



Review Article

Copper Nanomaterials Derived Preventive Technologies for COVID-19 Pandemic: A Review

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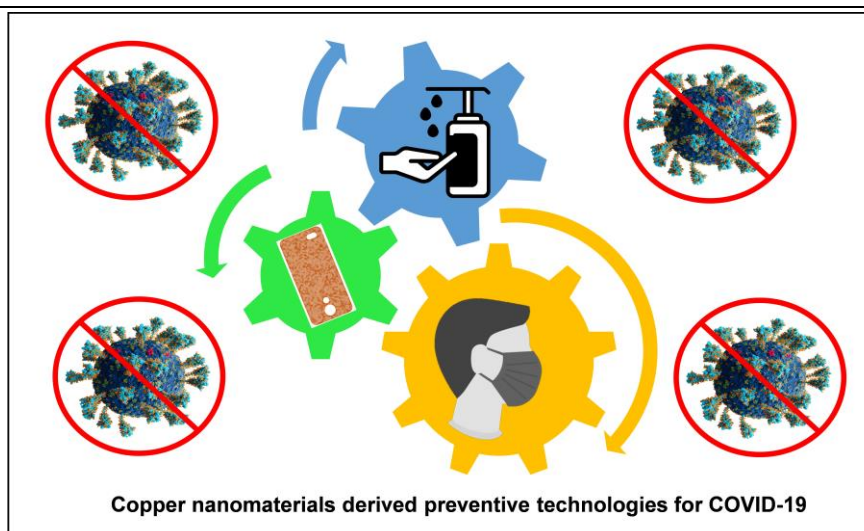
Hand sanitizer

Mobile phone case

ABSTRACT

Copper has been well-known for its antimicrobial properties, killing microorganisms and viruses. Scientific evidence attests the potential of copper and copper nanoparticle's derived surfaces to combat microorganisms and viruses in the surrounding environment. Coronavirus disease 2019 has affected people's life and undermined the economy worldwide. There are many preventive measures in practice to combat coronavirus disease as per local, national and/or World Health Organization (WHO) guidelines. However, with reference to the antibacterial and antiviral potential of copper and copper nanoparticles, respiratory face masks, phone cases and hand sanitizers are developed by incorporating copper and copper nanoparticles and made available in pandemic time. In this review, copper and copper nanoparticle's derived preventive technologies are summarised and discussed in detail.

GRAPHICAL ABSTRACT



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Introduction

The enormous challenge faced by humankind is the introduction of new microbial infections every day and its further consequences, including the death of human beings [1]. Coronavirus 2 (SARS-CoV-2) was detected in Wuhan, China, and has spread worldwide [2]. Coronavirus disease 2019 (COVID-19) was declared as pandemic disease in march 2020 by World Health Organization [3]. The outbreak of COVID-19 has killed more than 2.6 million people across the globe by February 2021 [4-5]. At present, COVID-19 pandemic has drastically affected public health and the economy worldwide. To overcome the COVID-19 pandemic situation, the whole world is in need of all possible preventive measures and permanent solutions as soon as possible.

Recent preventive measures against COVID-19 include social distancing, isolating the infected patients, the use of respiratory face masks, regular hand wash with soap, vaccination of non-infected people, development of more effective vaccines for prevention of COVID-19, the use of hand sanitizers and disinfectants [6-9]. Nowadays, all disinfectants, which are used to kill bacteria and viruses sitting on various object surfaces, are chemically derived and are typically based on sodium hypochlorite (bleach) or alcohol [10-11]. Moreover, the antibacterial effect of these disinfectants is not long lasting; they just clean the surface for that instant. The use of hand sanitizers has dramatically increased during COVID-19 pandemic [12]. The increased use of alcohol based hand sanitizers may lead to various health issues related to respiratory systems, skin etc. [13]. Therefore, there is a prime need to produce daily objects, which are durable, antibacterial and antiviral for minimizing the risk of infectious diseases like COVID-19 in future.

Since ancient times, few metals have been known for their antibacterial and antiviral

properties. Most often copper (Cu) bowls or silver plating was in use to minimize the spread of infectious disease [14-15]. Metallic nanoparticles encompass unique physicochemical properties because of their size at nanoscale resulting in high specific surface area, which facilitate their interaction with viruses and other microorganisms. Metal and metal oxide nanoparticles of copper, titanium, gold, zinc, silver have been proposed as antiviral agents [16]. In particular, antiviral activity of copper is well known [17-20]. Copper cations are capable of capturing negatively charged bacteria and viruses, also they are capable of penetrating into virus-infected bacteria. This activity inhibits viral replication and infection [21]. Copper nanoparticles (NPs) are advantageous over silver or zinc oxide metal NPs due to their enhanced antibacterial and antiviral activity [22].

