



View Point of Nanotechnology's Competence: Benchmarks of Covid-19 in the Post-Outbreak Period

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Abstract

The recent coronavirus 2019 (COVID-19) outbreak was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Finding newer therapeutic targets is necessary because, despite the fact that pandemics like SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) have been around for almost 20 years, no effective medication against the CoV family has been approved. Currently, research is being conducted simultaneously all over the world to find effective vaccinations or medications, including both new and traditional treatments like Nano medicine that were used to treat earlier, related diseases.

Keywords: Coronavirus; Nano Medicine; Pandemic; Respiratory; Syndrome

Introduction

The recent coronavirus 2019 (COVID-19) outbreak was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The first verified and documented cases of COVID-19 in China in 2019 quickly escalated to a global state of emergency that hasn't been seen since the Spanish Flu pandemic in 1918. The inability to stop the spread of COVID-19 has brought attention to how urgent it is to create diagnostic and treatment strategies for extremely contagious diseases [2,3]. To reduce the pathogenicity, morbidity, and mortality of SARS-CoV-2, numerous novel treatments are being developed that combine both conventional and cutting-edge techniques. One new area of study that has expanded into the medical field is nanotechnology. Nano medicine can overcome the challenges that conventional medicine faces because of its progressive nature. Above all, it will perhaps help bring about a revolution in 21st-century drug-based medicine. If properly utilized, the features of nanomaterials may enhance medications and vaccinations and offer safer and more effective means of combating illnesses [1].

Structure of virus

The CoV are enveloped positive single-stranded RNA viruses, and their 8.4–12 kDa genomes are the biggest known viral RNA viruses. The 5C and 3C terminals make up the viral genomes. A significant portion of the genome is made up of the 5C terminal, which has open reading frames that encode the proteins needed for viral replication. The spike protein (S), membrane protein (M), nucleocapsid protein (N), envelope protein (E), and hemagglutinin-esterase (HE) are the five structural proteins found in the 3C terminal [3]. The S protein facilitates the attachment and fusion of the virus with the membrane of the host cell as well as between the infected and nearby uninfected cells. In a vaccine, they are the main inducers of neutralizing antibodies. The RNA complexes that the N protein creates help transcription and assembly of viruses. The most prevalent structural protein, the M protein, also determines the form of the viral envelope. During the viral replication cycle, the E protein—the tiniest and most mysterious of the key structural proteins—is widely expressed within the infected cell. The HE protein is in charge of host specificity and receptor binding [4].

Mode of transmission

Common methods of human-to-human transmission include direct transmission, contact transmission, aerosol-borne

transmission, and transfer during medical procedures. Common ways of transmission include coughing, sneezing, inhaling droplets, and coming into touch with mucous membranes of the mouth, nose, and eyes. Other viral sources propagate as a result of viral shedding from the respiratory system, saliva, faces, and urine. Patients with severe COVID-19 have a greater and longer-lasting viral burden. There have also been reports of COVID-19 spreading from patients to medical personnel and airline attendants who had close contact with the affected patients [2]. Fever, cough, sputum production, dyspnoea, myalgia, lumbago, diarrhoea, rhinorrhoea, loss of taste and smell, and headache are among the symptoms that are frequently seen in COVID-19 [5,6].

Organs involved in COVID-19

An important target of the virus is angiotensin converting enzyme II (ACE2), a surface receptor present in human cells, which is essential for the effective uptake of SARS-CoV-2 in the host cells. During infection, the viral spike glycoprotein binds with the ACE2 of the host cell (peptidase domain of ACE2). Attachment of S protein with ACE2 is an important and the first step of infection, hence disrupting this binding process is a key approach in treatment. Initially, SARS-CoV-2 impairs the respiratory system and thereafter systemically reaches heart, liver and kidneys. ACE2 is expressed highly in the airways [4]. The respiratory system serves as the main entry point and binding place for SARS-CoV-2 due to the high expression of ACE2 in the lungs and respiratory tract. Hence, SARSCoV-2 can easily enter into the body by interacting ACE2 in the alveolar cells and this is described as the reason to develop immediate pneumonia and leads to ARDS and failure of multiple organs in severe patients. ACE2 is expressed highly in the cells of cardiovascular system and play a vital role in blood pressure regulation and myocardial contractility.

