Nanomaterial-Augmented Formulation of Disinfectants and Antiseptics in Controlling SARS CoV-2

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Abstract
The worldwide COVID-19 pandemic has brought significant consideration toward innovative strategies for overcoming the viral spread. Nanotechnology will change our lives in several forms as its uses span from electronics to pharmaceutical procedures. The use of nanoparticles provides a possibility to promote new antiviral treatments with a low possibility of increasing drug resistance compared to typical chemical-based antiviral treatments. Since the long-term usage of disinfectants and antiseptics at high concentrations has deleterious impacts on well-being and the environment, this review was intended to discuss the antiviral activity of disinfectants and antiseptics required for their activity against respiratory viruses especially SARS-CoV-2. It could improve the inhibition of viral penetration into cells, solvation of the lipid bilayer envelope, and ROS production, therefore enhancing the effect of disinfectants. However, significant concerns about nanomaterial's hazardous effects on individuals and the environment are increasing as nanotechnology flourishes. In this review, we first discuss the significant and essential types of nanomaterials, especially silver and copper, that could be used as antiviral agents and their viral entry mechanisms into host cells. Further, we consider the toxicity on health, and environmental concerns of nanoparticles. Eventually, we present our outlook on the fate of nanomaterials toward viral diseases.

Keywords Nanoparticles · Disinfection · Ecological safety · Biosafety · COVID-19 · SARS-CoV-2 · Toxic nanomaterials

Introduction
Severe Acute Respiratory Syndrome-Coronavirus-2 is a novel virus with a correlated illness called COVID-19. It is spreading worldwide since late 2019, and a few months later, the World Health Organization (WHO) announced it as an epidemic (Schrank et al., 2020).

Coronaviruses are an enveloped and extensive family of viruses, transmitting between humans and animals and commonly provoke upper-respiratory-tract diseases ranging from typical cold to severe infection (Howley et al., 2020). SARS coronavirus (2002) and MERS Coronavirus (2012) are two severe and lethal members of this large family (Rai et al., 2020). SARS-CoV-2 viruses are positive-sense, single-stranded RNA viruses having a genome length of 26–32 kb (Rai et al., 2020). In comparison, SARS-CoV-2 is of special concern due to challenging control, higher reproduction numbers, longer incubation times, latent infections, and delayed symptoms (Almasi & Mohammadipanah, 2020; Schrank et al., 2020).

Since one of the most conventional interventions to inhibit the spread of this virus is adequate surface disinfection, there is an urgent requirement for disinfectants with lower toxicity (Rai et al., 2020; Saadatpour & Mohammadipanah, 2020). As the effectiveness of disinfectants depends on multiple factors, efforts to enhance their impact are inevitable in the current situation of the pandemic. Therefore, the advancement of authentic, innocuous, and eco-friendly disinfection methods is of utmost importance for the widespread continuation of their applications. Enhancement of antimicrobial effect using the natural additive to disinfectant formulation is generally regarded as safe while the emerging usage of new nanomaterial in antiseptic formulations is of health and ecological associated concern (Saadatpour & Mohammadipanah, 2021). In the first section of this review, we will focus on nanomaterials with antiviral activity. The second section will highlight several instances of their
antiviral mechanisms. The third section will ultimately present the toxic impacts of nanomaterials on eukaryotic cells and the environment by their worldwide radically increased usage.

**Nanoparticles and Nanomaterials**

Nanomaterials (NMs) are materials constructed with a top-down or bottom-up nanotechnological approach. They are characterized by, at minimum, a single dimension fewer than 100 nm with a great surface area (Baroli, 2010). Depending on the composition, NMs are organized into four different groups: Based on metal, carbon, composites, and dendrimers (Kabir et al., 2018).

NMs based on carbon are concrete elements, which have been found in the form of nanoparticles (NPs), ellipsoids, sheets, and tubes that have specific and unusual physico-chemical, optical, mechanical, and thermal qualities (Kabir et al., 2018). Quantum dots, silver NMs, gold NMs, and nano metallic oxides like titanium or zinc dioxide are the main metal NMs (Kabir et al., 2018). The dendrimers are symmetrical particles comprised tree-like branches in a monodispersed construction. The superficial layer may encounter variations in form, size or bottom-up nanotechnological approach. They are characterized by, at minimum, a single dimension fewer than 100 nm with a great surface area (Baroli, 2010). Depending on the composition, NMs are organized into four different groups: Based on metal, carbon, composites, and dendrimers (Kabir et al., 2018).

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Depending on how many dimensions fall below the 100 nm limit, NMs can also be sorted into four large families: Core–shell (zero dimension), surface films (one dimension), strands or fibers (two dimensions), and particles (three dimensions) (Baroli, 2010).

The NMs might have various shapes (e.g., spheres, rods, cups, ellipsoids, cubes) and might be coated with inorganic or organic materials to stabilize them against aggregation (Baroli, 2010). Applications of NMs include drug delivery, biosensor, reaction rate enhancement agent, magnetic separation and detection, and last but not least, as the antimicrobial agent (Li et al., 2011).

**Nanomaterials with Antiviral Activity**

Depending on the dimension, form, and surface charge, NMs can possess various formations and antiviral characteristics (Abd Elkodous et al., 2020). New NMs are being developed to improve their performance in treating respiratory diseases through various mechanisms (Sivasankarapillai et al., 2020).

The primary NMs reported for their inactivation effect on respiratory viruses can be subdivided into the following groups.

**Polymeric NMs** Their impressive qualities include adjustable features, available combinatorial protocols, and excellent biocompatibility (Sivasankarapillai et al., 2020).

**Self-assembling proteins NMs** They are produced by the oligomerization of monomeric proteins.

**Inorganic NMs** This type of NMs often has records of antiviral activities (Sivasankarapillai et al., 2020). Some of the most critical inorganic NMs include copper, silver, zinc, Titanium Dioxide (TiO₂).

