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The potential of nanotechnology to combat the Covid-19 pandemic

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Abstract

In March 2020, the World Health Organization (WHO) announced that Coronavirus (2019) (Covid-19) was recognized as a global epidemic. In late 2019, a new type of the coronavirus family, known as Acute Respiratory Syndrome (SARS-CoV-2), emerged in Wuhan, China, called Covid-19. The Covid-19 epidemic has plunged the world into an unprecedented crisis, causing massive human and economic losses. As of July 6, 2020, this global outbreak has caused more than 167 million confirmed cases and more than 3.4 million deaths worldwide. The high rate of lung infection, long latency period, mild to moderate symptoms, cases that many people experience, or even cases of asymptomatic patients, has made Covid-19 a worrying disease. Challenges in addressing the illness involve the creation of vaccines, efficient large-scale manufacturing, and equitable global distribution. Nanotechnology can be regarded as a potential approach for both diagnosing and treating this hazardous virus. Nanoparticles, with their physicochemical properties, can be a promising treatment method to win the battle against coronaviruses. This review article aims to explore the disease of Covid-19 and the potential of nanotechnology as a bright and promising pathway for the diagnosis, drug delivery, and treatment of Covid-19.

Highlights:

The high rate of infection, the long incubation period, and the moderate symptoms have made Covid-19 a worrying disease.

Nanomedicine holds immense potential in combatting coronaviruses.

Nanotechnology can lend itself to identifying or extracting Covid-19.

Nanoparticle-based techniques are employed to design nanovaccines to enhance vaccine effectiveness.

Introduction

Drawing on past outbreaks such as SARS-CoV-2 and MERS-CoV, the world was expected to face another outbreak of pathogenic coronaviruses, common sources occurring between humans and animals (1, 2). In the latter part of 2019, the emergence of Covid-19 was caused by the appearance of SARS-CoV-2, a novel strain within the coronavirus family, particularly affecting the respiratory system and originating from Wuhan in China (3). As of July 6, 2020, this global outbreak has resulted in more than 11,327,790 confirmed cases and more than 532,340 deaths worldwide (4). The high rate of infection, the long incubation period, and the mild to moderate symptoms many people experience have made Covid-19 a worrying disease (6).

The sequence homology of the Covid-19 genome with SARS-CoV-2 and Mers-CoV is 77% and 50%, respectively. Data generated from research studies have shown that Covid-19 exhibits similar behavior and pathogenesis as betaCoV detected in bats (7). The rapid development, distribution, and administration of vaccines to the worlds' people is the most effective way to suppress this epidemic, and the only thing that leads to the complete removal of restrictions. Significant issues encompass the creation, manufacturing, and worldwide distribution of the vaccine, all of which pose challenges (8).

Due to owing to its unique physicochemical characteristics, nanomedicine holds immense potential in combatting coronaviruses (9). Nanotechnology usually deals with the designing and developing materials with dimensions from 1 nanometer to hundreds of nanometers, making it possible to design and manufacture materials with a specific structure and molecular structure (10, 11).

This study focuses mainly on the disease of Covid-19 and nanotechnology as a promising pathway for the diagnosis, drug delivery, and treatment of Covid-19.

2. Coronavirus and its transmission routes

For the first time in 2002, the transmission of SARS-Covid from bats to humans was seen in China. Then, in 2012, MERS-Covid appeared in the Middle East through camel transmission (12, 13). Now the seventh identified coronavirus, SARS-CoV-2, infects humans (14). Coronavirus particles are surrounded by a sphere of 80-120 nm (15). In the case of SARS-CoV-2, its genome (30,000 nucleotides) has about 79.5% sequence identity with SARS-CoV-2 (16).

Figure 1 shows the SARS-CoV-2 structure. To date, four subtypes of the coronavirus are known as α, β, ϒ, and δ (17). They are one of the most significant spherical RNA viruses covered by a positive single-stranded RNA genome (18). Although their stability is low, their potential for mutation is extremely high (19).

