

# Self-sterilizing Properties of Copper

Subjects: **Chemistry, Inorganic & Nuclear**

Contributor: JOJI ABRAHAM

It is confirmed that copper is a self-sanitising metal, acting on human pathogens in a way that does not let them survive exposure to copper or copper alloy surfaces for any reasonable length of time. Regarding the efficacy of copper surfaces, testing in an independent microbiology laboratory has led to 300 various copper surfaces being registered with the United States Environmental Protection Agency (USEPA) in 2008. The registration includes the following statement: "When cleaned regularly, the antimicrobial copper alloy surface kills greater than 99.9% of bacteria within two hours and continues to kill more than 99% of bacteria even after repeated contamination". This claim acknowledges that copper and its alloys brass and bronze can kill potentially deadly bacteria, and sometime later, it was further understood that copper nanoparticles (Cu-NPs) and laser textured copper also show enhanced antimicrobial activity.

health care

infection control

microbial infections

Copper

## 1. A Survey of the Antipathogenic Properties of Copper and Its Alloys

### 1.1. Copper as an Antibacterial Agent

The contact-killing ability of copper surfaces was studied with respect to bacteria in the early 1980s due to the emerging of hospital superbugs. In 1983, Kuhn <sup>[1]</sup> compared the bioburden on doorknobs made of brass and stainless steel and found that brass doorknobs showed reduced pathogenic growth in the healthcare environment compared to the stainless steel variety. Recently, Schmidt et al. <sup>[2]</sup> replaced the normal plastic rails of hospital patients' beds with copper and then tested for the microbial burden. It was found that the plastic surfaces on the control beds exceeded the recommended amount of bacterial concentrations, but it was not so on the copper beds (94% lower). Salgado et al. <sup>[3]</sup> installed copper alloys on common touch surfaces in the hospital environment such as bed rails, overbed tables, intravenous poles, arms of visitor's chairs, nurses' call buttons, computer mice, the bezel of the touch screen monitor, and palm rest of laptop computers in three intensive care units (ICU) of three large hospitals in the USA. A total of 650 randomly selected patients were observed in 16 ICU rooms, with eight copper alloy fitted and eight control rooms. The results showed that the MRSA and VRE concentrations were significantly lower (0.071 vs. 0.123;  $p = 0.020$ ) in the copper-alloy equipped ICUs compared to the standard ICUs <sup>[4]</sup>. It was also noticed that placing copper alloy surfaces in the ICU rooms reduced the risk of HAI by more than half during the study period, and no HAI outbreak of epidemiologically important organisms occurred in copper-alloy equipped ICUs. A detailed study was conducted in another 16 ICU rooms (eight experimental rooms and eight control rooms) of three hospitals in the USA over 21 months, replacing the normal hand-touch steel surfaces with

copper, and this study also found that copper materials at the hand-touch surfaces significantly reduced the microbial burden (698 vs. 6102 CFU per 100 cm<sup>2</sup>, 88% reduction) [5].

A three-year-long study was conducted in France in five extended care facilities, replacing the doorknobs and handrails with copper alloys. Around 1400 samples were collected and analysed and found that copper doorknobs and handrails revealed significantly less microbial burden (59% and 33% reduction, respectively) than the normal doorknobs and handrails [6]. Other studies conducted in the health care environment have also reported the benefits of replacing plastic hospital beds with copper or copper alloys due to the significant reduction in the microbial burden [7][8][9][10]. However, the studies revealed that the contact-killing property increases with an increase in copper concentration, and a minimum of 60% copper concentration is required in alloys to get the best result [11][5][12][13][14]. Souli et al. [14] studied the antibacterial efficacy of two copper coatings (99% and 63% copper concentrations) on various multi-drug resistant Gram-negative pathogens responsible for nosocomial infections such as *E. coli*, *Enterobacter* spp., *K. pneumonia*, *P. aeruginosa*, and *Acinetobacter baumannii* (*A. baumannii*). They found that copper coatings worked against all strains of the above microbes, with those having greater than 99% copper concentration being able to kill the microbes below six hours (2 h for *A. baumannii*, 3 h for *Enterobacter* spp., 5 h for *K. pneumoniae*, and 6 hr for *P. aeruginosa*) [14]. The contact-killing efficacy of copper surfaces on *Clostridium difficile* (*C. difficile*) (a major cause of hospital-acquired infection globally) showed similar characteristics to alloys with higher copper concentrations (>70% copper), killing the *C. difficile* (vegetative cells and spores) after 24–48 h [15]. This microbial contact-killing efficacy of copper has also been found to be successfully applied in wound dressings (Figures 1–3 in [16]).

Apart from the copper concentration, the biocidal efficacy of a surface depends on many other factors such as atmospheric temperature, humidity, length of exposure, microbial type, and concentration [16]. It does seem that contact-killing capability remains high across all standard temperature ranges [17][18]. Noyce et al. [19] studied the characteristics of copper alloys at 22 °C and 4 °C with MRSA and found that at 22 °C, all the three MRSA strains (10<sup>7</sup> MRSA, EMRSA-1, and EMRSA-16) were completely killed after 45, 60, and 90 min respectively, but it took six hours to completely eradicate these strains at 4 °C [19]. Michels et al. [18] observed a >6.4 log reduction of MRSA when the temperature was 35 °C and humidity was >90%, whereas it was a >6.1 log reduction when the temperature was reduced to 20 °C. It is also noted that the alloys with higher copper concentration (85% and above) were able to completely kill *E. coli* bacteria at a lower temperature [20]. Similar studies were conducted by Wilks et al. [21][22], who found that antibacterial properties exist at all temperatures but were superior when copper concentrations exceeded 85%. Testing for MRSA at 20 °C on four copper alloys—C19700 (99% Cu), C24000 (80% Cu and 20% Zn), C22000 (90% Cu and 10% Zn), and C77000 (55% Cu, 27% Sn, and 18% Ni)—showed that for C19700, there was a drop off within 75 min and for C22000, drop off was after 270 min. Both are considered to be more than 99% effective [18]. In a similar investigation, Bleichert et al. [23] looked at the biocidal effects of copper surfaces on bacterial and viral biothreat agents and revealed that cells of bacterial biothreat agents exposed to copper surfaces are inactivated within a few minutes. On the other hand, the cells on the control surface (stainless steel) showed a slower decline of the viable cells over time [23].

