Hindawi
Journal of Nanomaterials
Volume 2022, Article ID 4568443, 13 pages
https://doi.org/10.1155/2022/4568443

Review Article

Nanomaterials and Bioactive Compounds against SARS-CoV-2

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Received 3 March 2022; Accepted 27 March 2022; Published 8 April 2022

Academic Editor: Palanivel Velmurugan

Presently, an outbreak of coronavirus is of global concern, as it causes various respiratory problems. It was first detected in December 2019 in China's Wuhan City where various patients got admitted to the hospitals with a symptom of pneumonia. As the number of cases increased, scientists isolated the samples from patients. Initially, it was named as a novel coronavirus (2019-nCoV) and now renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This virus spread from Wuhan to other cities of China, and currently it is affecting worldwide. Transmission of this virus occurs from one human to another and spreads through contaminated hands or surfaces. Various researchers are trying to explore the potential role of bioactive compounds from plants and different nanomaterials against this virus. Therefore, in this review, an overview of SARS-CoV-2, preventive measures against this viral infection, potential biocides against this virus, and role of phytochemicals and nanomaterials against this virus have been discussed.

1. Introduction

SARS-CoV-2 is one of the deadly viruses which has spread rapidly over the world with 455 million confirmed cases and 6 million deaths globally as per the reports of the world health organization (WHO) [1]. The chronology of the events of this pandemic began in December 2019 when it was first detected in Wuhan, China. Several patients were admitted to the hospitals with pneumonia symptoms. In a very short period, the number of cases increases drastically. Considering the global threat, the WHO declared it a "Public Health Emergency of International Concern." Coronaviruses belong to the subfamily *Orthocoronavirinae*, and within the *Orthocoronavirinae* subfamily, there are four genera: alpha coronavirus, beta coronavirus, gamma coronavirus, and delta coronavirus [2]. These viruses are a group of enveloped viruses with single-stranded RNA genomes with size ranging from 26 kb to 32 kb. Both α- and β-coronavirus genera are known to infect mammals, while gamma and delta coronavirus infects birds. They are mainly able to cause enzootic infections and infect various vertebrates such as chickens, pigs, and birds [2].

In the last two decades, along with two other severely pathogenic human viruses, namely, the severe acute respiratory syndrome (SARS) coronavirus and the Middle East respiratory syndrome (MERS) coronavirus [3], SARS-CoV-2 is the third one that causes severe health problems and deaths worldwide. SARS-CoV-2 is a β-coronavirus and belongs to the *Orthocoronavirinae* subfamily [4]. Based on available data on its pathogenicity, it shows 3% pathogenicity, which is comparatively lower than the SARS coronavirus (10%) and the MERS coronavirus (40%) [5], but the transmissibility is quite high compared to the other two types. This virus has been transmitted from one person to another [6]. In most cases, symptoms include cough, fever, and myalgia or fatigue. Coronaviruses can be transmitted from

contaminated surfaces, self-inoculation of the mucous membranes of the eyes, nose, or mouth [7]. There is a crucial requirement for fast diagnostics, vaccines, and therapeutics to detect and prevent this disease. Worldwide, various disinfection (primarily in healthcare) has been used as biocides, including alcohols, hydrogen peroxide, sodium hypochlorite, and benzalkonium chloride [8]. Currently, various bioactive compounds from plants have been researched against SARS-CoV-2. Similarly, nanomaterials are another substances that have been used as a potential agent against this virus. The present review provides an overview of available information on coronavirus, evidence of various biocides, the role of various phytochemicals, and role of various nanoparticles that can be used against this virus.

2. Taxonomy and Structure

Coronaviruses are belonging to the Coronaviridae family with the subfamily of *Orthocoronavirinae* in the order of Nidovirales [9] (Figure 1). Coronavirinae is further divided into four genera: alpha, beta, gamma, and delta coronavirus [10]. MERS-CoV and SARS-CoV belongs to the β-coronavirus family [11]. The sequence analysis exhibited that SARS-CoV-2 showed a characteristic genome structure of coronavirus and belonged to the β-coronaviruses genera [6]. It has more than 82% similarity with SARS-CoV [12]. The genome size of SARS-CoV-2 is 30 kb, which encodes for an open reading frame of 1a/b, large nonstructural polyprotein, four structural proteins, and five accessory proteins.

Four structural proteins contain spike surface where envelope protein, glycoprotein, membrane protein, and nucleocapsid protein are present that are important for the virus assembly and infection. The surface glycoproteins play an important role in the attachment of this virus to host cells and can also be cleaved by proteases present in the host into an N-terminal S1 subunit and a membrane-bound C-terminal S2 region. The binding of subunit 1 to the host receptor can disrupt the prefusion trimer, leading to the shedding of subunit 1 and conversion to another subunit 2 which is a very stable conformation after fusion. To involve a host receptor, the subunit (S1) has a receptor-binding domain that undergoes hinge-like conformational movements, which quickly hide or expose the determinants of receptor binding. Understanding the structure and function of spike protein can help in the design and development of monoclonal antibodies and vaccines.

