
# Literatures Review Nanotechnology as a novel strategy for prevention, diagnosis, control, and treatment tools against COVID-19

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ABSTRACT

On January 30, 2020, the World Health Organization's (WHO) Emergency Committee declared a worldwide health emergency. Now world health faces a risk for the novel serious respiratory disease known globally as the COVID-19 pandemic called Coronavirus 2 (SARS-CoV-2). The infection responsible for COVID-19 is thought to have originated in the Wuhan Province of China. This virus has raised concerns around the world due to its rapid dissemination, great mobility, and high fatality rate. Unfortunately, there isn't even an active and specific antiviral medication or vaccine for COVID-19. Regretfully, while the majority of currently available treatments aid these medications, infections are not completely eradicated. These medications lessen side effects and problems.

Many health issues and infections that are expected to pose a serious threat to human health can be addressed by nanomedicine and nanotechnology. Nanomedicine can be detected in the case of viruses that cause respiratory illnesses. A few studies on the application of nanomaterials in the detection of anti-infections and treatment of certain coronavirus strains have been carried out. Based on earlier findings from numerous different coronavirus types, vaccinations associated to nanotechnology have demonstrated a more strong immune response. To imagine the possibility of using nanomaterials in the delivery of a highly effective COVID-19 approach, a review of studies on the potential use of nanoparticles for prevention, identification, monitoring, and care aims was undertaken.

Even though there isn't enough research on novel and dramatic therapeutic nanotechnology methods to COVID-19, the next paper review can examine them in order to develop SARS-CoV-2 nanomedicine that is both efficient and successful.

**Keywords:** COVID-19, SARS-CoV-2, Nanotechnology, Nanoparticles, Antiviral, Viruses

## Introduction

The global healthcare system has been in a dangerous state since beginning 2020 because of the continuous spread of a new severe acute respiratory syndrome known as coronavirus 2 (SARS-CoV-2). In a worldwide emergency on the

basis of a large number of confirmed cases and on 11 February 2020 it was officially named for the outbreak: COVID-19 (Corona Virus Infectious Disease–2019). On January 30, 2020, the World Health Organization (WHO) emergency committee declared a worldwide emergency. The virus has caused alarm worldwide due to its rapid rate of infection, great mobility, and fatality [2,3,4,5].

The virus was raised as a novel human diseases affecting severe acute respiratory syndrome (SARS). The growing rise in respiratory diseases is causing significant problems in public health as well as the health districts [6], according to the World Health Organization (WHO). The coronaviruses in people produce a wide spectrum of virus, causing general flu and severe respiratory problems such as respiratory disease in the Middle East (MERS). Since coronaviruses are known as Zoonotic Infections, they can be spread between animals and humans. Previous study showed that, prior to spreading to humans, MERS and SARS coronaviruses skipped people respectively from dromedary camels and civet cats. Many known coronaviruses will infect species which do not yet occur in human beings [7]. COVID-19 with vaccines, monoclonal antibodies (mAbs) or medicines is currently not available. However, a detailed review on the development of the COVID-19 vaccine is being conducted and this may be predicted in the near future [6]. Today the majority of nations should adopt strategies like social distancing in order to reduce cultural diffusion. This can include quarantining unhealthy people, if possible (including voluntary home separation), institutional closures and telecoms [8]. Certain techniques-include In various areas of prescription medicine such as genomic supply [9], guided drugs supplies [10,11], imaging [12], biomedical implants [13], and public safety sensing devices, plus other biological-sensors, nanotechnologies have been already implemented [14,15]. It may also be used to treat or diagnose cancer [16] and develop effective agents to combat infections caused by viruses, bacteria and funguses. The source of this concern for nanotechnology in medicine is the nanometer scale of substances, which transfers to living systems cells and particularly the body [17,18]. This article discusses and sheds some light on numerous approaches for the use in collaboration in the battle against COVID-19 of nanotechnologies and nanomedicine in recent years.

## 1. Recommended Conventional Treatments

No COVID-19 success vaccines or other antiviral therapies are currently approved. The major medications currently in use are helpful, but these medications are unfortunately given to minimize symptoms and side effects, they do not completely kill the virus. A detailed review is still also required immediately. A detailed understanding of the mechanism of action for the virus is necessary to build a successful COVID-19 strategy. SARS-CoV-2 is identical with Coronaviruses SARS and MERS and uses a "lock and key" mechanism in which angiotensin conversion II (ACE2) acts as "key" on some cells retaining "lock" [19]. However, high dosages of oncological drugs (Sunitinib and Erlotinib) are necessary for these inhibitors, but may lead, regrettably, to serious adverse events [20]. Alternative therapies with protease inhibitors of the human virus (HIV), such as Lopinavir and Ritonavirin, was given by several other COVID-19 inhibitors [21]. Until being utilized against malaria and autoimmune disorders, the usage of chloroquine, hydroxide chloroquine, antiviral and traditional medicines was a quite successful therapeutic choice which has been implemented in a number of countries [22]. A regimen involving the application of dimethyl-chloroquine with azithromycin demonstrated positive results for successful COVID-19 therapy. However, the initial disability of contacts showed potential effectiveness, and due to issues about the risk of arhythmic mortality caution should be taken under near doctoral supervision [23].

