Tackling COVID-19 pandemic through nanocoatings: Confront and exactitude

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ABSTRACT

After the eruption of the most deadly influenza flu pandemic in 1918, also known as Spanish flu, infected about 500 million people with a death toll of approximately 50 million globally, the second most devastating pandemic flu emerged in December 2019 at Wuhan (Hubei Province) of China. This viral disease caused by a novel coronavirus SARS-COV-2 was named COVID-19 by World Health Organization (WHO). The COVID-19 virus affected 213 countries globally with 5.6 million cases and 353,373 deaths as of May 28, 2020 [1] Fig. 1. Still, there is no promising solution known to tackle this severe epidemic disease worldwide. For protecting the global population from COVID-19, we must follow three steps – early detection, monitoring, and treatment. At the same time, it is important to follow WHO guidelines on preventive measures. Many countries have restricted the movement of people completely and lockdown was enforced to maintain social distancing. But lockdown alone is insufficient to prevent resurgence, can upend economies and roil society. People need to step out to perform essential tasks and may get exposed to this deadly virus. Learnings from previous outbreaks suggest the usage of nanotechnology as an important avenue to develop antiviral drugs and materials. So, to effectively minimize the acquired infection of COVID-19 in public places like hospitals, transport, schools, worship places, stores, malls, etc. Antimicrobial nanocoatings at these places and development of targeted antiviral drugs through capped nanoparticles will be a major effective option to tackle the spread of this disease.

1. Introduction

Viruses are submicroscopic infectious entities that multiply only inside the cell of macro and micro-organisms. They contain genetic materials DNA or RNA, capsid proteins that encircle nucleic acids, and an outer lipid envelope. Based on the presence/absence of lipid envelope, they are grouped into enveloped and non-enveloped viruses, respectively. The most common human pathogenic viruses like Dengue, Hepatitis C and B, Yellow fever, Influenza, Measles, Zika, Respiratory syncytial, Ebola, Epstein–Barr, and COVID-19 are enveloped viruses. Transmission of these viruses occurs through an infected vector viz. insects, animals, or directly through human contact (by coughing, sneezing, faecal-oral route, blood transfusion, or through sexual contact) [1].

By continuous infection from one organism to another, genetic complexity in these viruses increases, making them more pathogenic than their earlier form. For example, viruses from coronaviridae family, SARS-COV-1, evolved from horseshoe bat and later transmitted to human beings in a more pathogenic form [2]. Moreover, COVID-19 also originated from bats [3] and is more pathogenic than its original form (Fig. 1).

The genetic study of COVID-19 revealed that it has many similarities to SARS-COV-1, zoonotic origin, and belongs to the genus betacoronavirus [4]. Transmission of COVID-19 to human beings occurs mostly through the respiratory tract. Goblet cells and ciliated cells of the respiratory tract compete with this infecting virus. Goblet cells try to trap them in mucus and ciliated cells bearing hair-like structure struggle to remove trapped viruses from the human body. According to Letko et al. **

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entry of COVID-19 through respiratory cells occurs by a receptor-binding domain of viral spike glycoproteins to host cell receptor ACE2 (angiotensin-converting enzyme). After attachment of the virus to host cell, transmembrane serine protease 2 (TMPRSS2) of the host cell is generated by its protease activity supporting the entry of virus inside the host cell [6]. After entering the cells, they start their replication and translation process to produce more infecting virions for further infection to healthy cells. After two to fourteen days of viral exposure, symptoms such as fever, cough, fatigue, breathing difficulties, and shortness of breath start to appear. In case of severe infection, the patient develops pneumonia, acute respiratory syndrome, organ failure, and ultimately death. Researches are underway on many epidemiological parameters like viral shedding period, transmission mode, incubation period, subclinical infection, viral survival period in the environment, and people resistance towards it.