2.1. Symptoms of SARS-CoV-2. The symptoms of SARS-CoV-2 include sore throat, runny nose, fever, cough, and difficulty in breathing. Initially, it was thought that the viral incubation period was 14 days; however, several cases have also come up with a shorter incubation period. Guan et al. [13] conducted a study, where the average incubation period was four days in a lower interquartile range of two days and an upper interquartile range of seven days. They observed that during hospital admission, 43.8% of patients suffer from fever and 88.7% developed it through hospitalization where cough was found as a common symptom. Wu and McGoogan [14] reported that in the age group of 30-79 years, there were confirmed cases of 87% where the mortality and fatality rate increased with growing ages, that is, 8% and 15% fatality rate in the age group 70-79 years and 80 years or older, respectively. Cai et al. [15] performed a study in which 10 children were observed for coronavirus and found that 80% had a fever while 60% had a cough and they all showed mild symptoms but recovered. It was found that even in the recovery stage, children had prolonged virus shedding in the feces and respiratory tract. Wei et al. [16] studied nine infected infants belonging to the age group of 1-11 months, and they found out of nine, four infants showed feverish symptoms, one infant did not show any symptom but tested positive, and no one required any mechanical ventilation.

2.2. Coronavirus Presence on Non-living Surfaces. From the literature survey, it was found that in the case of human coronavirus strain (HCV) 229E, it remains infectious in various materials from 2 hours to 9 days [7]. High temperatures like 30-40 °C can reduce the persistence of MERS-CoV, transmissible gastroenteritis virus, and mouse hepatitis virus. However, at a low temperature such as 4 °C, the persistence of mouse hepatitis virus and transmissible gastroenteritis virus increases to 28 days. Ijaz et al. [17] reported that at room temperature, HCoV-229E persists better at 50% compared to 30% relative humidity. Duan et al. [18] reported that the presence of SARS-CoV on a metal surface at room temperature was for five days, whereas in the case of paper, it was 4-5 days, and correspondingly the P9 strain was isolated. In the case of wood and glass surfaces, the presence was for four days at room temperature, and the same strain was isolated [18]. A study reported the presence of SARS-CoV on the surface of disposable gown, where the presence of virus was for two days at room temperature and the GVU6109 strain was isolated [19]. Chan et al. [20] reported the presence of SARS-CoV on the plastic surface that remains for less than five days at 22-25 °C and isolated was strain HKU39849. Warnes et al. [21] reported the presence of human coronavirus strain 229E at 21 °C on the surface of ceramic, Teflon, PVC, silicon rubber, surgical glove, plastic, glass, and steel for 5 days.

2.3. Potential Biocides for Coronaviruses Inactivation. The presence of human coronaviruses on nonliving surfaces at room temperature can be infectious. More than 30 °C temperature can be a shorter viral persistence. Frequent contamination on surfaces in healthcare is a probable source of viral transmission. According to WHO, proper cleaning and disinfection measures has to be followed inconsistently. Thoroughly surfaces cleaning with water and detergent and the use of commonly hospital-level disinfectants are effective and sufficient procedures (WHO). Various chemicals/solvents are utilized as a disinfectant such as ethanol (70-95%), formaldehyde (0.7-1%), and 2-propanol (70-100%). These disinfectant solvents can easily able to inactivate the viral infectivity. In a study, it was reported that 70% of ethanol was able to inactivate the mouse hepatitis virus after 10 min of exposure and the viral infectivity reduction (log10) was more than 3.9 [22]. Rabenau et al. [23] reported that after 30 seconds of exposure to 85% and 95% ethanol,