## 2. Nanotechnology

The word 'nano' for the dwarf is taken from the Greek language. A nanometer (nm) is the same as one-billionth of a metre, or around one hundred thousandth of a human hair's diameter. In 1974, first use was made of the

word "nanotechnology." It reflects the functional application and administration of the nanometric scale. While there are many explanations for nanotechnology, researchers believe that technology is related to the material's properties, including its nature and/or the modification of its characteristics (improvement and reduction). The small material has numerous physical and chemical properties including increased reactivity and solubility. This substance 's stability increases when the active component is at nanoscale. Because of their small sizes, these materials can have stronger biological effects when they need to infiltrate cells, tissues, and organs than larger particles [24, 25, 26, 27].

### 2.1. Nanotechnology in Medicine

Nanomedicine, a modern science focused on nanotechnology-medicine integration. It is used in many medical specialties, particularly when drugs are transported to the target site. In cancer therapy in recent years and new for infectious diseases, the study of nanostructured drug loading and storage devices has been developed. In addition to transporting nanocarriers effectively to the site of infection, the dosage volume and duration are controlled, thereby avoiding drug toxicity [24, 25, 26, 27].

#### 2.1.1. Nanoparticles Antiviral Activity and Infection Mechanism of Viruses

The four primary steps of an infectious virus' life cycle are attachment, penetration, replication, and budding. Antiviral nanoparticles are employed to suppress or block the virus at each of these stages. Here, we can talk about the different ways that nanoparticles work against viruses. The most common and straightforward method of eliminating viruses is to render them inactive. However, certain nanostructures can interact with viruses, reducing the amount of capsid proteins they accumulate and, consequently, their virulence. This can be used in conjunction with physical and chemical methods to reduce the number of viruses that are active. Our view is that the greatest viral infections are typically linked to the target receptor protein by attachment to the host cells. The host cells can then be freed from the disease if the nanoparticles can effectively break the link [28]. By altering the cell surface membrane and protein composition, viruses can also be killed by preventing their entry and penetration into infected cells [29]. Blocking the pathogen-host cell pathway is another effective way to treat viral infections.

The last, practical method of preventing the virus from infecting cells is to stop the expression of specific enzymes that aid in the replication of virus DNA or RNAs. In this instance, the virus prevents replication. The novel approach aims to prevent and eradicate viral emergence from host cells. In this instance, the virus prevents replication. The novel approach aims to prevent and eradicate viral emergence from host cells. The virus may exhibit increased virulence; however, if functional nanoparticles stop the virus and significantly reduce the next generation, the virus's virulence may decline to a remarkable degree [30].

#### 2.1.2. Antiviral Assay Methods for Functional nanoparticles

##### 3.1.2.1. Plaque assay

Plaque test results can similarly assess the antiviral potency of work nanoparticles, as the infectivity of a virus can be assessed via plaque testing [31].

##### 3.1.2.2. TCID50 assay

A common quantitative test for determining each virus's infectious titer is the infectious dose tissue culture (TCID50), which can cause cytopathic effects in tissue cultures for a duration of five to twenty days while maintaining cell viability [32].

##### 3.1.2.3. Confocal imaging assay

Functional nanoparticles are typically tested for antiviral properties using confocal microscopy, an active technique that simulates the process of viral infection in host cells (33).

##### 3.1.2.4. β-Galactosidase assay

It is typically used as a reporter gene in the functional antiviral characterization of nanoparticles to track the expression levels in host cells, providing indirect evidence of the functional nanoparticles' capacity to combat viral infections by demonstrating the physiological state of infected host cells [34].

#### 3.1.2.5. Transmission electron microscopy (TEM)

TEM readings could show the viricidal capacity of the functional nanoparticles and provide a visual depiction of infected cells. Another crucial method is transmission electron cryo-microscopy, which may examine and operate on unfixed or unmodified specimens in their natural environment. An antiviral investigation could define the presence of functional nanoparticles in virus cells [35].