**Copper** Since copper NMs (CuNPs) contain a smaller size and high surface-to-volume rate, they are extensively realized antimicrobial, antifungal, and antiviral metals for use on surfaces (Imani et al., 2020; Ingle et al., 2014; Vincent et al., 2017).

**Silver** They have unusual physicochemical and biological features that lead to having many applications for antiviral purposes in the shape of ions, NPs (AgNPs), and hybrid coats (Gurunathan et al., 2020).

**Zinc** Zinc oxides are n-type semiconductor metal oxides having remarkable antiviral qualities. It has many advantages like low production costs, readiness preparation, distinctive UV filtering qualities, high catalytic and photochemical activity (Jayaseelan et al., 2012; Nisar et al., 2019).

**TiO₂** TiO₂ has many technical purposes such as water treatment, air disinfection, UV absorber, food, semiconductor, and agricultural industry (Hossain et al., 2014).

**Other Inorganic Antiviral Matters** Other inorganic matters and NPs like gold, magnesium, transition metals, and silica have significant antiviral activities (Imani et al., 2020) (Table 1).

**Peptide-based NMs** Earlier research has shown that the applications of peptide restrainer and modifications of amino acids may probably act against infections, especially the ones associated with SARS-CoV (Sivasankarapillai et al., 2020). Some of the most significant NMs that have shown activity against several respiratory viruses are summarized in Table 2.

**Antiviral Mechanisms of Nanomaterials**

In recent years, several NMs have been suggested as an alternative material for advanced diagnostic and therapeutic uses and carriers for antiviral agents. The mechanisms of action are limited to the specific type of NMs or viruses. Some of the main mechanisms are discussed below. The antiviral activity of NMs in any form depends on the dose and the target virus (Castro-Mayorga et al., 2017; Sportelli et al., 2020).

**Silver** The interaction with the envelope, genome, surface proteins, replication factors, preventing cellular pathways, and viral penetration into cells are the main mechanisms (Rai et al., 2016). Silver as an antiviral interacts directly with
| Nanomaterial   | Virus Name          | Virus Envelope | Genetic material | Virucidal Activity Level | Contact Time | Proposed Applications                                                                 | Reference          |
|---------------|---------------------|----------------|------------------|--------------------------|--------------|----------------------------------------------------------------------------------------|-------------------|
| **Copper**    |                     |                |                  |                          |              |                                                                                       |                   |
| Solid state   | Influenza A         | Enveloped      | Negative-sense ssRNA | $2 \times 10^6$ decreased to 500 infected viral particles | 6 h          | Replacing steel instruments with copper                                                | Noyce et al. (2007) |
| Copper alloys | Murine norovirus    | Non-enveloped  | Positive-sense ssRNA | Dependent on alloy composition | Dry: 5–120 min | Application of copper alloys in medical and environments settings                      | Warnes, et al. (2015) |
|               |                     |                |                  |                          | Wet: Virus TCID50 = 0 or $2-4\log$ reduction | Wet: within 2 h |                                                                                    |                   |
| Cuprous oxide | Influenza A         | Enveloped      | Negative-sense RNA | Following exposure to 2.1 μmol, 3.7log reduction | 30 min       | Block new viral shapes and potential resistance to drugs to decrease transmission     | Imani et al. (2020) |
| **Silver**    |                     |                |                  |                          |              |                                                                                       |                   |
| Hybrid coating (ionic) | HIV-1 | Enveloped | Positive-sense ssRNA | 99.5% reduction | 20 min       | Broad-spectrum antimicrobial surface coating in hospitals                               | Hodek et al. (2016) |
|               | Dengue virus        | Enveloped      | Positive-sense ssRNA | 1.1log TCID50 reduction | 4 h          |                                                                                       |                   |
|               | HSV                 | Enveloped      | dsDNA            | Virus TCID50 = 0        | 4 h          |                                                                                       |                   |
|               | Influenza           | Enveloped      | Negative-sense ssRNA | 0.7log TCID50 reduction | 4 h          |                                                                                       |                   |
| Silver nitrate in solution | Feline calicivirus | Non-enveloped | Positive-sense ssRNA | 3log decrease in 2.1 mg/L | 75 days      | In effective covering and contact surfaces                                              | Imani et al. (2020) |
|               | Murine norovirus    | Non-enveloped  | Positive-sense ssRNA | 1log decrease with 2.1 mg/L | 75 days      |                                                                                       |                   |
| NM in solution or film | Murine norovirus | Non-enveloped | Positive-sense ssRNA | In solution: primary 3log decrease, increased to Virus TCID50 = 0 with more than 10.5 mg/L concentration As film: 0.14log reduction at 25 °C and 0.86log reduction at 37 °C | 1 day         | The technology offered here would provide the In adequate covering and contact surfaces | Castro-Mayorga et al. (2017) |
| **Zinc**      |                     |                |                  |                          |              |                                                                                       |                   |
| Nanomaterial | Virus Name | Virus Type | Genetic Material | Virucidal Activity | Contact Time | Proposed Applications | Reference |
|--------------|------------|------------|------------------|-------------------|--------------|----------------------|-----------|
| Rigid phase  | Murine norovirus | Non-enveloped | ssRNA | 1 log decrease for pure zinc | 2 h | The insertion of copper alloy surfaces to hinder pathogens | Warnes et al. (2015) |
| Zinc oxide filopodia-like structures | Herpes simplex virus type 1 (HSV) | Enveloped | dsDNA | 100 μg/mL ZnO-MNSs leads to the entrance under 20% | 90 min | Development as a local agent for inhibition of viral infection | Imani et al. (2020) |
| Ionic solution | Human rhinovirus | Non-enveloped | Positive-sense ssRNA | 99% decrease in quantity of plaques with the use of zinc chloride | 1 h | It developed as an antiviral agent to block the cleavage of viral protein precursors and prevent the maturation of viral RNA and capsid polypeptides | Imani et al. (2020) |
| TiO₂          | Influenza virus | Enveloped | Negative-sense ssRNA | 3.6 log decrease (UVA severity 0.1 mW/cm²) | 4 h | Adhesion into high-touch settings to decrease the contamination from spreading | Nakano et al. (2013) |
| Solid-state coating | Feline calicivirus | Non-enveloped | Positive-sense ssRNA | 1.7 log reduction | 8 h | Disinfection of high-touch surfaces such as light switches, bed rails, door handles and disruption of organic contaminants | Moongrakset al. (2019) |
| Ag-doped solid-state coating | Influenza A | Enveloped | Negative-sense ssRNA | ≥ 4.17 log reduction (15 W UVA light at a distance of 35 cm) | 20 min | | |
| Additional inorganic antiviral substances | Modified gold NMs | Virus-like particles (VLPs), replicating human norovirus, GI.1 VLPs | Replicates non-enveloped | Virus TCID₅₀ = 0 of VLPs at 0.37 μg/mL with the application 0.083 μM AuCuS NMs | | Recommended as an antiviral agent | Broglie et al. (2015) and Imani et al. (2020) |
| | Multivalent gold NMs with sulfate ligands | HIV | Enveloped | Positive-sense ssRNA | Lower than twenty percent contamination rate of T-cells | 30 min | Construction of a remedial anti-HIV system | Imani et al. (2020) |
| | Silica NMs in coating | Influenza A/PR/8/34 (H1N1) | Enveloped | Negative-sense RNA | Virus TCID₅₀ = 0 following incubation of virus suspension on surface | 30 min | Usage as a microbicidal coverage | Imani et al. (2020) |

