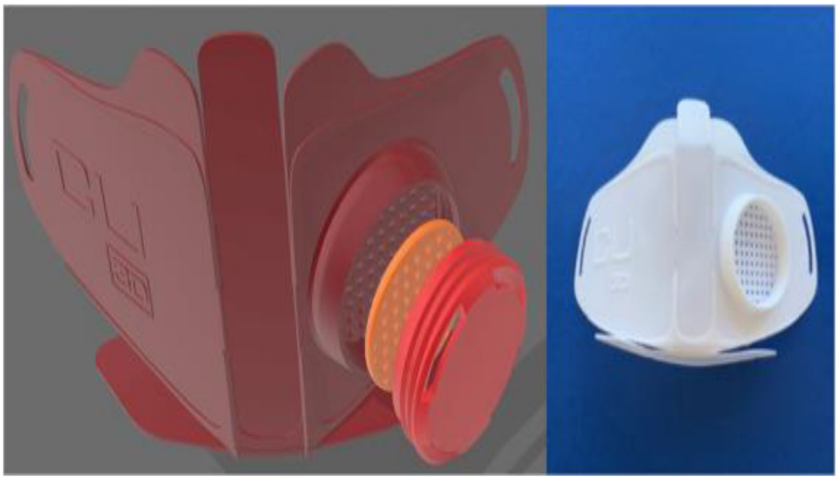

Fig. 3 Copper3D NanoHack mask model demonstrating an intermediate stage in mask completion, left. A 3D printed model of this mask, right [27]

directly without the extraction or elution of the viral RNA from the magnetic beads. This mechanism helps in reducing the time and contagious risks which assists in improved diagnosis with very less negative reports. The 10 copies of the magnetic nanoparticle-based elution of viral RNA procedures could be useful for the development of COVID-19 molecular diagnosis. In another study, they have used magnetic nanoparticles to detach or isolate the virus particles instead of extracting viral RNA. They reported that the enriched virus particles are strongly bound to the nanoparticles because of the functionalised target receptors. The nanoparticles acquired the magnetic nature by the encapsulation of super paramagnetic iron oxide nanoparticles (SPIONs). These SPIONs help in detaching the virus from the nanoparticles using the external magnet, and this supports in detecting the virus by cell-based tittering assays, quantitative reverse transcription-polymerase chain reaction (qRT-PCR) assay and immunochromatographic strip tests. The biomimetic super