#### 3.1.2.6. Western blot assay

After working with functional nanoparticles to characterize them as antiviral agents, the Western blot assay will assess variations in the protein structures of viruses [36].

#### 3.1.2.7. Real-time polymerase chain reaction (RT-PCR)

Once the DNA virus has interacted with functional nanoparticles, it can be identified using the RT-PCR approach [37]. For instance, it is known that host cell gene expression is a good indicator of viral infectivity, and PCR results can reveal information about the growth and metabolism of infected host cells as well as the maintenance of functional nanoparticles. As such, the PCR method provides indirect proof of the functional nanoparticles' antiviral effectiveness.

#### 3.1.2.8. Flow cytometry assay

The virus-infected cells can be measured and the effectiveness of viable nanoparticles to destroy them tested using flow cytometry, a technique for assessing the physical and chemical characteristics of a cell culture [38].

#### 3.1.2.9. In-vivo analysis

Research conducted on individual living cells or plants using different biological species is referred to as an "in-vivo" study. The Zika virus strain glycoproteins that encode the pre-membrane were, for instance, enveloped by lipid nanoparticle-encapsulated modified mRNA (mRNA–LNP), which Pardi and Hogan's group created as a single low-dose intradermal immunization [39]. According to research, mRNA-nucleoside-modified LNP may be a good option for an anti-Zika vaccination. A useful and efficient method for evaluating the antiviral efficacy of functional nanoparticles is an animal vaccination essay, according to these in vivo mice results [30].

#### 3.1.2.10. Computer simulation

Computer simulation includes reproducing a biological or chemical process by following a system to replicate the results of a mathematical model linked to order. In antiviral research, computer simulation is an auxiliary way to test improvements across virus and functional nanoparticles interactions in a particular DNA and protein site, providing clear indirect proof to model virus and host cell variations following functional nanoparticles intervention [40].

### 3.2. Novel Advancement of Antiviral Functional nanoparticles

Latest advances in nanoparticulate drug delivery pathways demonstrate great potential for the efficient dosing and targeting of active molecules [24, 25, 26, 27]. These carriers protect from chemical and biological destruction the active molecules. New advances in nanoparticulate drug delivery technology represent a tremendous potential to optimally dose and target the active molecules [24, 25, 26, 27], These carriers shield the active molecules from chemical and biological degradation.

#### 3.2.1. Inorganic Nanoparticles

Significant attention given to engineered inorganic nanoparticles because of their capacity to target sites, but also to have stimulus-responsive properties and the intrinsic potential of some forms (i.e., magnetic or gold nanoparticles) to be detected following

in vivo treatment of the human body using non-invasive medical imaging [41].

### 3.2.1.1. Quantum dots

Quantum has been widely used for virus and cell labeling, identification, and image tracking [43,44,45]. It also functions as a conventional delivery system for the effective delivery of loaded cargo dots (QDs), semiconductor nanocrystals with unusual size-dependent optical and electronic properties [42]. For instance, Szunerits et al. According to the paper, the inhibitory activities of carbon nanodots (C-dots) against the human coronavirus vary depending on the ligand modification. The CQDs made with 4-aminophenyl boronic acid surface modification exhibited the highest level of viral inhibitory activity [46].

### 3.2.1.2. Silver nanoparticles

Due to their unique physiochemical and chemical characteristics, silver nanoparticles (AgNPs) have been employed in the production of synthetic drugs [47,48,49.50]. AgNPs, for instance, have been characterized as biological therapeutic impacts found in burn care products and injury dressings [51]. Although several studies have been written concerning the viricidal effect of silver nanoparticle-bound antiviral drugs, these agents are still in the early stages of development [52, 53]. According to recent research, silver nanoparticles exhibit antiviral action against the human immunodeficiency virus, herpes simplex virus, hepatitis B virus, influenza A virus, and human parainfluenza virus [54]. Sreekanth et al. Rendered quasi-sphere metal nanoparticles. It has been discovered that exceptionally potent silver nanoparticles can kill influenza A viruses [55]. An anti-influenza A zanamivir virus containing silver nanoparticles was created by Chen, Zhu, and colleagues [56]. This virus inhibits the influenza H1N1 virus.

