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Review

Nanotechnology as an alternative to reduce the spread of COVID-19

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Abstract: The current emerging COVID-19 pandemic has caused a global impact on every major aspect of our societies. It is known that SARS-Cov-2 can endure harsh environmental conditions for up to 72 h, which may contribute to its rapid spread. Therefore, effective containment strategies, such as sanitizing, are critical. Nanotechnology can represent an alternative to reduce the COVID-19 spread, particularly in critical areas, such as healthcare facilities and public places. Nanotechnology-based products are effective at inhibiting different pathogens, including viruses, regardless of their drug-resistant profile, biological structure, or physiology. Although there are several approved nanotechnology-based antiviral products, this work aims to highlight the use of nanomaterials as sanitizers for the prevention of the spread of mainly SARS-Cov-2. It has been widely demonstrated that nanomaterials are an alternative for sanitizing surfaces to inactivate the virus. Also, antimicrobial nanomaterials can reduce the risk of secondary microbial infections on COVID-19 patients, as they inhibit the bacteria and fungi that can contaminate healthcare-related facilities. Finally, cost-effective, easy-to-synthesize antiviral nanomaterials could reduce the burden of the COVID-19 on challenging environments and in developing countries.

Keywords: COVID-19, Nanotechnology, Nanomaterials, Antiviral, Sanitizers, Nanomedicine, Infectious Diseases

1. Introduction

Save from a natural disaster of cataclysmic proportions, or an all-out man-made nuclear war, infectious diseases pose the only global threat to human life on Earth. Infectious diseases have plagued humanity and represented the major cause of morbidity and mortality through the millennia, and in the process shaped human evolution. They still constitute the leading cause of premature death in the developing world. However, our modern society has become extremely complacent about the threat posed by infectious diseases, mostly due to the availability and increased access to hygiene and sanitization techniques, vaccines, and antibiotics.

Despite this unjustified level of complacency and the false sense of security, epidemiological experts and sentinel organizations around the world have provided ample warning signs, yet often ignored, of our global vulnerability against infectious diseases and their broad and borderless impact -microorganisms do not need a passport and do not understand about artificial geopolitical boundaries. This is further aggravated by globalization and climate change. In particular, the newest epidemics caused by a virus such as SARS, MERS, Ebola, and H_1N_1 since the beginning of the century have raised the awareness of the major threat that viral diseases still pose to humanity as a whole. However, these preoccupations were often short-lived and fast forgotten once the resulting epidemics were seemingly under control, which left us completely unprepared despite our conviction and anticipation that it was only a matter of time for the next epidemic or pandemic to come. Sure enough, we did not have to wait too much longer, and as of early 2020, humanity is confronting a pandemic in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease, abbreviated as COVID-19.

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2. The SARS-CoV-2 virus and the current COVID-19 pandemic

The SARS-CoV-2 is a large, enveloped, positive-stranded RNA virus, with a nucleocapsid, with a similar structure to the SARS-CoV-1; and a diameter size range from 80 to 140 nm [1]. This zoonotic coronavirus has become a major cause of emerging respiratory disease [1] and has rapidly spread around the globe, affecting billions of people, and triggering unexpected changes in the healthcare system, global economy, and interactions in the societies worldwide.

So far, there are over 8.4 million confirmed cases with COVID-19 worldwide, with an estimated death toll of over 450 thousand people [2]. The costs related to this communicable disease are expected to be in the trillions of dollars globally, but the real cost cannot be estimated [3]. Implementing strategies to reduce its spread requires the participation of the whole society, as well as the development of innovative ways of social, work, and health policies. Several measures have been implemented to control COVID-19, from campaigns aimed at improving personal hygiene practices to community approaches such as social distancing and quarantines. Among the suggested public health activities to address this pandemic are 1) efficient stay-at-home implementation, 2) fast SARS-CoV-2 testing, and 3) efficient health care response. The last point considers protecting the health care professionals by providing tools to prevent nosocomial infections, from making appropriate PPE available to ensuring sanitizing procedures.