Learnings from previous disease outbreaks such as chickenpox, mumps, polio, measles, etc. indicate that some part of the population is immune towards a particular disease and they indirectly protect the transfer of virus to susceptible individuals, through a phenomenon called ‘herd immunity’. In the case of COVID-19, herd immunity would also play an important role to minimize transmission. But this type of control measure depends upon the proportion of the population showing immunity to these viruses. One of the possible ways used to develop partial immunity was to use antibodies generated in the population already infected and recovered from SARS-COV-1. The same principle could be applied for COVID-19, by harnessing antibodies from infected people who have recovered from this as well as asymptomatic people who got infected and cured without any treatment [7]. Interestingly, an impediment towards the spread of COVID-19 infection was found in countries (India, Peru, Portugal, and Saudi Arabia) that have mandated the Bacillus Calmette Guerin (BCG) vaccination program for infants to protect from tuberculosis, reporting lower number of cases and death rate than those who do not have BCG mandate [8]. Researchers are trying to get a clear picture between neonatal BCG vaccination and COVID-19 infection.

There are a number of antiviral drugs that are now being tracked in the clinical trials. In India, anti-malarial drug ‘Hydroxychloroquine’ received the government approval to treat severe COVID-19 cases, but some hospitals also started using plasma therapy, as a part of registered clinical trials, to treat severely ill patients. In China and France, a trial of ‘Chloroquine phosphate’ is underway and has shown some indication of possible benefits on infected individuals. Similarly, other drugs like ‘Lopinavir’ with ‘Ritonavir’, used against HIV; ‘Interferon-beta-1a’ with

Table 1
A united trial from the different organization by WHO for the development of safe and effective vaccines against COVID-19 virus (source: WHO).

| Organizations | Vaccine types | Platform | Clinical evaluation phase | Date of instigate |
|---------------|--------------|----------|--------------------------|------------------|
| Moderna/NIAID, US | LNP-encapsulated mRNA | RNA | Phase 1 | 3 March |
| Inovio Pharmaceuticals, US | DNA plasmid vaccine Electroporation device | DNA | Phase 1 | 3 April |
| Beijing Institute of Biological Products/Wuhan Institute of Biological Products, China | Inactivated | Non-Replicating Viral Vector | Phase 2 | 10 April |
| CanSino Biological Inc./Beijing Institute of Biotechnology, China | Adenovirus Type 5 Vector | Non-Replicating Viral Vector | Phase 1 | 17 March |
| Sinovac, China | Inactivated + alum | Inactivated | Phase 1 | 13 April |
| University of Oxford, UK | ChAdOx1 | Non-Replicating Viral Vector | Phase 1 | 23 April |
| BioNTech/Fosun Pharma/Pfizer | mRNA | RNA | Phase 1/2 | Approved, not yet started |
lopinavir and ritonavir, used against multiple sclerosis; and ‘Remdesivir’, that bind with viral RNA polymerase are also under trial against COVID-19. Some researchers are trying to target viral entry point receptor proteins ACE2 and TMPRSS2 for the development of antiviral drugs/vaccines. But the problem with this approach is that ACE2 is recognized as a potential therapeutic strategy in cardiovascular disease, hypertension, lung abnormality and diabetes, and TMPRSS2 is involved in a different vital activity of the cell. Dysfunction or blockage of these proteins may lead to developing various abnormalities or disorders in human beings.

WHO has developed a global blueprint of research teams for the outcomes of novel vaccines or antiviral drugs against this pandemic within a short period. List of these organizations with their respective platform and types are given in Table 1.