### 3.2.1.3. Gold nanoparticles

Gold nanoparticles have remarkable optical and electrical characteristics [57,58,59,60]. Functional gold nanoparticles have been found to suppress the HIV, herpes simplex virus, and influenza virus [61]. Gold nanoparticles are a useful scaffold for the synthesis of viral inhibitors. For instance, according to Christian Melander, multivalent gold nanoparticles may prevent HIV fusion through a variety of molecular mechanisms [62]. He claimed that gold nanoparticles cannot inhibit viruses alone and that gold nanoparticles can increase antiviral activity exponentially by multivalent interactions if they are covalently bound to other particles that bind to the viruses. In addition, Javier and colleagues synthesized a range of dendronized anionic gold nanoparticles and found that dendronized AuNPs were more effective than single dendrons at inhibiting HIV [63]. Well-known prescription medications called zanamivir and oseltamivir are used to treat infectious disorders brought on by influenza viruses. However, the influenza virus is quite likely to become more vulnerable to this illness because of the high intrinsic risk of mutation. Fortunately, sialic acid nanoparticles coated in gold can stop influenza viruses from attaching to their infected cells by decreasing the possibility of medication resistance spreading. Gold nanoparticles give us a particular way to produce antiviral chemicals as well as a scaffold for inhibiting viruses. Interestingly enough, Rainer Haag and his co-author have similarly found that gold nanoparticles' antiviral behavior is highly reliant on their sizes [65]. Tens to hundreds of gold atoms make up gold nanoclusters (Au NCs), which are usually less than 2 nm. Even if there is no bulk gold, Au NCs with a diameter of 1 nm or the size of a subnanometer exhibit unique and appealing physicochemical properties [66]. The effect of surface modification on the antiviral activity of Au NCs was examined using two different types of gold clusters: Au NCs (MES-Au NCs) that stabilized mercaptoethanol sulfonate and histidine, and histidine-stabilized Au NCs (His-Au NCs) [67]. Findings from functional nanoparticle antiviral test methods indicate that His-Au NCs, not MES-Au NCs, were able to efficiently suppress the PRV. The findings show that surface modification is a very effective way to increase the antiviral potential of functional nanoparticles.

### 3.2.1.4. Graphene oxide

Graphene oxide [68,69,70], a novel single-atom, two-dimensional carbon composite composed of a hexagonal lattice [68,69,70]. Graphene oxide has been thoroughly studied, previously. For example, Tang and his co-authors discovered that graphene oxide is an enabling candidate for inhibition of viruses [71]. Graphene oxide is normally functionalized with additional antiviral factors to create a synergistic virus-preventive agent on the virus' destructive activity to maximize its antiviral effectiveness. For example, Huang and his co-authors created a curcumin-functionalized graphene oxide to fight the respiratory syncytial virus by loading a large amount of curcumin onto the cyclodextrin-functionalized graphene oxide composite [72]. It has been demonstrated that the charged graphene oxide with curcumin has good biocompatibility with host cells and a notable inhibitory effect on respiratory syncytial virus disease.

### 3.2.2. Inorganic Nanoparticles

### 3.2.2.1. Polymers Nanoparticles

Polymer-based nanoparticles have been described as an active delivery system [73], their size, form and load can be efficiently optimized to provide controlled load release in external circumstances [74]. Researchers may recognize that polymers with long chains and branches have a high antiviral potency relative to the mono compound [75]. Because of the compact molecular structure, polymers may be set as predetermined parameters based on viricidal activities. Various polymers were designed to fulfill the needs of pervasive viral/bacterial agents. Organizing composites contain a number of notable value antiviral medicines [76]. Because of their non-toxic nature, biodegradability, biocompatibility with non-toxic in vivo materials, the ability to open up near links between epithelial cells [77], and the ability to easily turn them into desired shapes and sizes [78], these made of chitosan attracted particular interest in intranasal treatment from the different formulations of polymer nanoparticles. Chitosan in conjunction with therapeutic syntheses can enhance the survival of polymeric NP in the mucosal conditions and the entry into the mucosal tissue.

3.2.2.2. **Dendrimers Nanoparticles**

Dendrimer NP can be synthesized in highly branched 3D networks with a greater capacity to bind various functional groups to their surface and encapsulate hydrophobic therapeutic, non-water-soluble agents in their core [79]. This allows for the potential application of these nanoparticles for bacterial, virus, and viral infections in multiple therapies [80]. Dendrimers have demonstrated improved antiviral activities in the aggressive interactions they execute in viruses, thus minimizing inflammation of the host. Yet they have been a major tool in controlling viral outbreaks such as influenza virus infection [81]. Sierra's unit, for example, using the self-assembly of amphiphilic dendrimers in water to build micels for encapsulation of camptothecin as an HCV therapy [82]. A variety of attempts are currently under way to improve antiviral effectiveness in dendrimers. *Daniel*, and the others. A triple mixture of carbosilane dendrimers, tenofovir, and maraviroc has been reported as a potential agent to prevent sexual transmission of HIV-1 [83]. They concluded that the triple-drug combination increases antiviral potency and acts synergistically as a possible microbicide by regularly inspecting the HIV target cells and topical concerns, promoting our awareness of dendrimers' viricidal role. *Nandy. et al*. noted the development of Poly-L-lysine (PLL)-based dendrimeric NPs with anionic naphthalene disulphonate surfaces that can prevent the entry of HIV viruses by binding to the gp120 viral protein envelope and inhibiting the output of the CD4-gp120 complex [84]. *Chahal* and his team developed a dendrimer NP encapsulating antigen-expressing replicon mRNA. This nanoformulation provided essential CD8 + T-cell and antibody response capable of effectively protecting against fatal exposure to certain deadly pathogens including H1N1 influenza, Ebola, and Toxoplasma gondii [85].