*HIV* human immunodeficiency virus, *TCID₅₀* median tissue culture infectious dose
sulfur and phosphate groups to interrupt the cell membrane. Besides, silver ions generate ROS (Reactive Oxygen Species) inside the cells, providing significant antiviral activity (Imani et al., 2020).

**Zinc** The antiviral mechanisms of zinc are based on interference with the replication of the virus, such as inactivation of the free virus, suppression of viral uncoating, transcription of the viral genome, translation of viral proteins, and the process of the polyprotein (Scott A Imani et al., 2020; Read, 2019).

**Copper** In general, viruses are more susceptible than fungi and bacteria to copper by the lack of repair mechanisms (Borkow, 2012). The viral genome is targeted by copper, especially a gene encoding VPg (viral-genome-protein-linked, a viral protein essential for viral infectivity) leading to a gene copy number reduction (Vincent et al., 2017). Moreover, ROS formation contributes to the death of the cell via interaction with viral envelope or capsid (Imani et al., 2020).

**TiO2** The antiviral mechanism of TiO2 is based on electron/hole generation, absorption of light, and the oxidation of organic matter via ROS, which disrupts the lipid membrane and genetic materials, eventually leading to viral inactivation (Imani et al., 2020).

Since the initiation of the COVID-19 epidemic, new disinfectants and antiseptics formulations are being developed to limit disease transmission. As aforesaid, one of these changes is the use of NMs in their formulations (Abd Elkodous et al., 2020).

The action mechanism of NMs against the COVID-19 virus could be classified in distinct stages, before and after the viral entry inside the host cell (Fig. 1). Various kinds of NMs, like polymeric or virus-like NMs (Abd Elkodous et al., 2020), can inhibit the entrance of the virus inside the host cell by preventing it from attaching to the angiotensin-converting enzyme 2 (ACE2), which is the host cell receptor or the spike protein of the virus, through which the virus penetrates via the clathrin-mediated endosomal pathway (Almasi & Mohammadi Panah, 2020). The spike protein NMs of virus can inhibit the viral entry or provoke the immune system to produce antibodies against it. Moreover, liposomes and nanoemulsions could break down the lipid bilayer envelope, which destroys its structure. Inorganic NMs could also produce extracellular ROS to kill viruses. Once the virus enters the host cell, Nanomaterials could provoke ROS, improve the propagation of lymphocytes, cytokines overexpression (IL-1B), and the generation of neutralizing (IL-4, IL-5, and IL-13) or opsonizing (C4b, IgE, C3b, and IgG) antibodies via Th1 or Th2 immune reactions, respectively (Abd Elkodous et al., 2020).

## Approved Nanomaterial-Based Disinfectants

The antimicrobial activity of NMs depends on numerous factors, including (i) size of the NMs, since there is an optimum size that results in optimum antimicrobial activity because of the quantum size effect (Morones et al., 2005). The size difference between the NMs (10⁻⁹ m) and microorganisms (10⁻⁶ m) favors the antimicrobial action because some NMs can penetrate through the cell membrane. (ii) the shape of the NMs, since the more faceted the particle, the greater its antimicrobial efficiency due to more outstanding adhesion and contact with microorganisms (Cacciatore et al., 2020; Pal et al., 2007). (iii) surface charge, since the electrostatic interactions are favored when the NM has positive zeta potential as microorganisms present negatively charged bacterial wall. (iv) microbial sensitivity to NMs, since the organisms have different sensitivity due to their morphology (Cacciatore et al., 2020). Some of the approved disinfectants containing NMs as the main component are shown in Table 3.

## Nanomaterials with Antiviral Activity Against SARS-CoV-2

As mentioned in previous sections, the main NMs with antiviral coronavirus features are Quantum dots, synthetic virus-like particles, nanostructured lipid carriers, polymeric nanoparticles, carbon nanotubes, carbon dots, metal nanoparticles, nanostars, and magnetic nanoparticles (Table 4). The effect of Lipid Nanoparticles (LNP) and Virus-Like Particles (VLP) on SARS-CoV-2 have often been investigated in cell line and animal models including HEK 293 T, HeLa, Vero E6, and Freestyle CHO-S cells and animal models like transgenic hACE2 mice, C57BL/6 mice, BALB/C mice, Rhesus macaques, and Syrian golden hamsters (Geng et al., 2021; Ma et al., 2020) (Table 4).