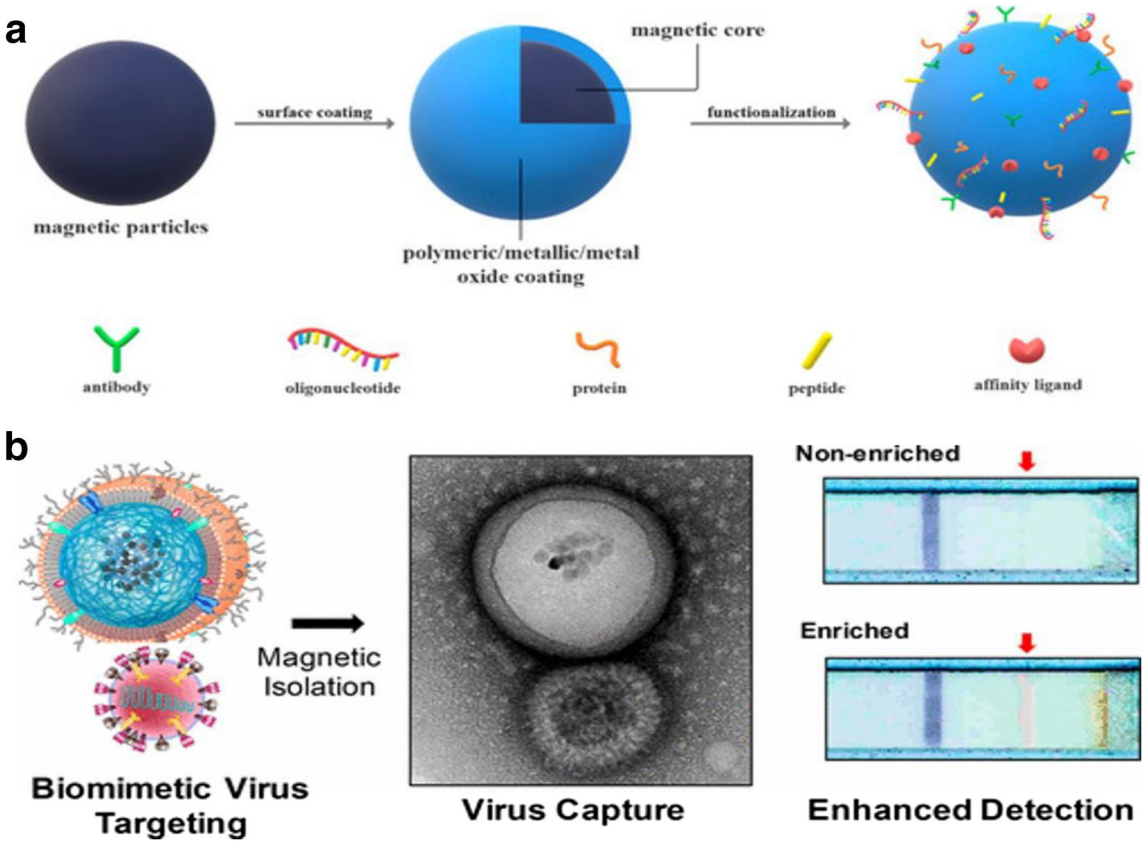

Fig. 4 **a** Functionalization of magnetic nanoparticles. **b** Biomimetic magnetic nanoparticles mimic the cell membrane of viral host (Reprinted with permission from American Chemical Society [37])

paramagnetic nanoparticles enrich the virus samples for the enhanced detection of virus [37]. Roh et al. used quantum dots containing fluorescent nanoparticles for the development of very rapid, sensitive viral detection techniques. They have used conjugated RNA aptamer to the fluorescent quantum dots, and if there is virus in the sample, it interacts with the RNA aptamer which causes difference in the optical signal of the quantum dots. This method is useful in detecting 0.1 pg ml^{-1} of the concentration of virus particles [38–41].

Zhu and Wang et al. utilised the combined RT-LAMP along with the nanoparticles for the diagnosis of COVID-19. They have used nucleoprotein and opening reading frame 40 F lab genes from the SARS-CoV-2 virus as the two primer sets for the amplification process in the isothermal condition. It can be easily detected visually by the easy display on the platform of nanoparticles-based biosensor. This biosensor shows very high sensitivity and specificity without cross reaction from non-SARS-Co-V-2 patterns (Fig. 4b). Similarly, Wang et al. combined the RT-LAMP along with nanoparticles for the detection of virus. They have used the isothermal amplification process in which the conjugated nanoparticles bound to the RT-LAMP viral DNA. It involves the process of chemiluminescence in which the probe molecules binds to the streptavidin-modified alkaline phosphate (ALP) enzyme. This ALP will convert the substrate molecules for the emission of chemiluminescence signal and that will detect the virus in the sample. This simplifies the extraction process of virus in the RT-PCR technique which enables the improved detection with less time consumption [42, 43].

4.2 Point of care testing (POCT)

This type of testing is useful for diagnosing the infected persons without sending the samples to the laboratory. Particularly this POCT process will be useful for those people who do not have the facility and infrastructure. This type of biosensors are called as colorimetric biosensors in which it functions with the changes in the colour of the sample [32, 44–46]. A study exhibited that paper-based DNA colorimetric sensor detects the virus sample very rapidly. The probe used in this paper-based biosensor is cationic pyrrolidinyl peptide nucleic acid (PNA) with improved hybridization, and they are very stable compared to the DNA and RNA probes. This sensor is useful for detecting COVID-19 and MERS-CoV, and the main mechanism is that the lysine in the probe has a positive charge, and this will interact with the silver nanoparticles and the DNA which are negatively charged. The probe PNA particles bound to the nanoparticles lead to the aggregation of silver nanoparticles in the absence of viral DNA, whereas, in the presence of viral DNA, it forms a complex with the COV virus without aggregation of the nanoparticles. This is due to the electrostatic repulsion which occurs during the complex formation between the particles. The analysis shows a colour change of the sample if there is presence or absence of the viral DNA and estimated using the paper-based analytical device (PADs) which acts as a point of use testing device (Fig. 5). The detection limit of this point of care testing method is 1.53 nM [47, 48].