### 3.2.2.3. Lipid Nanoparticles (LNPs)

The efficient biocompatibility of the lipid material makes nanoparticles made from lipids

especially suitable for medical applications. LNPs are new carrier systems intended to offer an alternative to current NP vehicles. Solid lipid nanoparticles (SLNs), lipid-drug conjugates (LDCs), lipid-core nanocapsules (LNCs), nanostructured lipid carriers (NLCs), and lipid-polymer nanoparticles (LPNs) are vehicles with a lipid matrix that have advantages by using biocompatible and biodegradable lipids for various purposes [86,87]. LNPs have particular characteristics due to their high surface area and ultra-small size which enhance drug targeting, treatment efficacy and decrease drug toxicity. LNPs are widely used as controlled release mechanisms, which were often used to enhance the bioavailability of drugs. It has been observed that the structure of LNPs is a key aspect that can affect their therapeutic output in different parts of the body [24, 25, 26, 27].

#### 3.2.2.4. Liposomes

Among the numerous lipid-based preparations adapted for intranasal delivery are liposomes, which are rounded capsules with an outer phospholipid bilayer and an inner hydrophilic core formed for carrying aqueous therapeutic drugs [86,87]. As any other type of NP, surface charge plays an important role in the modification of liposomal pharmacokinetic properties. Study on cationic liposomes performed after intranasal administration provided higher absorption and greater bioavailability relative to their counterparts with negative charges. This is due to the negative charge of the mucosal membranes resulting in the electrostatic penetration of these positively charged NPs, as well as the mucosal cilia limiting their clearance [88]. Furthermore, liposomes have been documented to have high potential for mucosal vaccines because their preservation in the nasal cavity promotes strong immune activity which contributes to the development of higher levels of immunoglobulin [89].

### 3.2.3. Additional functional nanoparticles

Preparation of Novochizol NPs aerosol can be performed to administer and carry any potential anti-COVID-19 treatment to the lungs of ill patients. Bioavanta-Bosti, a pioneer in chitosan NP chemistry, has announced the introduction of Novochizol 's unique polysaccharide nanotechnology that can be applied to any effective pharmaceutical product formulation-a small molecule for controlled delivery and continuous release into any tissue. Inventor of Novochizol technology notes that chitosan NPs are completely biocompatible and ensure consistent release without a systemic distribution [90]. Earlier studies on peptide-based NPs has demonstrated that the use of peptide inhibitors and amino acid mutations can protect against infections linked to SARS-CoV [91]. A vaccine moiety, P6HRC1, was formed in another study by binding a peptide ligand from the spike protein SARS-B HRC1 with a B-cell epitope, and was self-accumulated by dialysis in the presence of refolding buffer. Results indicated that the researchers could generate the necessary conformation-specific antibodies that could potentially neutralize infections of SARS-CoV by NPs-based systems [92]. Nowadays, researchers are also seeking to formulate successful peptide-based approaches to molecular dynamics that rely on experimental simulation studies. In new study, a peptide inhibitor isolated from ACE2 has developed large traces to block SARS-CoV-2. In addition, it has been reported that multiple binding of nanocarrier-linked peptides will increase the binding efficacy [93]. "LIF nano," a novel class of mesenchymal stem cells, is also reported to improve the patient's biological resistance to COVID-19 utilizing stem cells [94]. This kinds of strategies are very useful because as part of an infection with COVID-19 they can overcome the significant decline in health that is happening in cases affected by pneumonia.