Proper sanitizing measures are critical. A recent study revealed that SARS-CoV-2 can be detected on plastic and stainless-steel surfaces up to 72 h, whereas on copper, no viable SARS-CoV-2 was measured after 4 hours of application [4]. The inactivation of the virus by copper is not surprising, as it is known that transition metals can inactivate viral particles [5]. Thus, nanotechnology may provide an alternative for sanitizing surfaces, via antimicrobial and antiviral nanomaterials.

3. The *state-of-the-art* of antiviral nanomaterials: from research to the clinic.

There are different definitions of the nanomaterial concept. In general, nanomaterials can be described as single-structures which size is less than 100 nm in at least one of their three dimensions. The increasing interest in nanomaterials is due to their novel or improved physicochemical properties such as endurance, chemical reactivity, biocompatibility, conductivity, or reduced toxicity. The chemical composition of nanomaterials can be organic or inorganic, and they can be found as single structures, composites, embedded in a matrix, etc. Nowadays, nanomaterials are found in a wide range of existing products, such as in electronics, health and fitness, paints and other surface coatings, food, and clothing, among many others [6,7]. Moreover, medicine is one of the fields with a growing interest in the use of nanotechnology. Just for silver nanoparticles, the global consumption for healthcare-related nanotechnology is expected to be over 50 tons in 2020 [8].

Nowadays, nanomaterials are widely used in different healthcare-related applications, such as sanitizers, diagnosis, imaging tools, wound dressing, wearable devices, antimicrobial drugs, anticancer therapies, pharmaceuticals, drug delivery, and vaccine development, diagnosis, and even implants [9–11]. Nanomaterials have been researched due to their properties against multiple pathogenic, microorganisms [12–15] s.

The antiviral activity of nanomaterials against different viral families has been studied (**table 1**). Silver nanoparticles (AgNPs) inactivate different types of viruses, such as HIV-1 [16], monkeypox virus [17], hepatitis B [18], Tacaribe virus [19], and the Rift Valley Fever Virus [20]. Also, AgNPs display activity against influenza viruses like H_3N_2 [21] and H_1N_1 [22]. Moreover, nanomaterials have been used for inhibiting other viruses from the *Coronaviridae* family [23]. Also, non-silver-based nanomaterials display antiviral activity against viruses that cause Respiratory Syndromes. Titanium oxide nanoparticles inhibit the H_9N_2 [24], Carbon fullerene lipidosomes inactivate H_1N_1 [25], and a peptide–nanoparticle complex is capable of inactivating the influenza A virus [26]. Regarding other viruses, ivermectin-nanoparticles complexes can inactivate the Zika virus [27]. Therefore, nanomaterials can inactivate a wide variety of viruses, regardless of the viral structure and strain. In a recent review, Cojocaru *et al* described the potential mechanisms that allow nanomaterials to inactivate both DNA and RNA viruses [28]. Briefly, among the main mechanisms are the viral DNA/RNA synthesis inhibition; viral protein synthesis inhibition; and inhibitors of the entry, fusion,

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or integration of viruses into the cell. Back in 2005, Lara *et al* showed that silver AgNPs interact with the receptors from the HIV, inhibiting its infectivity [29].

Table 1. Examples of antiviral nanomaterials that inactivate different types of viruses.

Antiviral nanomaterial				Virus	Reference
Type/Composition	**Shape**	**Size [1] (nm)**	**coating**		
AgNPs	Spheroid	2.08	BSA	HIV-1	[16]
	Spheroid	25, 55, 80	chitosan	Monkeypox	[17]
	N/A	10, 50	N/A	Hepatitis	[18]
	Spheroid	10, 25	Uncoated & Polysaccharide	Tacaribe	[19]
	Spheroid	35	PVP	RVFV	[20]
	Spheroid	9.5	Organic	H3N2	[21]
	Spheroid	3.5, 12.9	Chitosan	H1N1	[22]
	Spheroid	5-25	Graphene oxide	Coronavirus	[23]
TiO_2NPs	Poly-shaped	52.9	N/A	H9N2	[24]
Carbon fullerene [2]	N/A	N/A	N/A	H1N1	[25]
Peptide–NPs [3]	Dendritic	2.4 & 29.8	N/A	Influenza A	[26]
Ivermectin-NPs [3]	Spheroid	60-140	IVM	Zika	[27]