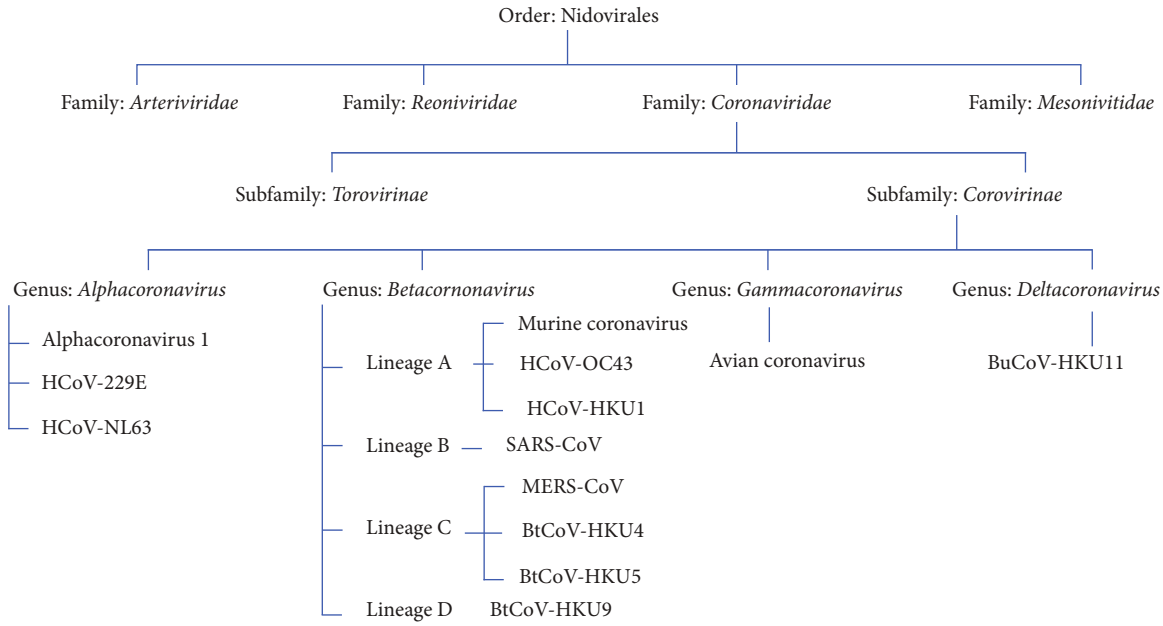

Figure 1: Taxonomy of human coronavirus [2].

SARS-CoV was inactivated, and the reduction in viral infectivity was greater than 5.5, while 80% ethanol was able to inactivate the Middle East respiratory syndrome-CoV, and the reduction in viral infectivity was greater than 4 [24]. Rabenau et al. [23] also reported that a combination of 2-propanol and 1-propanol benzalkonium chloride at 45% and 30% was able to inactivate SARS-CoV with 30-sec exposure and reduced viral infectivity greater than 4.3. A study reported that exposure of 70% and 100% 2-propanol for 30 seconds was able to inactivate SARS-CoV with a reduction in viral infectivity greater than 3.3 [23]. Rabenau et al. [25] reported that 0.7% and 1% formaldehyde exposure for 2 min can inactivate SARS-CoV with viral infectivity reduction of more than 3. Dellanno et al. [26] reported that 0.21% sodium hypochlorite exposure for 30 sec was able to inactivate the mouse hepatitis virus with 30-sec exposure and viral infectivity reduction more than 4. Omidbakhsh and Sattar [27] reported that 0.5% hydrogen peroxide was able to inactivate the human coronavirus strain 229E after 1 min of exposure and a reduction in viral infectivity reduction more than 4. Kariwa et al. [28] reported that 2.5% glutardialdehyde exposure for 5 mins can inactivate SARS-CoV with viral infectivity reduction of more than 4. A report suggested that 0.009% of formaldehyde exposure for 24 h hours can inactivate canine coronavirus and viral infectivity reduction more than 4 [29]. Hulkower et al. [30] reported that 70% ethanol, 0.55% ortho-phtalaldehyde, and 0.06% of sodium hypochlorite exposure for 1 min can inactivate transmissible gastroenteritis virus with viral infectivity reduction of 3.2, 2.3, and 0.4, respectively. They also suggested that at the same concentration and exposure time, mouse hepatitis virus was inactivated with viral infectivity reduction of 3.9, 1.7, and 0.6, respectively. Eggers et al. [31] reported that 15-sec exposure of 1%, 4%, and 7.5% of povidone-iodine can inactivate MERS-CoV with viral infectivity reduction of 4.3, 5, and 4.6, respectively. Siddharta et al. [24] reported that exposure to 75% 2-propanol for 30 s was able to inactivate SARS-CoV and MERS-CoV with a reduction in viral infectivity of more than 4. Eggers et al. [32] reported that 15 sec exposures of 0.23% of povidone-iodine can inactivate MERS-CoV and SARS-CoV with viral infectivity reduction of more than 4.4.

2.4. Phytochemicals for Possible Treatment of SARS-CoV-2. The absence of standard therapeutic options for COVID-19, such as vaccines and antibiotics, has led to supportive therapies that involve the use of natural agents. Extracts derived from bioactive or natural products play a vital role in the fight against coronavirus. Various studies have shown the involvement of different phytochemicals against COVID-19. Some of the observations like the use of Chinese qing fei paidu decoction (QPD) suggested how its preparation alleviates immune response as well as decreases the inflammation generated by the virus. Apart from this, traditional Chinese medicine also plays a role since its natural composition contains bioactive compounds which reduce the signs for COVID-19 via inhibiting inflammatory agents and reviving the body for the damage caused [33]. According to a trial by Chojnacka et al. [34], approximately seventeen prospective SARS-CoV-2 Mpro inhibitors were recognized. These Mpro inhibitors were assigned to the compounds belonging to pseudo-peptides, floronates, and flavonoids. One of the potential inhibitors for the virus is the phloroglucinol (1,3,5-trihydroxybenzene) oligomers isolated from *Sargassum spinuligerum*. Besides this, another active inhibitor for SARS-CoV-2 are composites of the phlorotannin group (8,8′-bieckol, 6,6′-bieckol, dieckol) extracted from *Ecklonia cava*. These examples show that plant-derived compounds that could be extracted could be a potential origin of the SARS-CoV-2 Mpro inhibitor and

therefore repress the generation of SARS-CoV-2 [35]. Recently, it has been indicated that traditionally used Chinese medicine may be an efficient alternative to interception [36] and treatment [37], even though clinical trials are poorly designed and treatment options are largely practical. Ling et al. [38] pointed out the effective use of these traditional medications as an alternative drug candidate based on their antiviral activity. Some of the other illustrations by Pang et al. [39] on therapies for this virus involved natural-based therapeutics but did not inspect the bioactive compounds or even their action mechanisms. Zhang et al. [40] also virtually showed 115 compounds of the same origin as mentioned in the previous study, highlighting 13 of them for further examination. Many of these were naturally derived polyphenols such as quercetin and kaempferol, which are already considered as a promising treatment alternative for additional types of disease [41–43]. Lianhuaqingwen, a Chinese traditional medicine comprising a fusion of different plant species, displayed antiviral activity, but its EC50 was very high (approximately 411 μg/mL) as compared to redesivir (a commercial drug used for COVID-19) with an EC50 of 0.39 μg/mL via using similar assay [44].