Today nanotechnology plays an important role in the treatment of viral infections [9]. Kalantar-Zadeh et al. [10] recently reported the possibility of using nanotechnology in monitoring COVID-19 infection and the development of effective therapeutic strategies with reference to gut microbiome modulation. Nanoparticles are suitable candidates for treatment against viruses due to small size that facilitates the transport of drug to target site, surface charge aiding drugs entry across the plasma membrane, increased surface area to volume ratio, large drug load capacity, biomimetic characteristics, mimic with the biochemical process and drug encapsulation [9]. The major advantage of nanoparticles in the formulation of vaccines are: they have a similar size to viruses, hence they can activate immune response rapidly, selective immune response development by binding with the receptor of specific immune cells, slow release of adjuvants or antigen molecules, resulting in enhanced cellular and humoral immune response [9]. Several nanoparticles have been studied to control the infection of enveloped viruses and developed as targeted antiviral drugs/vaccines for the prevention of the disease. Some researchers have also found that capped nanoparticles protect the host cell from viruses belonging to the coronavirus group by inducing the innate immune response. Thus, the application of nanoparticles in the form of drugs/vaccines could be an effective measure to control COVID-19 virus infection. Antimicrobial coating with nanoparticles at public places and on personal protective equipment (PPE) will be an effective preventive measure to minimize the transmission of COVID-19 to a susceptible host. Nanoscience will have the potential to tackle COVID-19 due to its proven effectiveness against other enveloped viruses [11].

### Table 2

Antimicrobial coating agents/nanoparticles with their virucidal effects.

| Viruses                     | Antimicrobial coating agents/nanoparticles | Mode of action                                      | References |
|-----------------------------|-------------------------------------------|----------------------------------------------------|------------|
| Influenza virus             | Hybrid coatings having silver, copper and zinc cations | Prevent the binding of the virus to host plasma membrane | [14]       |
| Hepatitis B virus (HBV)     | Silver nanoparticles                      | Interfere in the replication of viral DNA and attachment | [15]       |
| Herpes simplex virus type 1 (HSV-1) | Tin Oxide nanowires                      | Prevent the entry of virus to host cell            | [16]       |
| Tacaribe virus (TCRV)       | Polysaccharide-coated Silver nanoparticles | Before the entry to host cell, it inactivates the infective virus | [17]       |
| Human immunodeficiency virus type 1 (HIV-1) | Hybrid coatings having silver, copper and zinc cations | Interfere viral attachment to host cell             | [18]       |
| Respiratory syncytial virus | Hybrid coatings                           | Destroy the viral membrane                         | [14]       |
| Herpes simplex virus type 2 (HSV-2) | Zinc Oxide Tetrapod Nanoparticles (ZOTEN) | Bind with virions and prevent the entry in the cell | [19]       |
| Dengue virus type 2         | Green-synthesized silver nanoparticles    | Inhibit the production of dengue viral envelope    | [20]       |
| Vaccinia Virus              | Zinc Chloride                             | Inhibit the growth of virus on the host cell       | [21]       |
| Rhinoviruses                | Zinc ion                                  | Inhibit virus replication                          | [22]       |
| Monkeypox virus             | Polysaccharide-coated Silver nanoparticles | Block virus-host cell interaction and penetration  | [23]       |

Fig. 2. A mechanism to control the infection of enveloped viruses through the hybrid coating.
Bacteria present in these biofilm secrete extracellular polymeric substances which may allow the entrapment of enveloped viruses. Like other coronaviruses, COVID-19 is also an enveloped virus and has four different structural proteins; nucleocapsid (N), spike (S), membrane (M) and envelope (E). The S, E, and M protein develop viral envelope, while N protein clutch the RNA genome [12]. This spike protein of COVID-19 is responsible for its transmission by attaching on a different surface [12]. Surface survival of COVID-19 was studied by von Doremalen et al. [13]. They found that COVID-19 is present in infectious form for 4 h on copper, up to 24 h on cardboard, and two to three days on plastic and the stainless surface under given experimental conditions. Therefore, to prevent the transmission of COVID-19 from these surfaces, antimicrobial coating at common areas will be a major preventive measure.