[1] Average size. For the metallic nanoparticles, the size corresponds to their metallic core.
[2] Lipidosome complex
[3] Hybrid complexes

Research on nanomaterials for future antiviral treatments is still ongoing, as they have proven to effective for preventing HIV transmission [30] and pneumonia -influenza virus [31]-, in *in vivo* murine models. Also, AgNPs were effective at inactivating *in vivo* the Canine Distemper Virus in dogs [32]. Heparan Sulfate Proteoglycans (HSPG)-mimicking nanoparticles display broad-range antiviral activity, both *in vivo* and *in vitro* against herpes simplex virus (HSV), human papillomavirus, respiratory syncytial virus (RSV), dengue and lentivirus [33]. Also, some nanomaterials can be used as nanocarriers, for improving the bioavailability of current antiviral drugs [34].

Moreover, Singh *et al* reviewed recently different antiviral nanomedicines that are approved and under ongoing preclinical and clinical trials [35]. An example is Inflexal V©, a nanotechnology-based virosomal anti-influenza vaccine approved by the FDA [36]. Despite the current use of antiviral nanomaterials, research on other nanomaterials is still ongoing, to address their potential toxicity and side effects.

4. Current nanotechnology applications that can be used to combat COVID-19.

The typical shape of antiviral nanoparticles has an aspect ratio close to 1 (spheroids) with a usual range between 1 to 50 nm, and an average of 22 nm. Antiviral nanomaterials are typically smaller than the SARS-Cov-2 viral particle (**fig. 1**), therefore they may interact better with the surface proteins or even with the whole viral particle. Currently, nanomaterials are used in a wide range of commercially available applications, many of them related to healthcare. Some of the current applications that can be used against COVID-19 are described below.

4.1 Personal Protective Equipment (PPE).

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The application of nanomaterials-embedded textiles has been intensely researched. These textiles may be used for PPE, such as lab coats, and facemasks, as current research shows that they improve the physicochemical properties of textiles [37], such as fire-retardant, self-cleaning, UV-protection, antimicrobial, and antiviral, among others. Several patents consider the use of fibers embedded with metallic nanoparticles, such as copper and silver nanoparticles, due to their antimicrobial and antiviral properties [9,38]. The use of nanoparticles in textiles has been increasing rapidly, with a current global consumption of around 35 tons just for silver nanoparticles [8]. Moreover, wearable smart textiles for sensing have been under study, particularly for health-related applications. One area of interest is the early detection of pathogens [39], which may include viruses, such as the SARS-Cov-2.

4.2 Surface coatings.

Nanomaterials-based coatings are currently used for several applications, and different products are now available [9]. Numerous nanomaterials, such as silver, bismuth, or titanium nanoparticles, have been developed for coating surfaces, [37,40,41]. Also, nanostructured surfaces can physically reduce the attachment of pathogens [42] and even disrupt the structure of the pathogens due to the nanoscale topography organization [43]. Nanomaterials can be embedded in paint or coatings for medical instrumentation, gloves, and other highly-touched surfaces, such as doorknobs, handrails, other medical devices, etc. to reduce the viability of viruses and other pathogens.

4.3 Sanitizers.

Currently, disinfectants with silver salts are already available [44], as silver is deemed safe for sanitizing purposes [45]. In hospitals and other healthcare-related facilities, sanitizing with nanotechnology-based products could inactivate the viruses on surfaces. Moreover, sanitizers with nanomaterials could reduce the presence of the SARS-Cov-2 on surfaces.

4.4 Other current and potential applications.

Among other uses, nanomaterials can be used to improve the function of air filters in healthcare facilities or in other places that use recirculated air. Nanotechnology-improved air filters can reduce the spread of viral particles [46,47]. Also, the use of nanotechnology for producing wound dressings has been thoroughly explored [48–50], due to their ability to protect against infections and increase the healing speed rate. Future applications may include the development of improved detection kits, as it has been one of the major needs for the current strategies to contain and follow the virus spread.