In another study, Teengam et al. have used gold nanoparticles for the detection of COVID-19 and MERS-CoV virus. Here, they have used modified thiol molecules as probes which were paired with the upstream E protein gene and capped gold nanoparticles. The probes are combined with the gold nanoparticles through gold and thiol group interactions. In the absence of virus, the gold nanoparticles will aggregate which leads to a colour change. During the presence of virus, it forms a strong binding with the viral DNA, thereby inhibiting the aggregation of nanoparticles, and it stops the transition of the optical properties of nanoparticles. These colour changes were detected by the localized surface plasmon resonance shifts. These colorimetric assays were proved to be very rapid, less costly and efficient which has the detection limit of about 1 pmol μl^{-1} even with the very less quantity of sample. This paper-based analytical method is considered to be the portable detection technology which has been used widely for the testing [49]. This gold nanoparticle-based colorimetric test creates a gold nanoparticles solution which collects the virus, and it shows a detectable colour change in the liquid. This gives a rapid test for COVID-19 by shifting the colour of gold nanoparticles. This low-cost test performs much better than the other diagnostic techniques with a similar accuracy to the standard PCR tests. The main advantage of this test is that gold nanoparticles show certain colour because of their absorption of particular wavelengths. Then, to the gold nanoparticles, the sample containing SARS-CoV-2 is added which results in the aggregation of the virus, and it causes a shift in the absorption peak that results in change of colour of the solution. This shift in the colour will be visible to the naked eye, and the downside is that it is possible only when the load of virus is very high.

The sensitivity when compared to the PCR is that in the PCR method, it involves the extraction of RNA, reverse transcription and the amplification which has the complex procedure. This real-time PCR which can detect the viral RNA in the samples giving positive and the negative results by lacking information about the viral load. Because of its complexity in the analysis, the efforts are undertaken to overcome the blockage, and in particular, the metal nanoparticles-based biosensors were used. Because of their exceptional optical properties which makes it suitable for the rapid colorimetric diagnosis for POCT. Owing to its biocompatibility and the surface chemistry, the gold nanoparticles are considered as the preferred one than the other metals. Ventura reported that colorimetric biosensor used for the COVID-19 mass testing has the sensitivity and specificity of approximately 95% when compared to the standard real-time PCR technique. They explained the

functionalised colloidal solution of f-AuNPs against three surface proteins of SARS-CoV-2 such as spike, envelope and membrane. This technique can be used for the mass screening because its detection capability is based on the interaction between the virions, and it is a single-step detection method without involving any pre-treatments like RNA extraction, reverse transcription and amplification. The main significant feature of the AuNPs biosensor is that it completely depends on its sensitivity to the virion particles than the RNA. The two important aspects are: (i) this f-AuNPs biosensor is a powerful tool for quantifying the load of virus, and (ii) it is sensitive only to the virions which can detect only the presence of the active virus particles. This technique is the appropriate one to measure the definite degree of ineffectiveness of the samples. Thus, this single-step colorimetric detection of virions can be a common technique to be used for the laboratories and also the point of care testing [50]

4.3 Electrochemical biosensors

The electrochemical biosensors are one of the most efficient sensors for the detection of COVID-19 virus. In these sensors, they have slightly modified the electrochemical sensing process with the gold nanoparticles which helps in retaining the biomolecule functional moiety [52]. The gold nanoparticles act in the interface because it acts as electrocatalytic material and also has the intense electrical response. Layqah et al. in their study have developed a sensor for the diagnosis of COVID-19 virus. In their product, they have used carbon electrodes which are coated with gold nanoparticles, and it acts as an immunosensor. COVID-19 spike S1 protein was immobilized with the gold nanoparticles, and this immobilized S1 protein interacts with the virus present in the sample, and it binds to the antibody which is added in small amount in the sample. This binding process is measured by the changes in the current and in the absence of the virus; the antibody present in the sample binds to the S1 protein and will show a decrease in the peak current. Whereas in the presence of virus, the antibody will bid to the immobilized antigen of the virus and can measure the current changes. Because of the electrodes array, this immunosensor is capable of detecting different types of coronaviruses. As it can detect MERS-CoV, COVID-19 and HCoV viruses in the nasal samples, the detection limit for this kind of sensor is about 0.4 to 1.0 pg ml^{-1}[53].