Polyphenols are a group of compounds demonstrating antiviral activity according to various studies. Quercetin has an IC50 of around $8.6 \pm 3.2\,\mu$M [45]. Structurally similar polyphenols like myricetin and scutellarein show inhibitory levels against SARS-CoV-2 helicase [46]. Bioassay-based dissolution of an ethanolic extract isolated from the seeds of *Psoralea corylifolia* plant has also been recognized as compounds causing inhibitory pursuits in opposition to the virus [47]. In addition to this, six phytochemicals phenol-based phytochemicals were extracted from ethanolic extracts, namely, bavachinin, corylifolia, neobavaisoflavone, psoralidin, isobavachalcone isobavachalcone, and 4′-O-methylbavachalcone along with their antiviral activity (around IC50 values ranging from 4.2 to 38.4 μM). Compounds psoralidin, as well as isobavachalcone, displayed the highest antiviral activity out of these, with both of them being assorted and reversible PLpro inhibitors via a type I mechanism (that is, preferential binding with a free enzyme instead of enzyme-substrate complex) [48]. Plant lectins are the proteins that can bind with carbohydrate groups, specifically as well as reversibly [49] and might SARS-CoV. They have been proven to show antiviral properties against viruses such as influenza, herpes simplex virus [50], and the Ebola virus [51, 52]. Keyaerts et al. [53] conducted a study that involved screening of the activity of plant lectin lectin (total 33) against SARS-CoV-2 using a cytopathicity assay (CPE) with the observation of EC50 values around $0.45 \pm 0.08\,\mu$g/mL for *Lycoris radiata* agglutinin.

Other lectins also demonstrated good tolerability, according to clinical trials [54], proving to be one of the promising classes of bioactive compounds for SARS-CoV-2 treatment. Tryptanthrin (with EC5 around 0.06 μM), as well as indigodole B (with EC50 around 2.09 μM), displayed high virucidal activity against HCoV-NL63. Since the spike protein of HCoV-NL63 aims at the ACE2 receptor, it shows a similar conserved sequence and similarity in structure of SARS-CoV-2 [55]. Another crucial vine namely *T. crispa* was studied for finding out their bioactive properties. Its methanol extract led to the extraction of various compounds in silico, which were potent enough to alter the activity of the SARS-CoV-2 Mpro enzyme. The investigation further indicated phytocompounds of this methanolic extract such as benzeneethanamine, imidazolidin-4-ne, a derivative of TMS, (-)-globulol, androstan-17-one, camphenol, and 3-ethyl-3-hydroxy-(5 alpha) which have a finer binding capacity with SARS-CoV-2 Mpro compared to nelfinavir and also lopinavir [56]. In recent years, the AYUSH Ministry also highlighted the importance of developing drugs from natural compounds, including ayurvedic medicinal plants for COVID-19 treatment. Using different studies, few of these compounds have successfully shown a good binding affinity in opposition to the SARS-CoV-19 protease (6 LU7). These phytochemicals comprise diosmin, punicalin, naringin, and oleanolic acid [57]. Punicalin is generally present in edible plants such as *Punica granatum* (pomegranate) and *Combretum glutinosum*, *glutinosum*, as well as *Terminalia catappa*, used to treat dermatitis along with hepatitis [58]. It has played a role in the treatment of several other complications too like parasitic infections, microbial infections, diarrhea, respiratory problems, and hemorrhage [59]. Oleanolic acid is derived from *Olea europaea*, *Phoradendron juniperinum* (whole plant), *Rosa woodsii* (leaves), and *Prosopis glandulosa* (leaves and twigs) [60]. It exhibits antiviral, hepatoprotective, and antitumor properties [61]. Naringin is a flavone glycoside present in grapes as well as citrus fruits. It is also an antiinflammatory, antineoplastic, and blood lipid-lowering agent [62]. Diosmin, present in pericarp of citrus fruits, is a natural flavone that behaves as an antiulcer, antioxidant, antimutagenic, antihyperglycemic, and antiinflammatory agent [63]. In general, four of such compounds are also known for several therapeutic and medicinal characteristics, thus having the potential to act against SARS-CoV-19 through interaction with its prime protease. Another crucial natural product, honey, has been investigated and utilized as a potential treatment option and alternative medicine [64]. It has various properties such as being an antioxidant, antiviral, antiinflammatory, antitumor, antibacterial, antifungal, antimutagenic, and antidiabetic agent [64]. Even though there exists a variety of chemical compositions for honey, mostly found flavonoids included apigenin, pinobanksin, quercetin, pinocembrin, luteolin, genistein, chrysin, galangin, and kaempferol, while phenolic acids found comprised gallic acid, caffeic acid, chlorogenic acid, p-hydroxybenzoic acid, syringic acid, p-coumaric acid, and vanillic acid [65]. Both hesperidin and rosmarinic acid derived from plants have been proven to be present in honey and inhibit SARS-CoV-2 3CLpro according to a study involving computational data [66]. As a result, the consumption of honey helps in decreasing the SARS-CoV-2 severity, either directly by noting the antiviral properties or indirectly via boosting the immune responses.