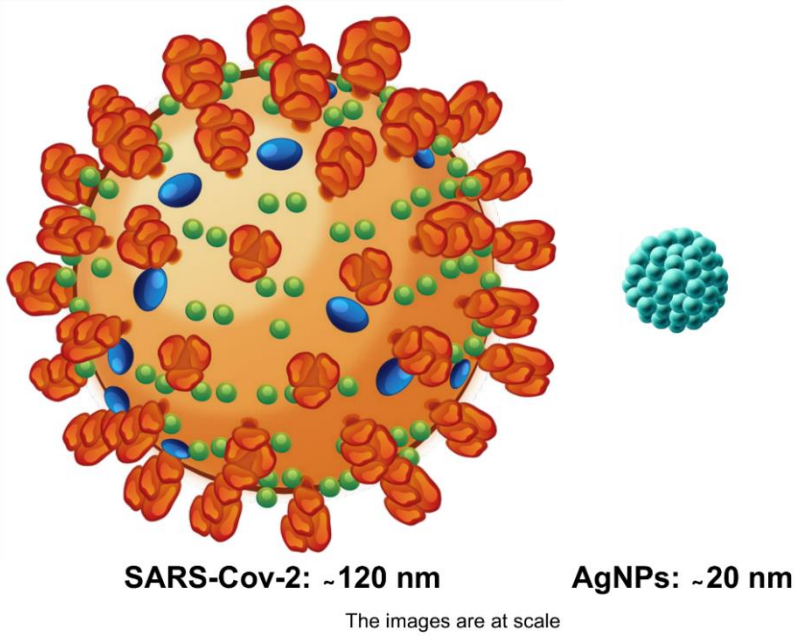

Figure 1. Size comparison between the average sizes of the SARS-Cov-2 coronavirus and a single silver nanoparticle (AgNPs).

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5. A silent risk: the microbial secondary infections.

The current COVID-19 pandemic has raised several health concerns beyond the disease itself. Among them, secondary infections are usually underestimated risks that may occur due to the burden on health caused by the COVID-19. Patients infected with the novel strain of coronavirus frequently show microbial dysbiosis and a decrease of probiotic bacteria [51]. Also, it is not uncommon for patients with COVID-19 to suffer from complications of acute organ injury and secondary infection [52]. Nanomaterials display a broad range of antimicrobial activity against bacteria [53,54], protozoa [55,56], and fungi [57–60]. In healthcare-related facilities, nanotechnology-based sanitizers could simultaneously reduce the presence of viruses and opportunistic microorganisms. Moreover, nanomaterials can reduce the microbial biofilms [58,59,61], leading to a reduced risk of secondary microbial infections.

In the long term, nanoantibiotics could be used to prevent or treat microbial secondary infections, particularly those that display multidrug-resistance profiles, which has been one of the rising concerns of our current crisis of communicable diseases. Nanomaterials are effective regardless of the drug-susceptibly profile of the microorganisms and may enhance the potency of the antimicrobial drugs [57,62,63].

5. Perspectives

What should be expected in the near future? Although more research is needed, antiviral nanomaterials represent an alternative to reduce the spread of COVID-19, as they have been effective against other viruses. Based on our current knowledge, nanomaterials may be potent sanitizers with broad antimicrobial activity. Nanotechnology-based sanitizers can improve safety in healthcare-related facilities and public spaces, particularly in developing countries. Moreover, their therapeutic use has proven to be effective and it will be expanded in the future, as more research becomes available. Also, as nanomaterials may enhance the antimicrobial potency of some drugs, they are an interesting alternative to control secondary infections, and for future treatments against multidrug-resistant microorganisms.

Finally, protocols that favor facile, rapid, cost-effective syntheses of antimicrobial and antiviral nanomaterials [53,64] produce potent nanomaterials that could reduce the spread of viruses and microorganisms. Affordable nanotechnology may benefit anti-COVID-19 sanitizing procedures in developing countries, where access to advanced materials is limited. Also, easy-to-synthesize nanomaterials may be used under non-favorable conditions, such as medical mobile-units, rural health care facilities, public spaces, and in medical posts for the military on the field [65,66].

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Conflicts of Interest: The authors declare no conflict of interest.

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