## Toxic Effects of Nanomaterials on Health

Nanotoxicity concerns are primarily raised by tiny dimensions of nanotechnological NMs and are secondly correlated to type and duration of exposure, NM penetration depth, preferential localization, and local delivery and/or systemic translocation (Baroli, 2010). Studies have shown that NMs may provoke the fragmentation of chromosomes, DNA strand breakage, point mutations, and modifications in gene expression (Singh et al., 2009). The toxicological studies of NMs so far have shown that the entry of NMs through inhalation, ingestion, and skin is of utmost importance, respectively (Laux et al., 2018). Repeated application of
Antiseptics can bring along the penetration of NMs through inhalation and skin. The entrance of NMs into the cells are demonstrated in Fig. 2.

Before any toxicological trial, a comprehensive and precise characterization of the contents of the nano-based antiseptics/disinfectants is essential. Duke et al. has proposed a three-stage solution for determining the properties of NMs, which includes (I) appearance properties of the composition like size, morphology, and surface area (II) dispersion properties including aggregation or agglomeration, and (III) interface of nano-bio (Laux et al., 2018).

### Skin Adsorption

The skin is the most extensive (~10%) body part, which has a pivotal protective function (Crosera et al., 2009). The epidermis has a complicated structure consisting of composite physical and chemical systems and barriers at the nano- and micro-scale that, all together, form what is generally referred to as the defensive barrier.

Based on physicochemical features and integrity of barrier, NMs can enter the skin in four ways, including intracellular, extracellular, and two transappendageal via follicles of hair and sweat glands (Crosera et al., 2009). Sometimes skin exposure to NMs is intentional, such as dispersion of a liquid or creamy fluid (sunscreens having titanium or zinc oxides) or textiles (antimicrobial gauzes containing AgNPs) (Baroli, 2010) even though, allergic reactions also occur due to this penetration. Studies with macroscopically non-compromised skin showed that nanotechnological NMs mainly accumulate in SC (stratum corneum) and HF (hair follicle) infundibulum (Table 5). Even small permeation of agents inside the superficial strata of SC may lead to fatal reactions (Baroli, 2010). Figure 3 has been shown that NMs could induce cytotoxicity, genotoxicity, endothelial activation, and impairment of NOS signaling.

### Epigenetic Effect

Inappropriate regulation of cellular epigenetic mechanisms can be deleterious to health making it a necessity to analyze the effect of NM exposure on epigenetic pathways. The mechanisms are methylation and hydroxymethylation of DNA, posttranslational adjustment of histones tails, remodeling of chromatin, methylation of RNA, and non-coding RNA. Epigenetic modifications, which can change in response to specific cellular and environmental status, could be permanent or even passed on to later generations (Table 6). Since these modifications play crucial roles in regulating various cellular activities like gene expression, DNA replication, and recombination, they could affect exposed people and their next generation (Sierra et al., 2016; Stoccoro et al., 2013) [52].

### Cell Accumulation

NMs are being used due to their novel features, while nanotoxicological studies are relatively neglected. NMs could...
enter the mucosal membrane by inhalation, and NMs lighter than 10 μm could rapidly penetrate the respiratory system. The extent of cellular destruction depends on the size of NMs, which means the smaller the NMs, the stronger their damage (Rai et al., 2020).

These NMs can accumulate in alveoli and cause inflammation in the lungs. Also, repeated exposure to them induces alveolar cell injuries, penetrates the blood vessels, and could be transmitted to other organs by systemic circulation (Rai et al., 2020).

Because there is no mechanism in the body to exclude the majority of NMs, NMs with low-solubility that have accumulated in the tissues and cells can remain for a longer duration. Metal NMs also reduce the viability of the cells and induce ROS, which leads to oxidative stress and cellular irreversible damages. The accumulated ROS inside the cell communicates with the cellular protein machinery and consequently can modify whole cellular processes, destroying mitochondria and nuclear DNA, leading to apoptosis (Cioffi & Rai, 2012; Rai, Ashok, et al., 2020; Rai, Bonde, et al., 2020).

**Biological Accumulation**

Detrimental effects of NMs on biology, particularly their toxic effects on plants, are among the most frequent study cases. NMs like carbon could even repress the plant nutrients absorption; others could restrain the content of plant protein, carotenoids, and chlorophyll. NMs can also be transferred from roots to leaves, entering the food chain. Generally, bio-accumulation factor (BAF) is a chemical mass per kg biomass in an organism to that in water (Hou, et al., 2013). As an example, Ag negatively affects the remediation process of the plant, ZnO, even at low concentration has a toxic effect
on Hydilla verticillata and Phragmites, and Ag, CeO2, Co, and Ni influence Ocimum basilicum L’s fresh weight (Zhu et al., 2019).

Environmental Impact of the NM Containing Wastes

Despite the progress mentioned earlier in NM technology, data on the potential impacts of NMs on personal health is insufficient. The remediation process of NMs is essential because they are not detectable and may have long-term destructive effects on the environment by their persistent presence in the environment. Although some approaches such as green nanoscience have been introduced to decrease the detrimental outcomes of NMs on health and the ecosystem, their environmental discharge must be avoided (Iavicoli et al., 2014; Kabir et al., 2018).