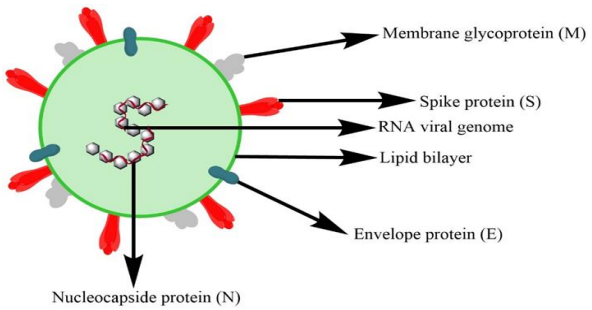

Figure 1. Schematic of the structure of the SARS-CoV-2

The four main structural proteins of β-coronaviruses are spike protein (S), envelope protein (E), membrane protein (M), and nucleocapsid protein (N) (Figure 1). The S protein is a desirable focus for vaccine development as it aids the virus's entry into the host cell during infection. The two spike protein subdomains, S1 and S2, are responsible for binding the ACE2 receptor to the host cell angiotensin-converting enzyme and integrating the host cell membrane,

respectively (Figure 2) (20). While the S1 domain varies throughout coronaviruses, the S2 domain is more consistent (21).

Coronaviruses are spread through person-to-person transmission (22). The virus is spread mainly through sneezing and coughing as saliva droplets, nasal discharge, and direct and indirect contact (23).

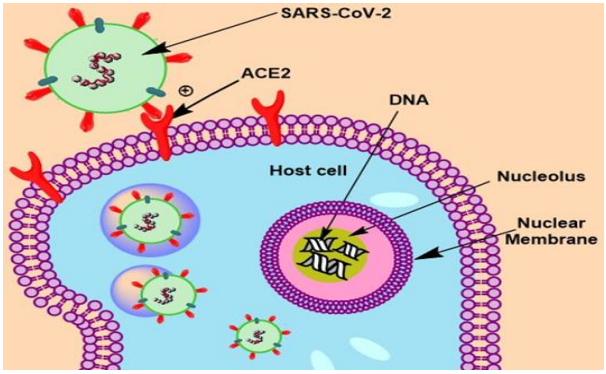

Figure 2. Schematic of Infection of the host cell with the SARS-CoV-2

3. Coronavirus diagnostic approaches

At present, laboratory diagnosis of viral infection can be made based on techniques.

Polymerase chain reaction (PCR) and sequencing: This is the predominant method for determining the types of coronaviruses (24). However, RT-PCR is the most effective tool for detecting SARS-CoV-2 (25). Viral RNA identity is determined by PCR (smear taken from the mouth and throat) (26).

Plain chest radiography: The examination focuses on the inflammation areas caused by the virus and the possible development of fibrosis and blockage in the lung connective tissue following the illness (27).

General and biochemical blood tests: Dynamic alterations in the typical levels of blood elements, such as white blood cells, neutrophils, and red blood cells, are linked to viral infections (28).

Immunology Assessments: A reliable antibody test against SARS-CoV-2 has the potential to detect the spread of Covid-19 throughout the population, which is critical for making informed health and economic decisions. The human adaptive immune system typically exhibits a distinct response against SARS-CoV-2, including producing specific IgM, IgG, and IgA antibodies (29).

4. Diagnosis of coronaviruses based on nanoparticles

Due to the critical necessity of promptly diagnosing Covid-19, nanotechnology can lend itself to identifying or extracting SARS-CoV-2 (Table 1).

