The 2nd International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/3/20220287

Nanotechnology for COVID-19: Vaccine Research, Detection and Therapeutic

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Abstract. COVID-19 has triggered a worldwide need for effective detection, treatment as well as infection control, with academic and industrial efforts around the world to control or contain COVID-19-related epidemic conditions. As in other fields, nanotechnology offers Therefore, faster, easier and more effective diagnostic methods based on nanomaterials and nanotechnology-based the variety of approaches and technologies with great potential and promise to address the COVID-19 crisis. One of the key elements to combat SARS-COV-2 is to diagnose quickly if the virus is mutated and to initiate therapy in time. Therapeutic methods as well as nanotechnology-based vaccines occupy an important position in combating COVID-19. In addition, the application of nanomaterials provides new ideas for the production of antiviral protective masks, gloves, and laboratory garments. We discuss ongoing nanotechnology-based treatment and prevention strategies to address health crises caused by pandemics, highlighting a key part of nanoscience involvement.

Keywords: COVID-19, mRNA vaccine, nanotechnology

1. Introduction

The COVID-19 pandemic is having a major impact on ordinary life around the world: by early 2022, the epidemic will have already killed more than 5 million people. Because of this high rate of infection, scientists around the world are searching for effective ways to mitigate this serious situation. Currently, there are no clinically proven treatments that can completely reverse the effects of SARS-CoV-2. The most effective solution is to interrupt and control the spread of the virus, for example through vaccination, isolation of confirmed cases, and the wearing of antibiotic masks and protective clothing.

Nanomaterials are a new type of material that has emerged in recent years, and their uniqueness has attracted a great deal of attention from the scientific community. Nanotechnology offers unique solutions to address epidemics, and researchers around the world are developing new applications for nanotechnology research. Although it is currently difficult to translate laboratory results into successful clinical applications in a short period of time, it is valuable to accumulate relevant knowledge to enable new futures.

Currently, the greatest challenge in controlling the epidemic is the development of effective vaccines and drugs. However, there are many problems in delivering proteins, drugs and RNA as carriers to the patient's target cells, as some carriers often dissolve, lose bioavailability, are excreted as toxic substances or do not reach the target accurately. Advances in nanotechnology have found many

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solutions to these problems. Due to the specific nature of nanoparticles, it is possible to overcome many of these limitations that are difficult to achieve with other technologies. For example, drugs and antigens coated with nanoparticles can avoid degradation and retain their activity after administration.

Nanotechnology has the potential to accelerate vaccine research and disease treatment, and it also plays an important role in disease diagnosis. Nanotechnology is expected to help develop rapid, accurate, and cost-effective tools to detect SARS-COV-2 and its variants, and nanotechnology-based biosensors could replace traditional laboratory monitoring devices. Nanomaterials can also be used to make masks and protective materials with germicidal properties. Since viruses are transmitted by droplets, ordinary masks and eye masks do not kill the virus directly, but only block it. The use of special invisible coatings that trap droplets, immobilize and kill viruses can greatly limit their spread. Overall, nanotechnology has the potential to address all aspects of COVID-19 and prepare for future pandemics.

This review focuses on the use of recently developed nanomaterials to apply nanotechnology approaches to diagnostic and therapeutic methods, drugs, and vaccines to prevent and stop the spread of this coronavirus.

2. Background

Coronavirus disease in 2019 is the most serious pandemic of the year. COVID-19 is an acute respiratory syndrome caused by the highly infectious SARS-CoV-2 virus. SARS-CoV-2 is an enveloped, positively charged RNA virus, 60-140 nanometers in diameter that closely resembles a virus in morphology. Thus, nanoparticles (NPs) acquire a high ability to mimic viruses and then interact with target proteins and cells. More importantly, nanoparticles exhibit significant activity against many viruses, including coronaviruses. Therefore, nanoparticles are highly competitive to other materials and nanoparticle-based strategies have great potential in the combat with the coronavirus, including vaccine research and drug delivery.

Since there is no absolute cure to control the virus, a vaccine remains the most effective means of controlling the spread of the epidemic. However, most vaccines against the virus are still under development. Different types of vaccines are being investigated, including traditional whole virus vaccines, recombinant vaccines, viral vector vaccines, and nucleic acid-based vaccines (DNA and mRNA vaccines). Nanotechnology research has led to the development of new vaccine delivery systems and pluripotent adjuvants. For example, several biopharmaceutical companies have recently worked to develop mRNA vaccines that encode SARS-CoV-2 proteins, including nano-coated spike proteins (S protein), some of which have passed clinical trials with initial success. The mRNA-based nanovaccines consist of mRNA that carries the genetic information of the protein antigen encapsulated in lipid nanoparticles (LNPs). One of the important components of COVID-19 mRNA vaccine are Lipid nanoparticles (LNPs), because they play a crucial part in protecting mRNA from degradation when delivered to the target cells.