NMs with various shapes as free NMs, functionalized NMs, aggregates, or embedded in a matrix can be found in the ecosystem (Nowack & Bucheli, 2007). The fate of NMs in environmental conditions is related to their interactions with different contaminants and their physicochemical features (Kabir et al., 2018; Maiti et al., 2016). According to their type, they may be discharged into the air and persisted in aerosols and the soil, sediment, and surface water for a long time or absorbed by organic molecules or biological systems. Therefore, their accumulation can cause an

Table 3 The commercial NM-based products approved for surface or skin disinfection (https://statnano.com/)

| Commercial name                          | Usage                                             | Type of NMs | Company               |
|-----------------------------------------|---------------------------------------------------|-------------|-----------------------|
| NPS 100 & NPS-200                       | All types of fabrics, Shoes, Air/Water Purification Filters | Silver NMs | NANOBIIZ.PL Ltd       |
| Copper Dispersion Antibacterial Coating | Hospitals, Personal protective equipment, Surface Coatings | Copper NMs | Nanoshel LLC          |
| Klenz Shoes Sanitizer                   | Shoes sanitizer                                   | Silver NMs | Maha Corporation      |
| Gel antiseptic nanoparticulate silver   | Hand sanitizer                                    | Silver NMs | M9 Ltd                |
| Soap antibacterial facial and body treat- | Skin sanitizer                                    | Silver NMs | M9 Ltd                |
| ments with NMs of silver                |                                                   |             |                       |
| Nanoever Dishwashing detergent          | Dishwashing detergent                             | Silver NMs | Nanoget Co., Ltd      |
| Nanoever Disinfectant Spray             | Surface disinfectant/household goods sanitizer    | Silver NMs | Nanoget Co., Ltd      |
| Nanoever Laundry detergent              | Laundry detergent                                 | Silver NMs | Nanoget Co., Ltd      |
| Nanoever Mouth wash                     | Mouth wash                                        | Silver NMs | Nanoget Co., Ltd      |
| Sanitizer (hand carry)                  | Hand sanitizer                                    | Essential oils nanoemulsion | Shepros SDN. BHD |
| Defender Series-Respirator masks        | Mask disinfectant                                 | Silver and copper NMs | Nexera Medical-Canada |
| MVX Nano Mask                           | Mask disinfectant                                 | Titanium and silver zeolite NMs | MVX Prime Ltd |

Table 4 Nanomaterials with anti-coronavirus activity (Carvalho & Conte-Junior, 2021)

| NMs                        | Size                        | Shape                   | Effective dose     | Application                      |
|----------------------------|-----------------------------|-------------------------|--------------------|----------------------------------|
| Ag                         | Colloids: 10 nm             | Spherical               | 3.125–12.5 (µg/mL) | Antiviral therapy                |
| Tellurium nanostars        | Nanoparticles: < 20 nm      | Spherical               | 15 (µg/mL)         | Antiviral agents                 |
| TiO2 Nanoparticles         | 57 nm                      | Triangular star shape   | 300 (mg/mL)        | Self-cleaning surfaces           |
| Gold nanoparticles         | Not Reported               | Predominantly spherical | Not Reported       | Antiviral agents                 |
| Nano-sized formazans       | 23.75 ± 7.16 nm            | Formazan analogs by dithizone and α-haloketones reaction | Not Reported | Antiviral agents                 |
| Carboxyl quantum dots      | 20 nm                      | Spherical               | Not Reported       | Antiviral agent                  |
| L-PLGA                     | Not Reported               | Not reported            | Not Reported       | Antiviral therapy                |
| Silica-copper nanoparticles| Not Reported               | Spherical               | Not Reported       | Superhydrophobic self-cleaning surfaces |
| Polymeric nanoparticles    | Not Reported               | Not reported            | Not Reported       | Antiviral drug                   |
| ZnS-NPs                    | 3.8 nm                     | Spherical               | 0.1 mM             | Antiviral drugs                  |
| Silver-sulfide nanoclusters| 5.3 nm                     | Spherical               | Not Reported       | Antiviral drugs                  |
Ecotoxicological risk, biodegradation, or bioaccumulation in the food chain. In this part, we present the destiny of NMs in various environmental matrices.

**Air** There is not enough information concerning the environmental destiny of NMs, particularly after releasing into the atmosphere. In all phases of the life cycle of NMs (e.g. generation, transportation, storage, and usage), it might swiftly release into the ambient atmosphere (Kabir et al., 2018).

**Soil** Soil is a multilayer matrix and complicated interface among several materials and organisms. Since NMs have a large surface area, NMs can adhere to the particles of the soil. Moreover, large aggregates of NMs through precipitation and purification could be immobilized in small holes. Plants could absorb and transport NMs from the soil, thereby affecting the germination and plant growth (Hong et al., 2014; Khodakovskaya et al., 2009).

**Water** NMs could immediately enter the aquatic ecosystems through industrial discharge, dumping of wastewater, and surface runoff from soils (Butley et al., 2011; Kabir et al., 2018). Several factors such as aggregation, distribution, reactions among different elements, organic matter, and aerobic, anaerobic, and abiotic degradation may influence the concentration of NMs in aquatic ecosystems. Exposure of NMs to aquatic organisms poses many detrimental consequences, such as DNA fragmentation, oxidative pressure, and growth reduction (Kabir et al., 2018).

**Concluding Remarks**

Numerous reports are available demonstrating remarkable bioactivities of NMs, including antiviral activity against RNA viruses, due to their unique physicochemical properties. Due to its potent antiviral nature, specific NMs have been used to prepare various nano-based disinfectants and antiseptics.

In this report, the latest advancement in studying NMs and disinfectants are discussed from three perspectives: positive impacts, toxicity, and their mechanisms of action. The type of nanomaterial that has been studied for augmentation of antiseptics and disinfectants included polymeric, self-assembling proteins, inorganic and peptide-based among which inorganic nanomaterial are more frequently studied and applied for these purposes.