### 3.3. Prospects in nanomedicine against coronaviruses

No research on radical and effective methods of treatment of nanotechnology for COVID-19 is available, but the thesis works against COVID-19 to produce both efficient and safe nanomedicine. The origin of respiratory entry is the respiratory mucosa for some viruses, such as influenza, and respiratory syncytial viruses. Since hitting the upper respiratory tract their

journey to the lower respiratory tract is causing breathing infections. Conventional vaccines have weaknesses such as pathogenic reversal of virulence that cause weak immune response and deficient or unsuccessful immunogenicity, respectively. These defects can be corrected by applying NP-based therapeutic techniques due to their properties such as size and form and structure, which effectively leads to better immunogenicity and enhanced antigen presentation [95]. New NPs that can enhance the efficacy in the treatment of respiratory diseases by means of a different mode of action which are (i) the development of polymers with more active mucus penetration and do not stay stuck, overwhelming this barrier, (ii) the formulation of biodegradable NPs with stability to bypass the cell membrane and function in the lung with reduced toxicity levels, thereby creating a low toxicity, No causing lesions by treatment, (iii) modifying the chemical structure of NPs by incorporating surface capping factors [96].

### 3.4. The nano-based vaccine in treatments for coronaviruses

Much focus has been given to the development of nano-based vaccines and multiple forms of coronaviruses. *Kim et al.* introduced an RNA vaccine-mediated ferritin-based NP assembly to MERS-CoV that can induce CD4 + T cells, which in turn contributes to the development of IFN-γ and TNF-α through stimulation of antigens [97]. Furthermore, *Jung et al.* Established a MERS-CoV immunogenic vaccine with a recombinant adenovirus serotype 5 encoding spike gene MERS-CoV (Ad5/MERS) and spike protein NPs using a heterologous prime-boost technique [98]. *Lin et al.* Developed a viromimetic NP-based vaccine connected to an agonist-adjuvant immunological stimulator for the interferon gene against MERS-CoV [98]. The development of hollow polymeric nanocarriers coated with antigens of the receptor-binding domain (RBD) has been followed by the loading of cyclic diguanylate monophosphate as an emerging form of agonist interferon gene stimulator. C57BL/6 mice were later immunized with the revamped vaccine. Sekimukai et al. tested the potency of two adjuvant models (AuNPs and Toll-like receptor agonists) with recombinant protein S against SARS-CoV infection in mice [99]. Results revealed that vaccination with AuNP-adjuvanted antigen did not result in the induction of antibody defense and reduction of eosinophilic infiltration compared to a Toll-like receptor agonist-adjuvanted vaccine, but provided a powerful IgG response. A self-amplifying RNA encoding the SARS-CoV-2 spike protein encapsulated in a lipid LNP as a vaccine and supporting the induction of effective pseudo-virus neutralization, equal to the quantity of unique IgG and higher than the recovered COVID-19 events. These results offer insight into the vaccine's design and evaluation of immunogenicity to facilitate rapid translation into clinic. It compares the immunogenicity of saRNA encoding a prefusion stabilized spike protein SARS-CoV-2 encapsulated in LNPs in a preclinical murine model to the immune response in recovered COVID-19 patients induced by natural infection. It characterizes both humoral and cellular-mediated reaction and the ability to neutralize the pseudotyped SARS-CoV-2 virus.

### 3.5. Nanotechnology for diagnosing coronaviruses

Sensory techniques for other microorganisms have been recorded in research. Unfortunately, due to its long incubation period and remarkably higher infectivity, some quick and delicate methods of diagnosis for COVID-19 are limited and are urgently checked. Present detection systems are based on the identification of nucleic acids and have several weaknesses (i) low-sensitivity laboratory procedures, (ii) long-term, (iii) high false-negative probability, and (iv) diminished precision. *Zhu* and others. Described a COVID-19 NPs-based biosensor system that operates via a one-step, single-tube reaction pathway [100]. This sensor utilizes a special-stage reversed transcription loop-mediated isothermal amplification (RT-LAMP) connected to an NP-based biosensor (NBS) assay. Furthermore, isothermal state processing equipment is required for 40 min, and the result analysis time from the collection of samples is only around 1 h. This SARS-CoV-2 RT-LAMP-