In another study, the researchers have fabricated a genosensor for the detection of SARS and COVID-19 virus which contains gold nanoparticles and a layer of thiolated oligonucleotides arranged in a self-assembled carbon electrodes screen. The sequence in the oligonucleotide exactly matches the small region in the viral nucleocapsid protein, and the presence of virus is detected by the enzymatic reaction of the virus. The enzymatic amplification is recorded by the hybridisation signal produced by the viral DNA and the probe, and the instrument is capable of giving highly sensitive measurements. For the accurate measurements, they have used casein molecule which acts as a blocking agent and also an enzyme conjugates to reduce the signals which are non-

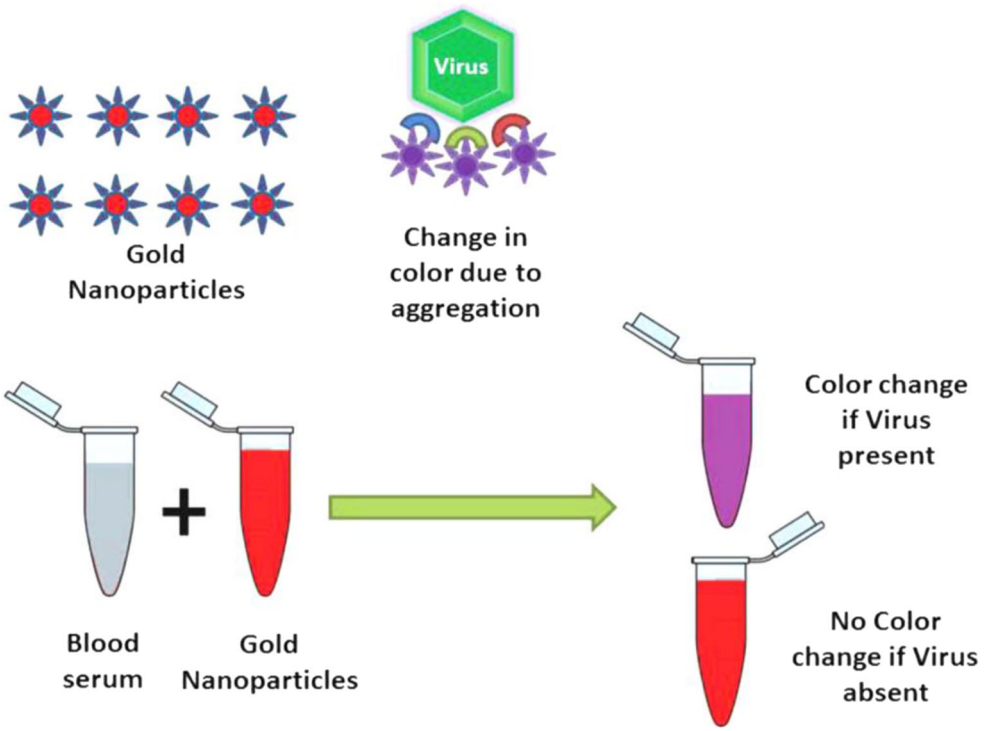

Fig. 5 Nanoparticle-based colorimetric detection of virus (Reprinted with permission from Elsevier [51])

specific. In this report, they have got the detection limit of about 2.5 pmol l^{-1}[54].

In another study, Ishikawa et al. have used nanowires instead of nanoparticles for the detection of SARS and COVID-19 virus which are very efficient. They have developed an In_2O_3 nanowire sensors and used fibronectin-based antibody mimic proteins for the detection of nucleocapsid proteins. These antibodies mimic proteins that have higher binding potential compared to the antibodies and the aptamers. The presence of virus affects the In_2O_3 nanowire sensor's electrical potential, and the electrical changes were measured as signal. The detection limit of these nanosensors is sub-nanomolar concentrations of the virus particles [55].

4.4 Chiral biosensors

Chiral sensors are very useful for the detection of SARS and COVID-19 virus. In a recent report, researchers have developed chiral zirconium quantum dots for the detection of COVID-19 virus. In the formulation, they have used zirconium quantum dots, magnetic nanoparticles and the coronavirus-specific antibodies. The zirconium quantum dots and magnetic nanoparticles strongly bind to the virus, and it displays a magneto plasmonic fluorescence in the presence of virus. The magneto plasmonic-fluorescent nanohybrids were separated by the application of external magnets, and the fluorescence intensity is measured to know the presence or absence of virus. The detection limit of the chiral sensor is found to be 79.15 EID/50 μl [56]. In another study, chiral immunosensor was used which has self-assembled layers of quantum dots and chiroplasmonic gold nanoparticles. This immunosensor can detect the COVID-19 infections in the blood samples. The gold nanoparticles conjugated antibody and the quantum dots were mixed with the virus sample, and the change in the chiral optical response is analysed by the circular dichroism method. In this method, they found that the chiro-immunosensor has a very low limit of detection which is 47.91 EID/50 μl for coronavirus [57].