Despite this remarkable antiviral effect at low concentration, there is a serious consequence in the long-term application of nanomaterial in the antiseptic formulation which has been underestimated. Although NMs have molecular targets...
Table 5  The skin absorption studies of NMs

| Composite (Size nm) | Module of the study | Outcome | Reference |
|---------------------|---------------------|---------|-----------|
|                     | In vitro            | In vivo |           |
| Polystyrene NMs     | Vertical diffusion cells by whole-width the skin of ear of porcine | Not Reported | The aggregation of NMs in follicular openings | Alvarez-Román et al. (2004) |
| Titanium Dioxide    | Human volunteers—tape stripping | Diffusion cells by human epidermis plus cultivated skin | Microfine titanium dioxide entered through the follicles of hair | Bennat and Müller-Goymann (2000) |
| Titanium Dioxide (20) | Human volunteers—tape stripping | Static diffusion cells with human skin | Titanium dioxide could not infiltrate into the follicles of hair | Mavon et al. (2006) |
| Zinc Oxide (15 to 40) | Not Reported | Franz diffusion cells with human epidermis | There were no NMs in the deeper layer of corneum or epiderm | Cross et al. (2007) |
| Silver (25)         | Not Reported | Full-thickness human epidermis with Franz diffusion cells | Penetration may occur via damaged skin | Larese et al. (2009) |
| 4 various formulations comprising Titanium Dioxide | The biopsies of pig skin | Not Reported | Penetration of NMs within granulosum layer through intercellular area | Menzel et al. (2004) |
| Ellipsoid (4.6) and Spherical QD (12 x 6) | Not Reported | Porcine skin within flow-through cells | Quantum Dots of various forms and surface coatings may enter intact skin in an appropriate dosage (62.5 pmol per cm²) | Ryman-Rasmussen et al. (2006) |
| Gold (15, 102, and 198) | Not Reported | Franz cells with ratepidermis | The permeability and diffusion coefficient decrease with the increase in the size of gold NMs | Sonavane et al. (2008) |

Fig. 3  Schematic illustration of toxic effects of NMs on endothelial cells. NMs could provoke cytotoxicity (necrosis, apoptosis), genotoxicity (DNA destruction), the activation of endothelial (adhesion molecules, the adhesion of monocyte), and NOS dysfunction (overproduction of ROS) in endothelial cells. LDH Lactate dehydrogenase, NOS Endothelial nitric oxide synthase (Zielińska et al., 2020)
and remarkable antiviral activity to inactivate several viral pathogens, these compounds have toxic effects on social health and the ecosystem due to the accumulation of their wastes in the environment and the inability to eliminate or detoxify them from the ecological cycles.

Some investigations have shown that these nanoparticles can produce critical impairment in respiratory sites and toxic effects on the skin, and even could weaken lung function. The oxidative stress, inflammation, fibrosis, and genotoxicity are among pathological consequences of the repeated exposure of human cell lines to nanomaterial (Imani et al., 2020).

**Table 6 Epigenetic effects of some NMs and their current applications**

| NMs          | Common applications                                                                 | Epigenetic effect                                      | NM properties | Reference                  |
|--------------|--------------------------------------------------------------------------------------|--------------------------------------------------------|---------------|---------------------------|
| Silver       | Antimicrobial agent to prevent wound infection and formation of dental plaque biofilms | Reduced histone methylation (H3K4me3 and H3K79me1)    | Spherical 25–30, Negative | Qian et al. (2015)         |
|              | Ultrasensitive recognition of biomarkers                                             | Modified DNA methylation miRNA expression changes     | ND 3–20       | 28 mV | Mytych et al. (2017)            |
|              | Food covering for longer shelf life Anti-caking matter in powder goods like salt     | Modified HDAC activity                                 | Spherical 10, 25–30, and 80 ND | Braydich-Stolle et al. (2010) |
| Gold         | Transfer carriers in biomedicine                                                     | The changes of expression on mi-RNA                   | Spherical 40, 100 ND | Balansky et al. (2013)      |
|              | Contrast factors in imaging techniques                                              | Condensation and reconstitution of chromatin expression changes of mi-RNA | ND 20 ND | Ng et al. (2011)               |
| Quantum dots | Imaging based on Fluorescence                                                        | Deacetylation of Histone                               | ND ND ND      | Choi et al. (2008)          |
|              | Anticancer purpose applying photodynamic UV or photothermal therapy                 | Modifications of Histone                              | ND 3.4        | Negative | Conroy et al. (2008)          |
| Silica       | Lighter, more durable, and powerful than concrete, steel, stick, and crystal         | Global genomic hypomethylation and reduced methyltransferase machinery | ND 15 ND | Gong et al. (2010)          |
|              | Nanosensors could be used to detect conversions caused via external agents           | Hypermethylation and inactivity of poly ADP-ribose polymerase 1 (PARP-1) promoter | ND 15 ND | Gong et al. (2012)          |
| Titanium oxide | Sunscreen and cosmetics lotions                                                        | PARP-1 promoter hypermethylation                        | Spherical 22 | 29.8 mV | Choi et al. (2008)          |
|              | Bleaching agents applied in soups, several kinds of toothpaste, and wet wipes       | Changed the methylation machinery expression levels and long interspersed nuclear elements 1 (LINE1) and ALU* expression levels | Spherical 21.0 | Negative | Lu et al. (2016)            |
|              | Remediation (elimination of organic contaminants of soil and water)                 | Dysfunction of methylation cycle                       | ND 10–100 ND | Tucci et al. (2013)         |
| Copper oxide | Doping substances in semiconductors                                                   | Global DNA and transposable elements methylation changes | Spherical 58.7 | Negative | Lu (2016)                   |
|              | Chemical sensors                                                                      | Hypermethylation of Alu                                 | Spherical 58.7 | Negative | Lu et al. (2016)            |

**ND** not defined, **HDAC** histone deacetylase, **ALU**, *Arthrobacter luteus*. 

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and remarkable antiviral activity to inactivate several viral pathogens, these compounds have toxic effects on social health and the ecosystem due to the accumulation of their wastes in the environment and the inability to eliminate or detoxify them from the ecological cycles.