NBS biosensor was successfully verified from non-SARS-CoV-2 models for COVID-19 confirmed cases with a possible sensitivity of 12 copies per reaction without a cross-reactivity. The labor-intensive and time-consuming features of conventional RT-PCR-based sensoring systems make them unacceptable for fast and accurate diagnostics. An effective approach for this strategy is the use of poly (amino ester) with carboxylic groups (PC)-coated magnetic NPs (pcMNPs) [101]. The designers developed pcMNPs, then incorporated the lysis and the binding step into the RT-PCR reaction in a single step. MNPs for their effective use in sensory systems have been mentioned before [102]. This system is capable of purifying viral RNA from several samples within 20 minutes, and 10 copies of immunity. These findings are so promising since the present molecular determination of COVID-19 reduces organizational demands, which help the early therapeutic determination of the affected individuals. *Wang et al*. Established a fast and synchronous recognition method using Nanopore Target Sequencing (NTS) for SARS-CoV-2 and other respiratory viruses [103]. The designers analyzed 61 nucleic acid samples from suspect COVID-19 samples and reported that NTS would be successful in detecting positive samples within 6 to 10 hours. NTS is based on the amplification using a primary line of 11 SARS-CoV-2 virulence-related and separate gene fragments (orf1ab), followed by a nanopore platform sequencing of the amplified fragments. This study is extremely important, as it provides valuable knowledge to establish sensory mechanisms for other respiratory pathogens. *Yu et al.* similarly used the NTS approach to identify changes in the homeostasis of intestinal microbiota in people affected by COVID-19 [104]. Recently papers on improved rapid detection of emerging COVID-19 diseases are available using colloidal gold testing of COVID-19 IgG-IgM hybrid antibody [105]. *Teengam et al.* developed a paper-based colorimetric multiplex analytical instrument that uses Ag NPs as a colorimetric reagent to classify DNA associated with a viral disease such as MERS-CoV. A detection limit of 1.53 nm had been obtained below a median condition in their study [106]. *Layqah* and *Eissa* reported an electrochemical immunosensor using a variety of carbon electrodes modified with Au NPs, which allowed the identification of individual coronavirus and MERS-CoV proteins in spiked nasal samples [107]. A self-assembled nanostructure of chiral gold NPs (CAu NPs) and quantum dots ( QDs) was used as a chiroimmunosensor for the detection of the infectious bronchitis virus (IBV) in broiler blood samples [108]. *Wang et al.* in another review developed an AuNP-based nano-nest PCR assay for variant and classical strain differentiation [109]; A total of 78 clinical specimens obtained from various regions in China were measured using both the nano-nest and conventional reverse transcription polymerasechain reaction (RT-PCR). Conclusions showed, with 100-fold sensitivity, that the nano-nest PCR assay was more effective than conventional PCR. Sona Nanotech has developed a lateral-flow screening technique, using its patented nanorod technology to classify the Covid-19 in less than 15 minutes. Meanwhile, the European Commission and the Spanish Ministry of Science and Innovation recently announced their proposal to finance a CONVAT research project to establish a fast, nanobiosensor-based COVID-19 study. CONVAT will introduce a new design based on optical biosensor nanotechnology that will allow the detection of coronavirus directly from the patient's sample within 30 minutes, without the need for testing in centralized clinical laboratories [110]. The Franklin team is focused on a protein that sits on the outline of the SARS-CoV-2 viral particle known as the 'spike' which binds to individual cells during an infection. This protein has a special region responsible for this binding activity – the receptor-binding domain (RBD). Nanobodies can retain the 'spike' to allow the best imaging at the atomic scale, using excellent imaging techniques such as cryo-electron microscopy (cryo-EM). In addition, the nanobodies allow the RBD to be kept bound to its target, enabling researchers to thoroughly understand how it acts in the body, and how it can be compared with current drugs. In addition , the team is exploring whether the nanobodies they recognize or drugs from which

they come could be used to build extremely sensitive 'blockers' that could contribute to COVID-19 medicines by blocking the SARS-CoV-2 virus from junction to human cells and inducing infection. In addition, nanobodies possess diagnostic ability, offering highly effective and fast testing [111].

### 3.6. Nanotechnology for prevention of COVID-19

Numerous nanotechnology devices are prepared to deliver COVID-19 fighting to people. Although enhanced respiratory masks and gloves are required for outdoor usage to minimize the amount of bodies exposed to potential hazards, detergents, sanitizers, disinfectants, and antiviral nanomaterial soap may be used indoors to prevent this pandemic. Nanodiamond, graphene, polymer nanofibers, and nanoparticles like platinum, copper oxide, and titanium dioxide are usually designed to provide experience in these types of products [112].

#### 3.6.1. Respiratory Masks

##### 3.6.1.1. Nanofibers Membrane Technology

Nanofibre membranes are composed of a thick spiderweb-like nanofibre-like fabric that produces large surface area. These sheaths are incorporated into respiratory masks which give great breathability and filtration capability thanks to their powerful and solid structures. Face masks usually filter out up to 95% of minor particles with a diameter of at least 300 nm, referred to as N95 masks [113]. The group of researchers at Queensland University has developed and tested a highly breathable, nanofibre-based substance based on cellulose that can extract virus size NPs. This new material that extracts NPs is created for use as a disposable filter cartridge is anti-pollution masks and is biodegradable. This is an important factor for those who are expected to wear masks for long stretches on their respiratory system or for those with disabilities. The higher the breathability, the greater the relaxation and the less fatigue [113].