After vaccination, mRNA protected by lipid nanoparticles is transported to the host cell membrane, where it serves as a template for the synthesis of protein antigens. Because protein antigens are synthesized in the recipient's cells, mRNA vaccines, unlike DNA vaccines, also induce immune responses, such as antibody production and T-cell responses. In addition, unlike other vaccines, mRNA vaccines have a time-limited antigen expression response, which ensures their safety after vaccination. These features suggest that this may be a new area of research for the development of viable, safe and cost-effective antiviral vaccines.

3. Lipid Nanoparticles（LNPS)─ as Protective Carrier

mRNA-based vaccines and corresponding therapies show promise in the fight against disease. Due to their high efficiency, short production cycle, ease of manufacture and low cost, mRNA vaccines have attracted the attention of many researchers and have contributed to the progress of vaccine development［1］. However, the rapid development of mRNA vaccines relies on advances in LNP

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nucleic acid transport technology, as mRNAs without packaging systems are typically degraded upon transport to the target site. In contrast, under the protection of LNPs, mRNA can be delivered to almost any host cell for protein expression［2］.

Nucleic acids have properties such as negative charge and hydrophilicity that reduce the efficiency of their diffusion across cell membranes. There are various barriers to the entry of mRNA into the host translation machinery, including uptake by phagocytes, binding to appropriate antibodies when recognised as an antigen, and degradation by enzymes. Therefore, mRNA packaging systems are required to prevent degradation during transport. Because of the size of the nanometer scale, nanoparticles have the ability to enter the host cell and enable the expression of nucleic acid antigens. Many nanoparticle-based drugs and vaccines take advantage of these properties, particularly lipid nanoparticles, which are widely used.

Lipid nanoparticles (LNPS) are promising as novel prophylactic and therapeutic vectors and are the most advanced non-viral gene delivery system in clinical practice. In the pharmaceutical industry, LNPS have proven to be versatile carriers as they can encapsulate and modify many different types of drugs, proteins or other items, and facilitate the safe and efficient transport of nucleic acids. Compared with the existing lipid nucleic acid delivery systems, LNPS has many advantages, such as high efficiency, good transfer efficiency, low cytotoxicity and immunogenicity. LNPS also have great potential in other areas such as cosmetics and food production, as well as in innovative areas such as nanosensors.

Both Pfizer/BioNTech and Moderna use LNPs to encapsulate mRNA to transport them into host cells safely without interference of extracellular substances. Compared to bilayer liposomes, LNPs provide a conductive and more stable transport structure, allowing better penetration of antigens into cells for expression［3］. In particular, the ionised lipid layer, whose surface charge varies with pH, plays an important role. It is neutral at physiological pH and becomes positive as pH decreases. This property reduces the risk of toxicity and provides payload to the mRNA during the process.

4. The use of Vaccine adjuvants nanoparticles (VANs)

A number of COVID-19 vaccines have been documented in clinical trials, and more than five of them have employed an antigenic adjuvant ligation strategy, suggesting that adjuvants can be an important component of vaccines. Therefore, there is a need to use vaccine adjuvant nanoparticles (VANs) to facilitate the research of modern COVID-19 vaccines. Vaccine adjuvant nanoparticles (VANs) have many advantages over molecular adjuvants previously used for vaccine delivery and appear to overcome existing limitations, such as lack of immune cell targeting.

It was revealed in clinical trials that vaccine adjuvants can promote vaccine efficacy and enhance immune responses, especially in elderly. They have the lowest immunity and the poorest health status in the population, and therefore have the highest morbidity and mortality after COVID-19 infection［4］［5］. Clinical cases have indicated that the addition of adjuvants reduces the risk of pneumonia and modulates the immune system response in the elderly. This supports to be tuned for vaccine studies［6］.

5. Advantages and disadvantages of Nanoparticles in vaccine application

5.1. Advantages

*5.1.1. Morphological peculiarities make the therapeutic accessible.*Unlike other materials, nanomaterials have a unique microscopic size and composition, which allows them to easily penetrate host cells and accomplish the expression of the delivered nucleic acid antigens, which is difficult to achieve with other materials. The lymphatic system is an important site for triggering the immune response, as APCs and other lymphocytes migrate through this system to nearby lymph nodes. However, the specific structural characteristics of the lymphatic system make it difficult for substances

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from outside the body to penetrate. Due to their small size, nanomaterials can cross the space and enter the surrounding lymph nodes.

5.1.2. Codeliver adjuvants. Nanoparticles can also work together in the delivery of adjuvants. In many cases, the adjuvant and antigen are encapsulated in nanoparticles and reach the target simultaneously. Some nanoparticles can even be used directly as adjuvants as well as packaged. The main role of adjuvants is to activate specific molecular receptors with recognition functions and to enhance the body's response to antibodies, especially innate immune cells. The mechanism of action of the vaccine is to to deliver antigens to lymphocytes to reorganize and stimulate the immune response, but not to target innate immune cells. However, B and T cell responses acquired after lymphocyte activation can activate innate immune cells［7］.