Table 1. Diagnostic methods based-nanoparticles for pathogenic coronaviruses

	Platform	Ligand	Target	Virus	Ref.
MNP-based viral RNA extraction	pcMNPs	Polycarboxyl groups	Viral RNA	SARS-CoV-2	(30)
	SMNPs	Probe (complementary to cDNA)	Target cDNA	SARS-CoV-2	(31)
NP-based detection	AuNP-based colorimetric assay	Thiolated ssDNA probe	Upstream of E protein gene and ORF 1a	MERS-CoV	(32)
	AuNP-modified carbon electrodes	Thiolated ssDNA probe	Target DNA	SARS-CoV-2	(33)
	Self-assembled star-shaped CAuNPs–QD	Virus-specific antibodies	Target virus	Avian influenza A, adenovirus, CoVs	(34)
	An array of AuNP-modified carbon electrodes	MERS-CoVID protein	Antibody	MERS-CoV	(35)
	SARS-CoV-2 antigens-AuNPs conjugates (Immunoassay strip)	SARS-CoV-2 antigens	IgG/IgM against SARS-CoV-2	SARS-CoV-2	(36)
	Antigens-AuNPs conjugates (Immunoassay strip)		IgG/IgM against SARS-CoV-2	SARS-CoV-2	(37)
	SFNPs	Probe (complementary to cDNA)	Target cDNA	SARS-CoV-2	(38)
	Streptavidin-AuNPs conjugates	Streptavidin	(FITC and biotin)-labeled RNA of MERS-CoV (N gene)	MERS-CoV	(39)

Magnetic nanoparticles can be involved in the separation of nucleic acids. For example, Zhao et al. (30) developed a one-step nucleic acid extraction technique using Magnetic nanoparticles modified with functionalized amines.

Gold nanoparticles are commonly used in color hybridization assays. One of these methods is the disulfide bond-based colorimetric method, designed by Kim et al. (40). An effective method for detecting SARS-Covid-like viruses involved utilizing specific hybridization of single-stranded DNA-gold nanoparticles and target DNA sequences (41). In addition, an electrochemical hybridization method based on gold nanoparticles using a gene sensor has been reported, including a thiol-stabilized DNA probe on a gold nanoparticle carbon electrode for the hybridization of SARS-CoV-2 biotinylated DNA (33). In addition, gold nanoparticles can be designed to detect specific antibodies to coronaviruses using electrochemical biosensors (35).

Beforehand, the identification of the N-gene of Mers-Covid was achieved through a combination of reverse transcription loop amplification method and visual detection technique called Vertical flow detection (VF) (39). As an experiment to improve the read signal, a combination of IgM and IgG detection is recommended, done using coating a strip with SARS-CoV-2 antigen-gold nanoparticles (42). This conjugate can produce a visible color line in 10 minutes (quality assay) (37). Baker et al. (43) reported the synthesis of polymerized gold nanoparticles stabilized with a polymer containing a sialic acid derivative and their interaction with the crown glycoprotein.

5. Nanoparticle-based vaccines

Nanoparticle-based techniques are employed to design nanovaccines to enhance vaccine effectiveness and optimize immunization methods. Nanovaccines are made by encapsulating coronavirus antigens or placing them on the surface of nanoparticles, and the nanoparticles produce a similar immune compound (44). Typically, the use of nanoparticles in vaccine formulations can serve three different purposes: (1) Boost the stability of antigens by safeguarding them from early deterioration caused by proteolytic enzymes, (2) augment their immunogenicity, and (3) focus on targeted delivery utilizing nanoparticles as a delivery system of antigens (45).

Nanoparticle-based vaccines offer potential benefits such as high payloads, adjustable size, adjustable surface properties, controlled drug release kinetics, and improved stability (46). Vaccines are made from live attenuated microorganisms or inactivated/killed pathogens (first-generation vaccines), synthetic peptides (second-generation vaccines), and DNA vaccines (third-generation vaccines) (47). Combining the vaccine with the adjuvant or delivery system must be safe, stable, and capable of inducing B and T cell responses with long-term memory (48). They also play an essential role in activating antigen-presenting cells (APCs), which may decide the viability of antibodies. Despite cytotoxic impacting nanoparticles (49), the risk is low compared to the benefits of vaccine delivery (50). The cellular uptake method depends on the nanoparticle size (51). Nanoparticles, such as gold, carbon, dendrimers, polymers, and liposomes, can trigger the production of cytokines and antibodies in the body (52, 53). An intriguing research found that introducing hollow pegylated liposomes resulted in the activation of the IgM response in a live model (54, 55). Altering the surface of nanoparticles using distinct targeting segments facilitates the delivery of antigens to particular receptors present on the cell surface and incites specific and focused immune reactions (56).