The spread of COVID-19 viral infection is transmitted via aerosols generated from coughs or vocalization of infectious people [23-24]. Since the beginning of this epidemic, the use of face masks and hand sanitizers has significantly increased, resulting in a scarcity of personal protective equipment (PPE) [25, 12]. However, for improved performance, copper and copper nanoparticles were widely incorporated in these PPE's, during COVID-19 pandemic. In this review, CuNPs based products (PPE's) used during COVID-19 pandemic are summarized and discussed in detail.

Discussion

Antiviral activity of CuNPs for prevention of COVID-19

Copper is needed as an essential trace element for human body [26]. Copper exposure to human coronavirus 229E fractured the viral genomes and permanently transformed virus morphology, including fragmentation of envelope and diffusion of surface spikes [27]. Cu alloys or Cu/Zn brasses with low concentration of Cu(I)

and Cu(II) moieties were reliable for the inactivation of coronavirus by generation of Reactive Oxygen Species (ROS) on alloy surfaces [28]. Copper based surfaces are highly sensitive to novel coronavirus which is accountable for COVID-19 pandemic [29]. SARS-CoV-1 requires papain-like protease-2 for its replication. In cell-based study, it has been found that Cu^{2+} hinders the growth of this papain-like protease-2 protein [30-31]. CuNPs and hydrophobic polymer based nanocomposite inhibit virus transmission in

three steps. Initially, virus droplets contact the hydrophobic surface in spherical shape with Cassie-Baxter wetting state. Secondly, droplets striking a superhydrophobic surface will either bounce back or roll-off from nanocomposite surface which suppress virus infection. Finally, traces of virus contaminating the nanocomposite surface are eradicated by CuNPs from the nanocomposite [32]. The schematic for COVID-19 virus eradication by nanocomposite of CuNPs and hydrophobic polymer is shown in Figure 1.

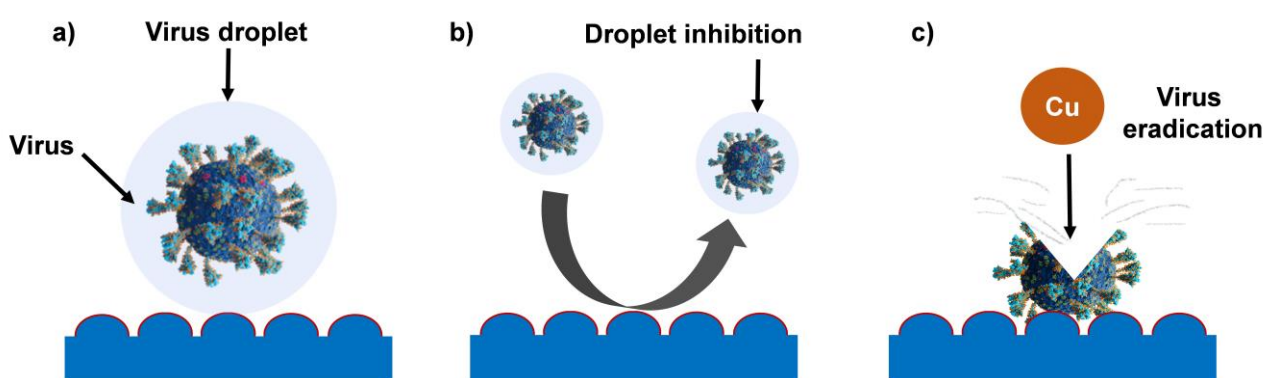


Figure 1. A schematic of COVID-19, Virus transmission preventing strategy: a) Virus interaction, b) infection inhibition, and c) virus eradication.

CuNPs derived respiratory face masks for prevention of COVID-19

For the ongoing COVID-19 pandemic, wearing a respiratory face mask is compulsory for everyone and not wearing a mask is punishable in most of the countries [33]. The wearing of masks is a preventive measure for outspread of the COVID-19 virus, exclusively for those infected patients, who may be symptomless, but transporting the virus without recognizing it [34]. There are some basic types of face masks that are used for protection against COVID-19, which include bandana, i.e. a triangle shape or square shape piece of cloth used to worn as a head or neck masking, homemade cloth mask, T-

shirt cloth based respiratory face mask, store procured respiratory cloth mask, filter based cloth mask, neck gaiters and balaclavas, surgical respiratory face masks, cone-style mask, N95 and other respirators [35]. Due to their low cost, high stability, and extensive antibacterial characteristics, Cu oxide nanoparticles are commonly employed in antibacterial products [36-37]. Considering the advantage of antibacterial and antiviral properties of Cu, there is a variety of respiratory face masks available in the market for protection against COVID-19. Table 1 below provides a list of commercial copper and CuNPs derived respiratory face masks available to use in COVID-19 pandemic and their features.