Some investigations have shown that these nanoparticles can produce critical impairment in respiratory sites and toxic effects on the skin, and even could weaken lung function. The oxidative stress, inflammation, fibrosis, and genotoxicity are among pathological consequences of the repeated exposure of human cell lines to nanomaterial (Imani et al., 2020).
As a result, the prevalent commercialization and usage of NM-based disinfectants during this pandemic can have long-lasting detrimental effects on human health and other animals, environmental microorganisms and plants in the ecosystem (Hossain et al., 2014; Imani et al., 2020; Zhu et al., 2019). According to multiple studies, these formations are influencing the environment by several mechanisms, e.g. (i) by raising the non-decomposable contamination level of air, soil, and water, (ii) through environmental accumulation, and (iii) via changing the life-cycle of living systems in the ecosystem (Kabir et al., 2018).

**Future Perspective**

The effect of NMs exposure is starting to be analyzed, and to reveal the full impact of such disclosure on human physiology, a great deal of effort needs to be made. However, precise prediction can calculate the toxicity potential of nanomaterial-based antivirals and decrease their long-term side effects. This prediction can be also achieved by a machine learning approach like the other lines of applications for control of SARS-CoV-2 (Sadeq et al., 2021).

Besides, the principal focus of later studies is to expand biocompatible and biodegradable NMs without any cytotoxicity, developing new techniques for nanotoxicology analysis, defining the level of exposure and level of discharge for different nanoparticles, understanding the biological effects of NMs in the environment.

Considering the ecological destiny and the possible consequence of NM on ecotoxicity, it appears essential to recognize the modifications of NMs during their diverse life cycle steps since they are capable of changing the toxic properties of substances in different conditions.

Moreover, NMs are extremely reactive constructions; they may interact with different contaminants and make more/less virulent forms. So investigations should also be included in the forthcoming analysis.

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**Declarations**

**Conflict of interest** There are no conflicts to declare.

**References**

Abbasi, E., Aval, S. F., Akbarzadeh, A., Milani, M., Nasrabadi, H. T., Joo, S. W., Hanifehpour, Y., Nejati-Koshki, K., & Pashaeei-Asl, R. (2014). Dendrimers: Synthesis, applications, and properties. Nanoscale Research Letters, 9(1), 1–10. https://doi.org/10.1186/1556-276X-9-247

Abd Eldokous, M., El-Sayyad, G. S., & Abdel-Daim, M. M. (2020). Engineered nanomaterials as fighters against SARS-CoV-2: The way to control and treat pandemics. Environmental Science and Pollution Research. https://doi.org/10.1007/s11356-020-11032-3

Almasi, F., & Mohammadipanah, F. (2020). Hypothetical targets and plausible drugs of coronavirus infection caused by SARS-CoV-2. Transboundary and Emerging Diseases, 68, 1–15. https://doi.org/10.1111/tbed.13734

Alvarez-Román, R., Naik, A., Kalia, Y. N., Guy, R. H., & Fessi, H. (2004). Skin penetration and distribution of polymeric nanoparticles. Journal of Controlled Release, 99(1), 53–62. https://doi.org/10.1016/j.jconrel.2004.06.015

Balansky, R., Longobardi, M., Ganchev, G., Iltcheva, M., Nedyalkov, N., Atanasov, P., Toschkova, R., De Flora, S., & Izzotti, A. (2013). Transplacental clastogenic and epigenetic effects of gold nanoparticles in mice. Mutation Research - Fundamentals and Molecular Mechanisms of Mutagenesis, 751–752(1), 42–48. https://doi.org/10.1016/j.mrfmmm.2013.08.006

Baroli, B. (2010). Skin absorption and potential toxicity of nanoparticulate nanomaterials. Journal of Biomedical Nanotechnology, 6(5), 485–496. https://doi.org/10.1166/jbnn.2010.1147

Batley, G. E., Kirby, J., & McLaughlin, M. (2011). Fate and risks nanomaterials in aquatic and terrestrial environments. Accounts of Chemical Research, 46, 854.

Bennat, C., & Müller-Goymann, C. C. (2000). Skin penetration and stabilization of formulations containing microfine titanium dioxide as physical UV filter. International Journal of Cosmetic Science, 22(4), 271–283. https://doi.org/10.1046/j.1467-2494.2000.00009.x

Borkow, G. (2012). Using copper to fight microorganisms. Current Chemical Biology, 6(2), 93–103. https://doi.org/10.2174/18723112801254723

Bragdich-Stolle, L. K., Lucas, B., Schrand, A., Murdoch, R. C., Lee, T., Schlager, J. J., Hussain, S. M., & Hofmann, M. C. (2010). Silver nanoparticles disrupt GDNF/Fyn kinase signaling in spermatogonial stem cells. Toxicological Sciences, 116(2), 577–589. https://doi.org/10.1093/toxsci/kfp148

Broglie, J. J., Alston, B., Yang, C., Ma, L., Adcock, A. F., Chen, W., & Yang, L. (2015). Antiviral activity of gold/copper sulfide core/shell nanoparticles against human norovirus virus-like particles. PLoS ONE, 10(10), e0141050. https://doi.org/10.1371/journal.pone.0141050

Cacciatore, F. A., Brandelli, A., & Malheiro, P. D. (2020). Combining natural antimicrobials and nanotechnology for disinfecting food surfaces and control microbial biofilm formation. Critical Reviews in Food Science and Nutrition. https://doi.org/10.1080/10408398.2020.1806782