3. Role of Nanomaterials in SARS-CoV-2

The emerging techniques that are based on nanotechnology can be used for the detection, prevention, and treatment of numerous viruses/viral infections. Various types of

nanoparticles (NPs) and nanomaterials (NMs) exhibit potential effects to detect, prevent, and kill SARS-CoV-2 virus (Figure 2). Further, NPs and NMs are preferred due to their biocompatible, safe, and nontoxic properties. Therefore, different types of NMs and NPs have been used for their applications in the development of vaccines against SARS-CoV-2: biosensors, facemasks, personal protective equipment, antiviral coating, drug delivery, and airborne virus filtration.

3.1. Carbon-Based Nanomaterials. There is not enough evidence that supports the applications of carbon-based NMs to fight against the SARS-CoV-2, but their commendable antiviral and physicochemical properties have an effective role against the virus. Carbon-based nanomaterials include fullerenes, graphene and graphene oxide, carbon nanotubes, and carbon quantum dots, which demonstrate excellent characteristics such as antimicrobial and antiviral effects and the detection of pathogens; therefore, they are considered ideal to fight against SARS-CoV-2. They also exhibit various applications for diagnosis in biosensors, filtration of the airborne virus, drug delivery, and antiviral coating [67].

3.2. Graphene and Graphene Oxide. Graphene and graphene oxide NMs containing two dimensions have been widely considered because of their antiviral and antimicrobial characteristics. Graphical sheets conjugated with antibodies can easily detect viral-targeted proteins and can also provide a great option for the diagnosis in a significant population and effectively improve filters and sensors [68]. Apart from this, the functionalized graphene demonstrated an acceptable capture capability of the virus when combined with light or heat-mediated inactivation, and, therefore, they are also utilized as disinfectants. Graphene sensors can be utilized for effective drug screening and conventional textile utility. There is an existence of biosensing techniques that can employ the antibodies to specifically detect the infection. Additionally, the field-effect transistors (FET) based on graphene act as potable sensors that have been developed to evaluate the viral load of SARS-CoV-2 through the nasopharyngeal samples, by employing the specific antibodies against the viral spike protein [69]. The immobilization using the FET technology of the SARS-CoV-2 spike antibody was done by its conjugation on the graphene sheets, using an interfacing substance as a probe linker. Using the antigen protein of the infected person, the cultural virus, and the nasopharyngeal samples, the FET device detects SARS-CoV-2 by analyzing its performance and therefore is an excellent biosensing technology [67].

3.3. Carbon Nanotubes (CNTs). Recently, CTs with dimensions of 10-100 nanometers exhibit significant conversion capability of light heat and possess antimicrobial and antiviral functions, which makes them useful for extensive application in biomedical and biological fields, and CNTs are also preferred due to their flexibility, large surface-volume ratio, ability to synthesize ROS (reactive oxygen species), small pore size, clinical compatibility with numerous drugs, slight density, enormous mechanical strength, and resistance to respiratory droplets and acids and bases [70]. The CNTs also demonstrate extraordinary characteristics such as effective rate of bio-absorption, large surface-area, targeted biomolecule alteration capability, significant biocompatibility, multienergy surface/tube chemical functional group capability, and extensive space for storage and provide effective permeability of biological barriers, etc., which ultimately leads to the new scope of solutions for SARS-CoV-2. Apart from this, they also have various applications as an inactivation substance of the virus, diagnosis process and filtration [71] [72], detection, and capturing of the viruses and viral proteins [73–78] and act as an anti-HIV substance [73, 74].

4. Quantum Dots (QDs)

QDs have a diameter of 1-10 nanometers and act as semiconductor NPs. They have a tunable optical wavelength that when combined with high fluorescent probes becomes a major aspect to determine the long-term fluorescence imaging of various cellular activities [79, 80]. Quantum dots as novel NPs, in addition to being used as fluorescent probes for cellular and molecular imaging, are also used as interceptor agents to restrict the entrance and interactive activities of SARS-CoV-2 with the plasma membrane of the host [81]. Hence, the materials of quantum dots possess an effective capability to deactivate the viral agents by interacting with the viral S-proteins and inhibit the RNA replication of the virus and the utilization of the fluorescent probes.