Table 1. List of commercial copper and CuNPs derived respiratory face masks available during COVID-19 pandemic and their features

No	Name of mask	Features	Ref.
1	Copper Compression Copper Infused Face Mask	- Cotton woven with copper and made up of four layers. - Washable and reusable. - Adjustable ear loops and nose bridge.	[38]
2	Copper infused organic cotton barrier face mask	- Organic materials based masks. - Made up of 17% copper strands woven with knitted fabric. - Both machine washed and reused.	[39]
3	Copper compression face mask	- High percentage (17%) of copper content. - Reusable.	[40]
4	FFP2 Certified Four- Layer Copper Face Mask	- Copper-infused fabrics to kill the bacteria, fungi and viruses in minutes of contact. - Copper treated.	[41]
5	Frido copper plus mask	- Washable and reusable respiratory face mask. - Made of breathable and stretchable fabric for ultimate comfort.	[42]
6	American giant face mask	- Non-medical grade masks is made with 100% cotton and also contain silver and copper.	[43]
7	Atoms everyday face mask	- Everyday use comfortable and breathable mask, made of out layer polyester blend. - Inner layer made of a copper-lined ionized quartz yarn which offers 84.6% filtration. - This mask made of pure copper	[44]
8	SUBHAG safe copper mask	- Has nose clip. - This is washable and reusable cloth mask made of melt blown fabric layer	[45]
9	Corp sanitizers copper self- sanitizing mask	- Self-sanitizing mask.	[46]
10	SUBHAG V Safe Mask	- Washable and reusable cloth mask. - Fabricated using melt blown fabric layer.	[47]
11	WONDERCHEF copper coated mask	- Copper coated respiratory face mask. - With melt blown fabric layer.	[48]
12	TKCK-Copper mask	- TKCK mask uses copper as core element to protect being washable and reusable, and last for six months. - Self-sterilising face mask, made of, copper oxide charged cotton.	[49]
13	CoProtex Self- sterilising cotton mask	- 98% of bacterial filtration efficiency. - Antimicrobial, antiviral, reusable and self-sanitizing mask.	[50]
14	Primeway P29 PU	- Non-toxic, anti-odour, and easy to breathe through mask. - Light, comfortable, breathable, antibacterial, and antiviral.	[51]

	Foam PM2.5 AirFilter	- Blocking and killing 99% viruses, germs and bacteria.	
	Antibacterial 2 Layer Featherlight Copper Mask	- The ability of being washed for 50 times and reused.	
		- Anti-fogging, water resistant, anti-odour and wrinkle free mask.	
		- More than 50 times washable and reusable mask.	
15	NSafe+ Mask	- Triple layer fabric filtration technology of mask provides extra protection to the user.	[52]
		- Having antiviral outer and middle layer which kills trapped virus including SARS-CoV-2.	

It was demonstrated that, copper oxide impregnation into disposable N95 respiratory mask (filter 95% of 0.3-micron size particles) provides potent anti-influenza biocidal properties in N95 respiratory mask, without hampering its physical barrier properties [53].

The design of N95 respiratory mask containing CuO particles, and four layers of protection, are shown in Figure 2. This N95 respiratory mask of US National Institute for Occupational Safety and Health (NIOSH) is also called test mask.