Carvalho, A. P., & Conte-Junior, C. A. (2021). Recent advances on nanomaterials to COVID-19 management: A systematic review on antiviral/virucidal agents and mechanisms of SARS-CoV-2 inhibition/inactivation. Global Challenges, 5(5), 2000115. https://doi.org/10.1002/gch2.202000115

Castro-Mayorga, J. L., Randazzo, W., Fabra, M. J., Lagaron, J. M., Aznar, R., & Sánchez, G. (2017). Antiviral properties of silver nanoparticles against norovirus surrogates and their efficacy in coated polyhydroxyalkanoates systems. LWT - Food Science and Technology, 79, 503–510. https://doi.org/10.1016/j.lwt.2017.01.065
Food and Environmental Virology (2022) 14:105–119

Choi, A. O., Brown, S. E., Szyf, M., & Maysinger, D. (2008). Quantum dot-induced epigenetic and genotoxic changes in human breast cancer cells. Journal of Molecular Medicine, 86(3), 291–302. https://doi.org/10.1007/s00109-007-0274-2

Cioffi, N., & Rai, M. (2012). Nano-antimicrobials: Progress and prospects. Springer-Verlag.

Conroy, J., Byrne, S. J., Gun’ko, Y. K., Rakovich, Y. P., Donegan, J. F., Davies, A., Kelleher, D., & Volkov, Y. (2008). CdTe nanoparticles display tropism to core histones and histone-rich cell organelles. Small (weinheim an Der Bergstrasse, Germany), 4(11), 2006–2015. https://doi.org/10.1002/smll.200800088

Cross, S. E., Innes, B., Roberts, M. S., Tsuzuki, T., Robertson, T. A., & McCormick, P. (2007). Human skin penetration of sunscreen nanoparticles: In-vitro assessment of a novel micronized zinc oxide formulation. Skin Pharmacology and Physiology, 20(3), 148–154. https://doi.org/10.1159/000098701

Dhalak, S., Hiremath, J., Bondra, K., Lakshmanappa, Y. S., Shyu, D. L., Ouyang, K., Kang, K. I., Binjawadagi, B., Goodman, J., Tabyнов, K., & Krakowka, S. (2017). Biodegradable nanoparticle delivery of inactivated swine influenza virus vaccine provides heterologous cell-mediated immune response in pigs. Journal of Controlled Release, 247, 194–205. https://doi.org/10.1016/j.jconrel.2016.12.039

Eom, H. J., Chatterjee, N., Lee, J., & Choi, J. (2014). Integrated mRNA and micro RNA profiling reveals epigenetic mechanism of differential sensitivity of Jurkat T cells to AgNPs and Ag ions. Toxicology Letters, 229(1), 311–318. https://doi.org/10.1016/j.toxlet.2014.05.019

Francica, J. R., Lynn, G. M., Richard Laga, M., Joyce, G., Ruckwardt, T. J., Morabito, K. M., Chen, M., et al. (2016). Thermostresponsive polymer nanoparticles co-deliver RSV F trimers with a TLR-7/8 adjuvant. Bioconjugate Chemistry, 27(10), 2372–2385. https://doi.org/10.1021/acs.bioconjchem.6b00378

Geng, Q., Tai, W., Baxter, V. K., Shi, J., Wan, Y., Zhang, X., Montgomery, S. A., et al. (2021). Novel virus-like nanoparticle vaccine effectively protects animal model from SARS-CoV-2 infection. PLoS Pathogens, 17(9), 1–20. https://doi.org/10.1371/journal.ppat.1009807

Gong, C., Tao, G., Yang, L., Liu, J., Liu, Q., Li, W., & Zhuang, Z. (2012). Methylation of PARP-1 promoter involved in the regulation of nano-SiO2-induced decrease of PARP-1 MRNA expression. Toxicology Letters, 209(3), 264–269. https://doi.org/10.1016/j.toxlet.2012.01.007

Gong, C., Tao, G., Yang, L., Liu, J., Liu, Q., & Zhuang, Z. (2010). SiO2 nanoparticles induce global genomic hypomethylation in HaCaT cells. Biochemical and Biophysical Research Communications, 397(3), 397–400. https://doi.org/10.1016/j.bbrc.2010.05.076

Gurunathan, S., Qasim, M., Choi, Y., J. D., T., Park, C., Hong, K., Kim, J. H., & Song, H. (2020). Antiviral potential of nanoparticale delivery of inactivated swine influenza virus vaccine provides heterologous cell-mediated immune response in pigs. Journal of Controlled Release, 247, 194–205. https://doi.org/10.1016/j.jconrel.2016.12.039

Hodek, J., Zajíčková, V., Lovetinská-Šlamborová, I., Stibor, I., Müllerová, J., & Weber, J. (2016). Protective hybrid coating containing silver, copper and zinc cations effective against human immunodeficiency virus and other enveloped viruses. BMC Microbiology, 16(1), 1–13. https://doi.org/10.1186/s12866-016-0675-x

Hondog, J., Peralta-Videa, J. R., Rico, C., Sahi, S., Viveros, M. N., Bartoń, J., Zhao, L., & Gardea-Torresdey, J. L. (2014). Evidence of translocation and physiological impacts of foliar applied CeO2 nanoparticles on cucumber (Cucumis Sativus) plants.
Zhu, Y., Liu, X., Yali, Hu., Wang, R., Chen, M., Jianhua, Wu., Wang, Y., Kang, S., Sun, Y., & Zhu, M. (2019). Behavior, remediation effect and toxicity of nanomaterials in water environments. *Environmental Research, 174*, 54–60. https://doi.org/10.1016/j.envres.2019.04.014

Zielińska, A., Santos, D., Campos, J. R., Santini, A., Severino, P., Shimojo, A. A. M., Souto, S. B., & Souto, E. B. (2020). Cellular and molecular toxicology of nanoparticles. *Handbook of Materials for Nanomedicine*. https://doi.org/10.1201/9781003045151-11

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