Heart fibrosis and inflammation may develop as a result of SARSCoV-2 binding to ACE2. Both direct infection harm and hypoxia injury are ways that the CoV-2 might infect the central nervous system. A cytokine storm and significant brain damage can result from the activation of brain immune cells caused by astrocyte, macrophage, and microglia infections. The BBB's integrity may be impacted by SARS-CoV-2's interaction with the ACE2 of brain capillary endothelial cells, which facilitates the virus's entry [7]. The liver and pancreas are possible targets of CoV-2 because they contain higher levels of ACE2 and TMPRSS2 (transmembrane

serine protease 2) than other intestinal epithelial cells. More ACE2 is expressed in the reproductive system, specifically in pregnant women's uterus, placenta, and foetus interface. The expression of ACE2 in CoV-2 can bind to foetal tissue, making it a crucial target location that increases morbidity and death [5]. Patients with COVID-19 have high levels of inflammatory chemokines and cytokines, which leads to cytokine release syndrome (CRS). Severe multi-organ failure and ultimately mortality can result from advanced types of CRS, especially when paired with ARDS. Tumour necrosis factor (TNF) or interleukins 1 or 6 (IL-1, IL-6) are the chemokines and cytokines that are involved [4].

Nano medicine approach

Although there are numerous treatment options available, the application of different Nano medicine techniques has been effective in accurately treating a number of illnesses; nonetheless, its application in pulmonary drug/therapeutic targeting as an adjuvant therapy is still pending. Improved lung infection treatment approaches are made possible by Nano engineering with possible medications. Pulmonary Nano-drug delivery systems are the perfect drug delivery system for treating COVID-19-like pulmonary infections because of their special physicochemical characteristics, which include mucosal penetrability, ease of ligand functionalization, enhanced permeation because of their small size, increased local concentrations of drugs, and high adjuvant properties for vaccine applications [6].

Antiviral activity of Nano particles

Antiviral compound delivery has demonstrated notable potential benefits with nanoparticles. Furthermore, nanoparticles exhibit direct antiviral action. Silver nanoparticles, functional gold nanoparticles, and quantum dots are among the different types of nanoparticle systems that have been shown to have antiviral properties thus far. For example, the majority of "antiviral" nanoparticles employ the well accepted tactic of preventing the virus from attaching itself to or entering the host cells [8,9]. The suggested medications Nano encapsulation may result in a safer way to treat COVID-19 and other viral illnesses. By permanently harming different viruses, these particles can stop their transcription, translation, and replication. To target infected cells, drugs can be enclosed in Nano carriers [5]. These systems based on nanoparticles have demonstrated an enhanced therapeutic effectiveness and lower related toxicity as

compared to free medications. It's interesting to note that their mucoadhesive quality is one of these characteristics that is highly valued while developing treatments for respiratory infections using nanoparticles. Numerous nanomaterial modifications using different functionalization techniques have been created in order to obtain this high mucoadhesive characteristic [7].

Nanoparticles in diagnosis of covid19:

Nanoparticles can be engineered as biosensors for the detection of biomarkers, such as nucleic acids (DNA, RNA), specific antigens (proteins, enzymes), or antibodies, in order to swiftly and accurately identify SARS-CoV-2. Recent advances in nanotechnology have made it possible to use graphene in conjunction with an anti-spike antibody as a SARS-CoV-2 diagnostic method. Other detection methods that have been developed include dual-functioning plasmodia biosensors that use the energetics of DNA-RNA hybridization and graphene oxide particles coated with fluorophore-bound DNA target strands that may detect viral helicase [10].

Nano medicine for vaccine adjuvant delivery

Adjuvants are occasionally needed to increase the immunogenicity of recombinant and inactivated protein vaccines. NPs can carry molecular adjuvants, and they frequently exhibit adjuvant properties for the integrated antigen on their own [11]. The drawbacks of the conventional method of administering molecular vaccination adjuvants can be addressed using vaccine adjuvant nanoparticles. Alum (aluminium salts), MF59 (a squalene-based emulsion adjuvant), AS01 (a liposome-based adjuvant), AS03 (a squalene-based emulsion adjuvant), AF03 (a squalene-based emulsion adjuvant), AS04 (which contains the TLR4 agonist MPL (3-O-desacyl-4'-monophosphoryl lipid A), and virosomes are among the adjuvants that have been licensed for use in vaccines. As a Nano adjuvant, MF59 demonstrated strong adjuvant action, including humoral and T helper type 1 immunological. DTap, Hib, hepatitis A, and hepatitis B are among the licensed vaccines that contain alum. Virosomes is a component of the hepatitis A vaccination (Epaxal®) and the influenza vaccines Inflexal® V and Invivac®. For influenza vaccinations intended for older adults, MF59 and AS03 have licenses [12,13].