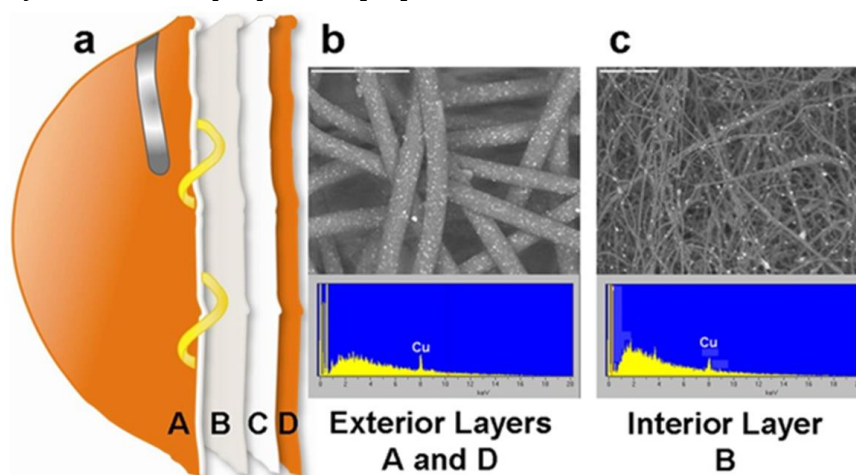


Figure 2. Schematic of test mask design with infused copper oxide: a) 2.2% Cu oxide particles (w/w) embedded spunbond polypropylene layers (A and D). Internal layer B is meltblown polypropylene containing 2.2% (w/w) Cu oxide and Internal layer C is polyester layer containing no Cu oxide particles. b) External layer (A) Scanning electronic micrograph and Energy dispersive X-ray analysis photograph. c) Internal layer (B) Scanning electronic micrograph and Energy dispersive X-ray analysis photograph. (Reproduced with permission from ref. 53 copyright 2010 Public Library of Science).

Considering inherent antibacterial and antiviral potential of copper metal, recently Hashmi et al., developed an antimicrobial breath mask with copper oxide loaded polyacrylonitrile (PAN) nanofiber membranes [54]. Vasilopoulos et al., developed graphene wrapped CuNPs which displayed admirable antibacterial activities against gram-negative and gram-positive

bacteria [55]. Maji et al., utilized silver and CuNPs in masks for COVID-19 virus protection [56].

Cu and CuNPs derived mobile phone case for prevention of COVID-19

In ongoing pandemic situations people tend to stay isolated from social gatherings and spend most of their time for using their smartphones.

On an average, smartphone users touch their phone for about 3-6 times per minute with exposure to over 25,000 bacteria per square inch. Relatively many mobile phones are dirtier than the average toilet flush handle. Phones are one of the culprits in disease transmission. Hazardous microorganisms can live on the phone

for a few hours to days and so, it necessitates to take due care while handling the phone [57]. As per online survey conducted, for analysing Cu based phone cases available in the market, two categories are found and they are summarised in Table 2.

Table 2. List of commercial Cu and CuNPs based phone cases available during COVID-19 pandemic and their features

No	Name of phone case	Features	Ref.
1	Aeris:The antimicrobial copper phone case	- On contact germ killing protect device from germs and germs drops. - Grippy and smooth feel with military grade drop safety.	[58]
2	Copp-The antimicrobial pure copper case for iPhone	-Fabricated with 100% recycled pure copper (99.90 %). -Naturally developing elegant patina.	[59]

CuNPs derived hand sanitizers for prevention of COVID-19

Alcohol-based sanitizers are widely used under current pandemic situation worldwide. Varieties of hand sanitizers are available with a variation of flavours. Alcohol evaporates quickly after its

application and leaving the user's skin unprotected. For sensitive skins of babies, alcohol is harmful. Copper and CuNPs engineered masks, hand sanitizers and phone cases for prevention against covid-19, are available in the market for sale. Below is the list of CuNPs based hand sanitizers:

Table 3. List of commercial copper and CuNPs based hand sanitizers available in COVID-19 pandemic and their features

No	Name of sanitizer	Features	Ref.
1	Nano Disinfekt Hand Cop	-Made with silver and copper nanoparticles. -Proven antibacterial/antiviral action against viruses, bacteria fungi, algae, microbes. A chemical free product which is safe and environment friendly	[60]
2	ALLOUT nano Hand Sanitizer Spray ULTRA	-Formulated with 75% isopropyl alcohol and copper, silver and zinc in parts per million (ppm) - Natural astringent and anti-bacterial properties, skin wellness and hydration, moisturize and nourish the skin. -FDA compliant and FDA registered.	[61]
3	Rubsafe sanitizer	-Made with skin friendly and non-toxic ingredients. -Having the capacity to sanitize broad spectrum of bacteria and many of the viruses such as SARS-CoV-2 virus. - Moisturising the skin and make it soft. - Being effective for 24 hours.	[62]

Conclusions

Copper metal has strong antibacterial and antiviral activities. In the current COVID-19 scenario, the world needs all possible preventive

measures. Along with other prevention methods, copper and copper nanoparticles integrated face masks, phone cases, and sanitizers are already made available to public during COVID-19 pandemic. Prevention technologies based on

copper and copper nanoparticles are playing a crucial role during COVID-19 pandemic. In the present review, copper and copper nanoparticles derived preventive technology were dealt with in detail.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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