4.1. Carbon Quantum Dots (CQDs). They are predominantly used as imaging probes such as biosensors and chemosensors; possess antiviral effects; have various applications like detecting infections, biological agents, and microorganisms; and are also used in the biocompatible deactivation process for infectious SARS-CoV-2. The CQDs have a dimension of 10 nanometers and exhibit a high water solubility, and for the synthesis of the carbon precursors, the CQDs were fabricated by hydrothermal carbonization. Thus, various novel approaches are being designed to detect the SARS-CoV-2 by using CQDs. Łoczechin et al. (2019) studied the antiviral characteristics of the 7 kinds of carbon quantum dots that were utilized for the prevention of contagious SARS-CoV-2 virus. They synthesized several categories of CQDs by hydrothermal conjugation and carbonization of the boronic acid. It was demonstrated that the virus was inhibited due to the interaction between the functional groups of the carbon quantum dots and the viral receptors [82]. A positive charge that is present on the surface of CQDs deactivates the viral spike protein and then interacts with the viral RNA (negative) [83, 84].

4.2. Zirconium Quantum Dots. Zirconium is a transition metal element that is nontoxic and is widely utilized in numerous biomedical applications due to its characteristics like mechanical strength, thermal stability, and capturing of ultraviolet light. Apart from its nanosize, Zirconium possesses unique chemical-physical properties because of its restriction to electronic states as compared to bulk

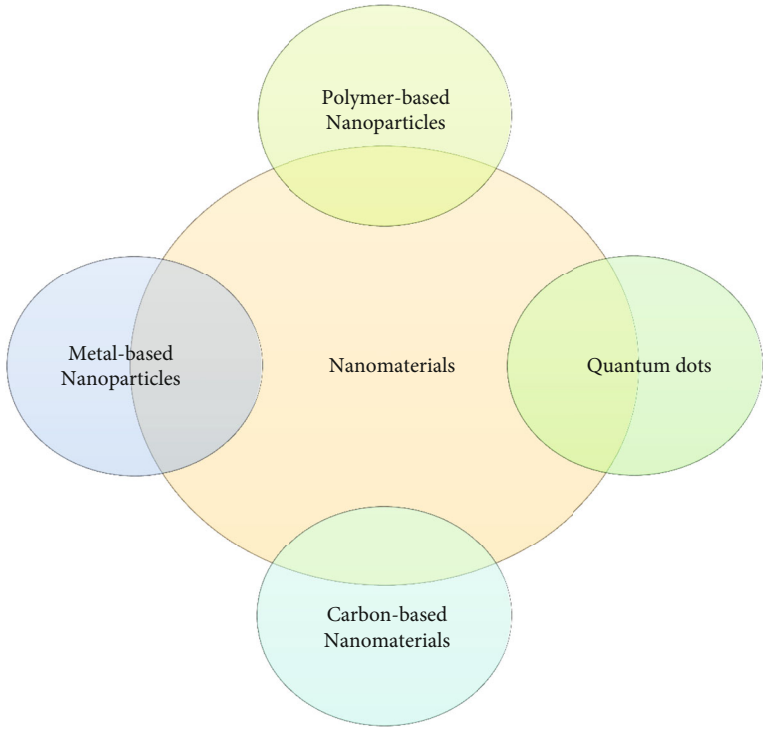

Figure 2: Different nanoparticles used for SARS-CoV-2.

substances and large surface area [78, 85–87]. Ahmed et al. utilized the zirconium quantum dots' magnetoplasmonic nanoparticles to research the detection of the IBV (infectious bronchitis virus). They also described a single-step process of the fabrication of the zirconium quantum dots from the zirconium NP by an autoclave [88]. As per the experimental inference, the zirconium quantum dots demonstrate the emission of blue fluorescence during the biosensing of the IBV. The conjugated antibody-magnetoplasmonic nanoparticles and the antibody-zirconium quantum dots were distinctly noticeable when there was an addition of infections. Now, the antibody-magnetoplasmonic nanoparticles and the antibody-zirconium quantum dots were linked together and a zirconium quantum dot- magnetoplasmonic nanoparticle nanocomposite was synthesized to transport the infections/viral agents, and consecutively, the composite was detached by utilizing an external magnet [89]. In another research, a rapid detection biosensor was developed based on antibody-functionalized MoS2, to detect the IBV [90].

5. Metal-Based Nanoparticles

The metal-based NPs are the most important and widely used since it exhibits numerous applications in the biomedical field and also due to their capability for effective drug delivery and stimulating the responsive characteristics and abilities of several substances (like gold or magnetic NPs) that are observed after the in vivo organization to the human body utilizing safe medical imaging [91]. The nanoparticles based on metals are extensively researched during the preclinical and clinical studies for detection, diagnosis, and prevention of various infections, but there is also an emergence of safety concerns associated with their clinical uses [92]. To overcome these challenges, various other types of metal-based NPs along with biocompatible compounds are widely examined due to their nontoxic characteristics.