5.2. Disadvantages
There are a number of issues that will need to be investigated in depth by scientists in the relevant research areas in the near future.

5.2.1. Storage limitation. In the case of mRNA vaccines, their stability is temperature-dependent and they tend to degrade and lose their activity at high temperatures. Therefore, the storage conditions of mRNA vaccines, especially in terms of temperature control, are challenging. Although their low cost and efficacy are major advantages over other vaccines, the need for complete refrigeration is one of the factors preventing their widespread use worldwide, as many underdeveloped regions cannot afford refrigerated facilities or refrigerated transport.

5.2.2. Short life. Unlike DNA, which has to be intergrated into the nucleus for antigen expression, RNA simply enters the cytoplasm to become active［8］. While this mechanism has the potential to reduce the risk of carcinogenesis and mutagenesis, it also means that the maintenance of mRNA and other expression is not durable and may cease in a relatively short period of time. In addition, the unmodified naked RNA is rapidly degraded in vivo and has a very short life span［9］. It is mportant to find ways to improve the stability and persistence of the spread.

6. Other applications of nanomaterials against COVID-19 health crisis

6.1. Antimicrobial textiles made by Nanomaterials for protection against pandemic
Besides vaccination, the use of personal protective equipment is an effective means of protecting health care workers and the public from viral infection. On the other hand, personal protective equipment (PPE) with antimicrobial and antiviral properties have not been developed, and existing PPE can isolate but not kill viruses［10］［11］. Therefore, in addition to the physical barrier effect, making PPE resistant may be effective in reducing the spread of COVID-19. Special nanofibers and coatings on the surface of protective clothing and masks can make the products resistant. On the surface of the product, the virus can be killed or bound to the virus, immobilizing it and preventing its further transmission.

6.2. Use of Nanotechnology to diagnosis SARS-CoV-2
Timely and accurate diagnosis is as important for epidemic control as it is for prevention and treatment. This is because patients with confirmed diagnosis can be isolated in time to stop the spread of the virus and receive prompt treatment. In particular, early detection of new coronavirus variants can lead to improved vaccine research and treatment.

In contrast to nanotechnology-based biosensors, traditional viral diagnostic methods, such as PCR, are poor efficiency, have low analytical sensitivity, and require special expertise. Nanobiosensors are expected to be an effective alternative to current laboratory equipment in clinical analysis and testing. Diagnostic methods using nanomaterials are more sensitive and can be performed efficiently with smaller equipment.

7. Future perspectives

Progress in nanotechnology in medicine has been slow to move from laboratory research to clinical applications due to technical difficulties. The spread of COVID-19 has significantly prompted the search for innovative nanotechnology solutions to combat SARS-COV-2. The initial success of nanoparticle-based mRNA vaccines has encouraged scientists to explore the development of nanomedicines and vaccines, which could be a tool for developing future cancer treatments.

Nanotechnology is already being used in the real world to detect SARA-COV-2, with detection kits being the most common nano-detection technology. The increasing demand for simpler and faster detection methods means that in the future, nanomaterials may be developed that can be detected by humans themselves.

In terms of treatment, there are no drugs specifically for novel coronaviruses, only antivirals are commonly used. Nanotechnology offers a new approach to the development of drugs specifically for the treatment of COVID-19. Drugs can be encapsulated in special nanomaterials, allowing for targeted and sustained release of the drug in the body. Once a specific drug is developed, it can directly aid in the recovery of an identified patient and take the fight against the epidemic one step further.

Overall, nanotechnology holds great promise in the medical field and plays an important role in the prevention, detection and treatment of COVID-19. The development of nanotechnology offers many strategies and approaches to control and treat possible future epidemics and cancers. Nanotechnology still has a long way to go and many challenges lie ahead.

8. Conclusion

Nanotechnology has greatly accelerated the development of the COVID-19 vaccine, but new confirmed cases continue to emerge in some regions, and nano methods alone cannot contain the spread of the current epidemic. The spread of the epidemic has not been halted and many questions remain unanswered.

The currently licensed COVID-19 vaccine has shown its usefulness in clinical trials, but it is not known how long immunity can be maintained and whether the in vivo immune effect will diminish over time. Therefore, it is important to study the duration of the immune response and changes in action after vaccine administration, as well as to design activation and defense methods to prolong the duration of action.

In addition, the spike glycoprotein (S protein) is susceptible to mutation. The spike glycoprotein is one of four major structural proteins of SARS-COV-2. Vaccines and dulcolax that have been effective in the past may not be effective in preventing or treating new variants, and there is a risk that routine testing will fail to detect new variants. Therefore, a timely and flexible response to emergencies involving new variants and variants is an important challenge that requires further research in the near future.

Overall, nanotechnology offers a major breakthrough in the development of antiviral vaccines. Although many challenges remain, it is hoped that these obstacles will be overcome in the near future to defeat pandemics.

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