Antimicrobial coatings are chemical substances that are either natural bioactive polymer/chemically synthesized polymer or nanoparticles that can kill or inhibit the growth of pathogenic bacteria, fungi, and viruses. These agents prevent the attachment of microbes on the surface by crossing the microbial membrane and interfering with the metabolic pathway resulting in changes in membrane structure and function. Inside the microbes, they induce oxidative stress leading to electrolyte imbalance, damage of protein, and enzyme inhibition which leads to alteration in gene expression and ultimately causes the death of microbes. According to Hodek et al. [14] hybrid antimicrobial coating with silver, copper, and zinc cations have great virucidal effects against enveloped viruses such as HIV-1, human herpesvirus 1, influenza H1N1 and dengue type 2 viruses, making them excellent virucides to be applied in common surfaces (Fig. 2). Most common antimicrobial coating agents that show virucidal effects are given in Table 2. Li et al. [24] developed a multifunctional antimicrobial coating from biocompatible polymer encapsulated chlorine dioxide with anti-adhesion, contact-killing, and release-killing. Prof. Yeung King Lun, a lead researcher from Hong Kong University of Science and Technology, China has developed an effective Multilevel Antimicrobial Polymer (MAP-1) coating that inactivates 99.99% surrogate feline calicivirus which is more resistant than

![Fig. 3. A hypothetical mechanism to tackle COVID-19 through the antimicrobial coating.](image)

![Fig. 4. Study of the virucidal activity of MONS (metals oxide nanostructures) against enveloped viruses.](image)
coronaviruses. Schematic representations of action of antimicrobial material on COVID-19 to prevent its transmission are given in Fig. 3.

Many researchers have found different nanostructures/particles to be effective in antiviral therapy against enveloped viruses, some of which are noted in Table 2. Various metal nanostructures like zinc oxide, tin oxide nanowires, zinc oxide tetrapod are widely used in novel antiviral therapy. A common mechanism involved in their study against enveloped viruses is given in Fig. 4. Similarly, capped silver, gold, silicon nanoparticles have been studied for their strong antiviral activity. They prevent the entry of viruses by mimicking cell receptors or inhibiting the genomic replication and viral assembly. Du et al. [25] studied the effect of capped nanoparticles (glutathione-Ag2S clusters) against porcine epidemic diarrhoea virus (PEDV), a member of coronavirus at Wuhan, China. These capped nanoparticles inhibit the synthesis of the viral negative-RNA strand and prevent the budding of viral progeny by inducing an innate immune response. COVID-19 is very much close to PEDV coronavirus and the application of different combinations of capped nanoparticles against different life cycle steps of COVID-19 would be a possible therapeutic option shortly. A possible molecular option to control the COVID-19 infection is given in Fig. 5.

3. Summary and future outlook

In summary, antimicrobial coatings would be an effective measure to control the transmission of COVID-19 at a community level. Metallic nanoparticles are an effective and economically sustainable measure to control any pandemic, even COVID-19. Metallic antimicrobial coating plays a multifunctional role and can minimize the spread of any disastrous disease in the populace. Impediments to the transmission of this disease will make it localized and much more manageable for any country. Broad-spectrum antimicrobial coatings will also inhibit the growth of those microorganisms which facilitate the spread of COVID-19. This method will be a novel therapeutic option against the resurgence and emergence of future pandemics that the world may face in the future. A multidisciplinary research collaboration between environmental, social and biomedical sciences is essential to understand the high rate of disease transmission and its prevention. Thus, our focus should be on curing COVID-19 disease, and at the same time controlling the transmission while reducing patient complications and maintaining life support for every level of individuals.

Declaration of Competing Interest

There are no any conflict among authors.

CRediT authorship contribution statement

Pradeep Kumar Rai: Writing - original draft. Zeba Usmani: Writing - review & editing. Vijay Kumar Thakur: Conceptualization, Supervision, Funding acquisition, Writing - review & editing. Vijai Kumar Gupta: Conceptualization, Supervision, Writing - review & editing. Yogendra Kumar Mishra: Conceptualization, Supervision, Writing - review & editing.

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