5.1. Gold Nanoparticles (Au NPs). They have gained profound recognition in the development of vaccines due to their convenient ability to stimulate the immune system by using the antigen introducing cells [93]. Apart from this, the Au NPs can activate the T-killer (CD8+) cell-mediated immune response by intranasal delivery which then gets diffused in the lymph nodes [94]. Furthermore, due to the high atomic number of Au NP, it demonstrates high biocompatibility and stability and can be used as a contrast substance for clinical imaging based on X-rays, specifically computed tomography (CT) [95]. By utilizing the electrocatalytic properties of gold nanoparticles' hydrogen evolution, the diagnosis of disease cells is being researched [96]. This biosensor functions by recognizing the interactions of the host cells' surface proteins with specific antibodies, using Au NPs. The same technique can be employed for the diagnosis of the virus by using the identified antigens and obtained antibodies.

5.2. Iron Oxide and Ferrite-Based Nanoparticles. Earlier, the USFDA (US Food and Drug Administration) has approved the use of iron oxide NPs as biocompatible substances for the treatment of anemia, and recently, there have been various studies that have demonstrated the antiviral properties of iron oxide NMs in vitro. There have been several reports about the antiviral characteristics of these NMs [97, 98] [99]. It has been also reported that the antiviral characteristics of

the iron oxide NPs have been examined to eliminate several viruses like that of rotavirus [100], influenza virus (H1N1) [101], and dengue virus [102]. As per the investigations, it is hypothesized that the antiviral function of the iron oxide NPs is because of its interaction with the surface proteins of the virus and prevention of the binding and entry of the viral agents into the cells of the host, leading to neutralization. As a result, the iron oxide NPs can be employed as a safe and appropriate remedy for the rapid diagnosis and the prevention of the COVID-19 virus in infected individuals.

5.3. Copper Nanoparticles. As per the report on CoV-229E in 2015, it has been observed that copper (Cu) can effectively decrease the effects of the virus in a very less amount of time [103]. The amalgamation of at least 70% of Cu and brass was found to be significantly effective for viral inactivation. The amount of copper determined the rate of inactivation [104]. The combination can be different to alter the antimicrobial characteristics using the nanostructures of metal species to act against SARS-CoV-2 [21, 105]. The utilization of copper salt and solutions can lead to antiviral effects [106–110]. Thus, this can be used for making the materials if personal protective equipment (PPE), such as copper ions, can lead to the elimination of the viral agents present on the PPEs. Generally, the metal ions reduce the effects of SARS-CoV-2 on these substrates. Presently, copper/cubic brasses can be used for surface treatment. Therefore, the inactivation of the virus is determined by the release of ionic metal [111, 112].

5.4. Silver Nanoparticles (Ag NPs). The antiviral characteristics of the Ag NPs are widely known, because of their ability to restrict the entry of the virus into the host cells. The interaction of the viral genome with the metal caused the inhibition of the replication of the virus [113]. The Au NPs when covered with the Ag NPs were able to combine with the gp120 glycoprotein present in the envelope of the HIV and thus caused the viral inhibition [114, 115]. Interaction with the virus, which was dependent on size, was studied [52]. Through numerous mechanisms, the functionalized silver nanoparticles demonstrated the ability to inhibit viral infection [116, 117]. It has been observed that the particles that are relatively smaller in size could easily reach the cell membrane, therefore causing the inhibition of the replication of the virus [118], such as the utilization of the Ag ions along with the nanotitanium dioxide that was studied for their significant MIC (minimal inhibitory concentration) [119].

5.5. Zinc Nanoparticles (Zn NPs). Zn NPs exhibit effective antiviral characteristics as well as immune-modulatory activities [120]. But the effect or use of Zn against SARS-CoV-2 has not been reported yet. The Zn ionophore pyrithione, when combined with Zn +2 ions, was also observed to inhibit viral replication [121], suggesting that Zn ions can be used as an antiviral substance. It was observed that chloroquine was used as an antiviral for the treatment of COVID-19 [122]. However, more evidence and research are needed to understand the antiviral mechanism [123].

5.6. Titanium Dioxide Nanoparticle (TiO2 NP). It has been observed that the photolytic NP was able to inactivate the SARS-CoV-2 virus and TiO2 is one of the well-known ones. The NM is less toxic, inert, and does not undergo photo corrosion when irradiated with ultraviolet light [124]. The photocatalysis of TiO2 can aid in the viral deactivation by the decontamination of the surface utilizing paint, air treatment system, aerosol, and water, containing these materials to fight against the SARS-CoV-2. The photolytic mechanism is widely known and discussed as the excitation of an electron from the VB (valence band) to the CB (conduction band) that causes the initiation reaction to release reactive oxygen species such as hydroxyl radical and superoxide anion [125]. The disinfecting property of TiO2 is achieved by the presence of hydroxyl radicals due to the oxidation of the H2O molecule [125].

6. Polymer-Based Nanoparticles

The NPs that are based on polymers include natural and synthetic polymers which exhibit noteworthy properties like effective biocompatibility, tunable characteristics, and easy synthetic protocols and, therefore, are extensively used in the field of biomedical sciences [126–128]. Such types of NMs are widely utilized due to their safe characteristics in clinical applications such as in vivo delivery, viral delivery system, and the release of controlled viral vaccines [126, 127, 129]. The vaccines for the viral infection can be administered in the form of protein, mRNA, or DNA [130], and once it enters the systemic circulation, they enzymatically get degraded [131, 132].