##### 3.6.1.2. Nanocomposite Membranes Technology

Copper3D offers a face mask, NanoHack, that incorporates a modern, integrated filtration system made from the revolutionary nanocomposites PLACTIVE® and MDflex®. This efficient filtration method includes three layers of saturated non-woven polypropylene with 5% copper oxide NPs, with high antiviral and antibacterial properties [114].

##### 3.6.1.3. Nanoparticles Technology

Promethean Particles Ltd is leading testing equipment to investigate the antiviral effects of its revolutionary copper NPs that were produced for use in personal protective equipment in the healthcare field. It was found that by embedding nano-copper into polymer fibers, like nylon, using a melt extrusion process, the antimicrobial effect persisted higher than other comparable antimicrobial fabrics. If approved, it could open the gate to be COVID-19 immune to the manufacture and sale of nonwoven fabrics and personal protective equipment [115].

#### 3.6.2. Air Filtration Systems

##### 3.6.2.1. Nanofibers Technology

Mack Antonoff HVAC launches COVID-19, mold and bacteria, pet dander, clean air filtration operations system. For families with asthma , allergies, bronchitis, the 5 "Hepa, Peco, and Nano filters with UV light inserted into ductwork are required to keep your home smelling fresh [112].

##### 3.6.2.2. Photoelectrochemical Oxidation Technology

In March 2020, the University of South Florida, a newly created air purification device named Molekule, was established to experiment with a virus that functions as a coronavirus proxy that destroys air pollutants including viruses , bacteria, molds and spores. The instrument uses photoelectrochemical oxidation, a process that uses UV-A light to activate a catalyst in

Molekule's NPs-covered filter to generate free radicals and oxidize air contaminants. This product has the potential to help reduce the spread of the virus-especially in hospitals and health centers, where he says medical workers around the world are now risking their own lives to work with patients who have fallen ill [112].

### 3.6.3. Disinfectants

#### 3.6.3.1. Nanopolymers Technology

Design.123 launched a platform specifically designed for COVID-19 sanitization and scanning, marketed as PRELYNX PORTAL. Based on equipment found in labs and quarantine locations, a high-powered nano-polymer disinfectant vapor blast wraps the underlying body. This disinfectant uses an active virucidal agent that inactivates on an individual's surface several of the many hydrophilic and lipophilic viruses. The virus cells will instantly start dying and they will all die by minutes [112].

#### 3.6.3.2. Nanoparticles Technology

Produced by NANO4LIFE EUROPE L.P., NANO4-HYGINELIFE surface sanitizer kills viruses and bacteria. If this substance is placed on the surface there would be a coating of "swords." Because of the positive charge of the "swords," the virus' negatively charged membrane is attracted and the cells will be destroyed until it comes in contact with the "sword." Therefore, by interfering with the metabolism, NANO4-HYGIENLIFE does not kill the cells; it is a brute force by which the cells are killed right after they touch the surface [116].

## 3.7. Conclusions

World health faces the most urgent condition surrounding the novel extreme acute respiratory syndrome called coronavirus (SARS-CoV-2), which is internationally referred to as the COVID-19 abbreviated pandemic. The drug design techniques against the virus are thoroughly reviewed in our study, including exploitations of experimental therapies and repurposed drug potentials. Although major implementations have been placed in place to develop an appropriate therapeutic approach against different forms of coronaviruses, no clear procedure has yet been identified. Numerous study has been carried out on the use of nanomaterials in the prevention, anti-infection, and detection of some forms of coronavirus, including the ones discussed in this paper. Therefore, a review of studies on the efficacy of NPs for therapeutic, preventive, regulation, and diagnostic strategies was presented that envisaged the possibility of using nanomaterials to produce a highly efficient coronavirus vaccine. The effect of nanomedicine is significant in the whole condition but only a few scientists have written their findings on the study worldwide. The latter was in the hospitalized contaminated cases due to several early studies and findings obtained from laboratories, and also some samples. It is expected to be possible to have the first (validated) vaccine on the market in the next year, but before then more testing needs to be completed to develop a dramatic medicine to deal with this unknown adversary, COVID-19. Nanomedicine applications may be evaluated through the use of certain basic nanomaterials including organic and inorganic substances, with special attention being given to biosensors based on NPs, which are important instruments for the identification of persons infected with pathogens. Traditional detection systems focus on identification of nucleic acids and have several faults. The basic hypothesis, however, is that COVID-19 is a new pandemic and can initially be treated with any already recognized nanomaterials added to previous SARS-CoV or similar viruses. This knowledge would be a significant instrument in the battle for this unusual virus.

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