The constituents of nanoparticles employed for administering vaccines typically comprise an assortment of natural polymers, synthetic polymers, minerals, lipids, and other materials. Agents that enhance immune responses or regulate immune system activity and molecules activate and boost the immune system. The composition of nanomaterials impresses an essential role in how nanoparticles move, attach to cells, move within cells, and can break down and be accepted by biological systems (Table 2) (18). A technique involves the utilization of virus-like particles (VLPs), which are specially crafted nanoparticles that share comparable physicochemical features to viruses but do not possess any genetic material or the capacity to replicate (57). Vaccines are being created with a tactic similar to that of antiviral drugs, specifically targeting the SARS-CoV-2 S protein to prevent the virus from taking up the ACE2 receptor (58). Nanoparticles have the potential to be engineered in a way that triggers the cleavage of S protein, preventing it from binding to its intended target (59). Gold nanoparticles are frequently utilized in nanovaccinations because they serve as immunostimulants and carry antigens (60).

Ye et al. (61) assessed the effectiveness of graphene oxide and various derivatives as agents to combat viruses. The discovery was made that GO can disable viruses before they enter into cells by disrupting the normal coating and spikes of the virus, thus preventing infection.

Chen et al. (62) fabricated of silver and graphene oxide nanocomposites, subsequently evaluated for their effectiveness in combating feline coronaviruses

Table 2. Nanoparticle-based vaccines against coronaviruses

	Platform	Antigenic component	Virus	Ref.
Self-assembled NPs	Spike protein NPs	Spike protein	SARS-CoV-2, MERS-CoV	(69)
	Spike protein-displaying VLPs		MERS-CoV	(70)
	RBD-displaying VLPs	Gene of RBD of the spike protein	MERS-CoV	(71)
	Chaperna-based NPs		MERS-CoV	(72)
	Polypeptide NPs	HRC1 epitope of the spike protein	SARS-CoV-2	(73)
AuNPs	S-AuNPs	Spike protein of avian CoV	Avian CoV	(57)
	S-AuNPs	Spike protein	SARS-CoV-2	(74)

(FCoV). The GO sheets were found to have silver nanoparticles ranging in size from 5 to 25 nm. The cytotoxicity of the cells used was higher compared to GO and GO-Ag.

Park et al. (63) have developed a new solution for neutralizing viruses by creating a silver-coated magnetic hybrid colloid (Ag-MHC). With time, the effectiveness of this approach improved, resulting in superior outcomes for the 30 nm Ag - MHC system. In a similar image, Chromogira et al. (64) prepared three copies of silver nanoparticles for carbon coating, polyvinyl pyrrolidone coating, and bovine serum albumin-bound (to determine the effect of silver on a virus) HIV-1. Lara et al. (65) confirmed this interaction using silver nanoparticles coated with polyvinyl pyrrolidone. A complete study of silver nanoparticles as antiviral agents has been presented by Galdiro et al. (66). Lazchin et al. (67) proposed quantum dots of functionalized carbon as a treatment for human coronavirus HCoV-229 E.

Applying nanoparticles composed of nitric oxide can serve as a substitute for Covid-19 therapy. Apart from preventing reproducing viruses, NOx also can avert the commencement of inflammatory reactions instigated by hypoxia/ischemia-reperfusion (68).

Conclusion

The Covid-19 pandemic is a global crisis that has caused the loss of many human beings and caused severe social and economic damage and damage to the health sector of countries worldwide. Despite many efforts in various fields, a cure still needs to be found. Conversely, permanence has not been proven to cure this disease. Accordingly, studying the virus life cycle and host response would enable us to produce an effective nanovaccine. Based on this information, the present study expects to develop an effective therapeutic nanoparticle-based vaccine for current and future coronavirus pandemics. Due to the rapid transmission of viruses surpassing the pace of vaccine and drug advancements, it is crucial for vaccine research to build upon the progress made in combating the Coronavirus.

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Ethical statement

This study was approved by the Ethics Committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1400.073).

Conflicts of interest

The authors declare that there is no conflict of interest.

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