6.1. Synthetics Polymer Nanoparticles. The NPs that are based on synthetic polymers exhibit the ability to alter their characteristics and activities as per the suitability of the delivery system. PLGA (polylactic-co-glycolic acid) is one of the well-known polymers of this type that has been ratified by the FDA due to its extraordinary properties of biodegradation and biocompatibility [133]. Zhao et al. researched the fabrication of poly (amino ester) together with carboxyl groups of pcM NP (PC-coated magnetic NPs) and synthesized the viral RNA extraction technology based on pcM NP [134]. Therefore, this easy and single-step process is based on binding steps and lysis that releases a complex of pcM NPs-RNA that is incorporated into the consequent reactions of RT-PCR. This procedure involved purification of the viral RNA in just twenty minutes using the automated high-throughput or easy manual method. This new, easy, and extremely efficient technology for the extraction of the viral RNA can significantly reduce the operational requirements of the existing molecular identification of the COVID-19 virus and also the turnaround time, specifically for the rapid clinical detection. Apart from this, the NPs of polymer are also utilized for the fabrication of the protective facemasks. Liu et al. created a novel self-powered electrostatic adsorption facemask based on the triboelectric nanogenerator and the poly (vinylidene fluoride) electrospun nanofiber film that can efficiently remove

99.2% of particulates and is better than other types of masks [135].

6.2. Nanocellulose. The NMs that are based on cellulose can be utilized for protection from SARS-CoV-2 in numerous ways like personal hygiene paper and paper-based medical products like a paper electrode, biosensors, filtration, biological tests, adsorption, and paper-based microfluidic chips [136]. Johnson et al. designed a model for 3D thermoplastic printing of NaCl coated facemasks or biocellulose or clay impregnated with NaCl to synthesize a purified deactivated surface that can further prevent the spread of SARS-CoV-2 [137].

6.3. Chitosan Nanoparticles. Chitosan is one of the well-known and second most used NPs based on natural polymers with the ability to alter into the required shape and size and is extensively utilized in the biomedical field [138, 139]. The controlled release of chitosan NPs enhances the stability and solubility of the drugs, reduces the toxic effects of the NPs, and improves its effectiveness [140, 141]. One of the most significant advancements in DNA-based vaccine technology is the use of chitosan NPs for delivery, which have proven to be an efficient means of preventing DNA vaccine destruction while also allowing bonding to the negative charge of DNA due to their cationic nature [142]. Based on extensive research, it was investigated that the administration of the plasmid DNA coding for the nucleocapsid SARS-CoV-2 incorporated into the chitosan NPs and administered through the nasal route demonstrated significantly positive outcomes [143, 144].

6.4. Lipid Nanoparticles (LNPs). LNPs are approved by the USFDA since they are clinically advanced and are used for the significant delivery of nucleic acid [145]. Apart from this, lipid nanoparticles act as efficient delivery systems of mRNA. These NPs are made of many constituents of lipids such as phospholipids, PEG lipid, ionizable amine lipid, and cholesterol, out of which ionizable amine lipids possess a major function in the endosomal release of nucleic acid. Various researches have been conducted to test the mRNA-based vaccine technology that is enclosed in lipid NPs for numerous infections like rabies, zika virus, HIV, influenza, and currently SARS-CoV-2 [146–150]. According to the findings of this study, these NPs can be used in mRNA vaccines based on lipid nanoparticles, against COVID-19.

7. Conclusions

Many potential developments in pharmaceutical interventions for SARS-CoV-2 are going on. Researchers are turning to nanotechnology instead of traditional approaches to combat SARS-CoV-2 due to the global demand for effective and remarkable strategies. Nanomaterials with antiviral characteristics play an important role in coating materials such as facemasks and medical equipment. NMs in biosensors provide several advantages, including improved detection capabilities, safety, simplicity of design, dependability, and low cost. Using NMs in facemasks, textiles, and filters, such as metal-based, carbon-based, and polymer-based NPs, has numerous benefits that not only reduce the risk of transmission, but also make the facemask, textile, and filters reusable. Furthermore, NPs such as polymer-based nanoparticles, carbon nanotubes, graphene and graphene oxide, quantum dots, iron oxide, and gold nanoparticles effectively enhance the functioning of the biosensors for identifying the SARS-CoV-2 virus, since they have previously demonstrated their ability to detect other viruses. Nanomedicine can drastically increase (or facilitate) a drug's or vaccine's effectiveness and safety. Lipid NPs are biodegradable and biocompatible, and there have been few reports of immunological reactions. Although metal-based and polymer-based NPs degrade more slowly than other types of nanoparticles, they may be advantageous based on the condition being cured and the medicine being administered. Furthermore, the nontoxicity and the large surface area-volume ratio of NMs utilized in nanomedicine are the most notable characteristics, allowing for significantly effective medication packaging. More research is required on the biocompatibility, and safety of NPs in living cells is required. In a nutshell, DNA and mRNA-based vaccinations would be ineffective without nanoparticles. Existing nanoparticles, lipid, and chitosan NPs are among the numerous types of nanoparticles used in vaccine research. As a result, the COVID-19 can be effectively managed in the community and environment by using nanomaterials.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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