The adjuvant qualities of virus-like particles, PLGA NPs, cationic liposomes, Nano emulsion, and cholesterol-bearing Nano gel are also

being investigated. By enhancing antigen presentation and utilizing their innate immuno activation capabilities, several nanomaterials on their own exhibit adjuvant activity. The properties of cyclic dinucleotides (CDNs) make them useful as vaccine adjuvants. CDNs were transported to the draining lymph nodes by cyclic di-GMP (cdGMP) loaded PEGylated lipid NPs (NP-cgGMP), which also enhanced the adjuvant activity of CDNs as an adjuvant to induce CD4+ and CD8+ T cell responses [14]. Adjuvants may be helpful for individuals with compromised immune systems and those with additional comorbidities that lead to immune dysfunctions in the case of SARs-CoV-2. It is anticipated that vaccine adjuvants will lower the COVID-19 antigen dose needed. Matrix-M adjuvant, a saponin-based adjuvant, along with a SARS-CoV-2 recombinant spike protein NPs vaccine, is undergoing a phase I clinical research to assess its immunogenicity and safety. Therefore, it is thought that a combination of vaccine and adjuvants is crucial, particularly for elderly and immunocompromised patients [9].

Preventive action with nano medicine

Because of their additional layers of nanofibers and tiny holes, Nano masks can keep viruses from accessing the respiratory system. As a result, Nano masks are far more effective than regular masks at preventing the spread of viruses. Without sacrificing the material's structure or breathability, face masks, lab or surgical aprons, and other items have been Nano engineered to incorporate novel qualities including hydrophobic and antibacterial activity [10].

In addition to providing comfort, nanomaterials, including nanofibers, can lower pressure and breathing resistance while protecting against tiny particles (less than 50 nm). Comparing this to traditional surgical face masks, the protection is far higher. Conversely, the mucous membrane serves as the coronavirus's entryway into the human body. Therefore, the strategies for preventing and providing Medication that passes through the mucosa is essential. When it comes to transport across mucosal membranes, nanotechnology has demonstrated enormous promise [15].

Challenges and limitations

One of the biggest challenges will be producing nanoparticles on a large scale, particularly when attempting to make these treatments reasonably priced. Although total health care costs could

be reduced if nanomaterials and Nano-vaccines are successful in preventing COVID-19, the cost of nanoparticles may increase due to the complexity of their manufacturing methods and intellectual property rights. Unwanted tissue interactions and toxicity, as well as unintended systemic dissemination and deposition, including unintended blood-brain barrier crossing, are additional drawbacks of nanoparticles [16]. Depending on the size and chemical makeup of the nanoparticles, accidental inhalation into the lungs is thought to result in fibrosis, pulmonary inflammation, and epithelial damage. Furthermore, it has been demonstrated that nanoparticles disrupt biological functions such as oxidative stress, inflammation, mitochondrial activity, and macrophage phagocytosis. as well as platelet activity. ROS production, cell membrane binding, DNA damage, altered cell cycle control, and protein denaturation are some of the ways that nanoparticles can be harmful, either acutely or over time. The lack of knowledge regarding the long-term impacts of nanoparticles on people and the environment is another significant problem [17].

Conclusion

Because they improve antigen stability, antigen processing, and immunogenicity as well as the sustained and targeted administration of antigens, Nano medicines like NPs, lipid NPs, and VLPs have drawn attention from researchers as therapeutic molecules and vaccine delivery vehicles [18]. However, a significant obstacle is the reproducibility and large-scale industrial manufacturing of target-specific ligand coupled Nano medicines loaded with drugs or vaccines. It is anticipated that Nano medicine will be a potent platform for repurposing current antiviral medications to enhance the treatment of COVID-19.

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