5 Limitations of nanotechnology-based approaches and nanoparticles

Although nanoparticles can be useful for biomedical applications, they have a reverse side, i.e. their toxicity, which needs to be addressed judiciously to optimize their use against COVID-19 treatment [58, 59]. One of the major challenges is to ensure the safe use of nanomaterials, since most of the studies have only evaluated the biocompatibility using in vitro approaches. The fate and behaviour of nanomaterials in the body can also change when they reach blood circulation due to the formation of protein corona [60]. Thus, reliable in vivo models are needed to better understand the toxico-kinetic behaviour of the nanoparticles in the body, especially for long-term exposure [61]. During the course of inhalation, nanoparticles can penetrate into the mucosal membrane lining of the respiratory tract. The particles smaller than 10 μm can easily enter into the respiratory system [62]. The inhaled nanoparticles entering into alveoli may get accumulated and cause inflammation in the lungs as reviewed by Campos et al. [59]. Another issue is the lack of standardized protocols for physicochemical and biological characterization of nanomaterials, as well as lack of a universally agreed upon definition of a nanomaterial [63]. Capacity for large-scale manufacturing is another hurdle that needs to be overcome for broader commercialization of nano-based formulations [63]. Due to the multifaceted interactions between nanomaterials and biological systems (in vivo), it is very challenging to foresee the behaviour of these materials under physiological conditions. Once within the body, the nanoparticles reach the blood circulation, which is a very complex matrix containing ions, small molecules, proteins and cells [64]. It is already known that nanoparticles are able to interact with biomolecules, mainly proteins, resulting in the formation of protein corona [65]. The composition of protein corona is mainly driven by the physicochemical properties of the nanoparticles. In other words, it is unique for each nanoparticulate system and influenced by several factors. Both protein-nanoparticle interaction and protein-protein interaction regulate the adsorption of protein on the surfaces of nanoparticles [65]. The formation of protein corona modifies the physicochemical properties of nanoparticles, consequently giving them a new biological identity, which is more significant in determining the biological response than the original properties of the nanoparticles [66]. Therefore, the characterization of protein corona is an essential step to be investigated in the process of nanomedicine development. It was reported that the toxicity of nanoparticles to the respiratory system depends upon the structure, composition and function of the mucosal membrane. For instance, bronchi and bronchioles are protected by the mucus layer wherein a single layer of cell separates inhaled air from blood capillaries. For efficient absorption of inhaled air, these cells have a larger surface area, which makes it prone to the damage caused by inhaled nanoparticles. During the normal functioning of lung tissues, all structural cells of the lungs including endothelial cells, alveolar macrophages, lymphocytes and mast cells form an inflammatory and repair system [67]. Nanotechnology has already been shown to enhance diagnostics, protection and therapies in other viral infections; therefore, there is a good chance that, with more researches, it will revolutionize the fight against COVID-19 offering processes, materials and tools to enhance sensitivity, speed and reliability of diagnosis, as well as providing more efficacious options for therapies [59].

6 Conclusion

The COVID-19 coronavirus turned from a small infection to a global pandemic, and the world is currently under a global health emergency. Nanotechnological research is one of the best weapons to fight against it as it can detect the SARS CoV-2 virus because of the unique properties of nano-sized materials. This will offer a more sensitive, specific, low-cost and easy to use diagnostic kits for detecting the pathogenic virus. 3D printing offers an automated solution for several manufacturing industries and other related fields to manufacture medical equipment during the COVID-19 crisis. With the current 3D printing technologies, competent production of PPE and other medical equipment is highly achievable. As the COVID-19 pandemic spreads across the world, 3D printing technology can be in forefront for the production of antibacterial bio-cellulose masks and ventilators, among other equipment, which is readily available to patients and prepare us better for such viral outbreaks in the future, probably and undesirably in the coming decades. One of the major limitations is that to ensure the safety of nanomaterials because only few studies have assessed the biocompatibility using in vivo studies. But when the nanomaterials enter the body, the fate of them changes due to the formation of protein corona when they enter the blood circulation. However ,there are few standardized procedures for physicochemical and biological characterization of nanoparticles. To overcome the aforementioned problems, a closer association between regulatory agencies, scientific experts in the area of material science, pharmacology and toxicology is required. Thus, it can be summarised that nanotechnological developments could significantly contribute in the diagnosis, detection, understanding and treatment of viral diseases and also help in mitigating the future viral outbreaks.

Authors' contributions AT conceived the original idea and designed the review paper. AT, RR and CJC equally contributed and wrote the manuscript in consultation with NK and ST. All the authors approved the submitted version.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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