Whilst most recent studies were in the hospital environment, Inkinen et al. [24] decided to study the antibacterial efficacy of copper in different environmental settings such as retirement homes, kindergartens, and office buildings. Copper replaced traditional materials at the common touch surfaces (such as door handles, light switches, corridor handrails, closet touch surfaces, toilet flush buttons, floor drain lids, and toilet support rails). The study found that the copper surfaces had a lower bacterial load than the reference products and concluded that copper touch surfaces functioned efficiently as an antibacterial surface [24]. It was found that *C. difficile* can form spores and survive on dry surfaces for up to five months, and cannot be killed by hospital-grade disinfectants [25]. However, copper, including its alloys with greater than 70% copper, can kill the *C. difficile*, including the spores [25]. The antimicrobial property of copper regarding *C. difficile* was also studied by Wheeldon et al. [26] in a clinical setting using carrier test methods against dormant and germinating spores and vegetative cells for three hours in the presence and absence of organic matter. It was found that within 30 min, the copper surface destroyed the vegetative cells and reduced the viability of spores exposed to germination within an hour, giving an additional positive signal for using copper in the hospital environment to reduce infection. Besides copper metal and alloys, a copper coating on a steel surface was also found to enhance the antibacterial property of the steel [27].

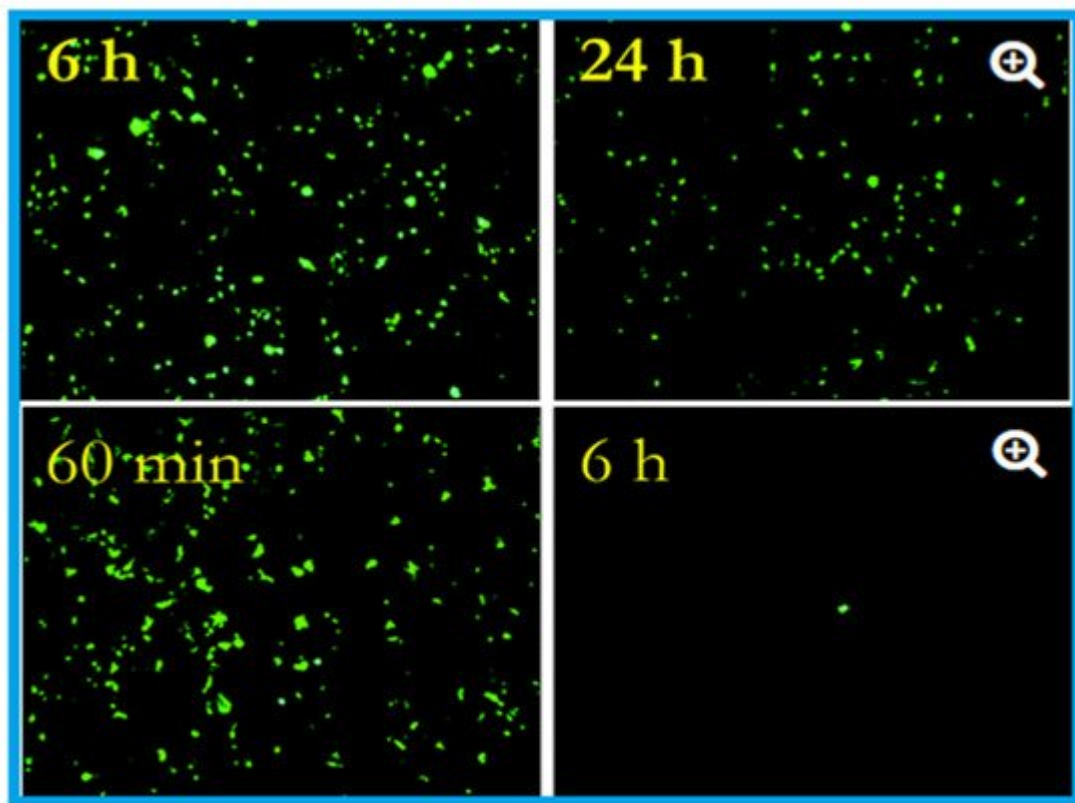
In the food industry, most bacterial contamination is due to *E. coli* O157 and is responsible for large-scale food recalls [20]. Noyce et al. [20] studied the efficacy of seven cast copper alloys with copper concentration ranges from 61% to 95% to investigate the ability to reduce *E. coli* strains in the food industry environment. The study found that without the addition of beef extract, three alloys completely killed the *E. coli* inoculum within six hours of exposure at 22 °C, but at a lower temperature (4 °C), only the copper alloys with higher copper concentration (>85%) were able to significantly reduce the inoculum [20].

*Listeria monocytogenes* (*L. monocytogenes*), commonly found in soil, water, plant materials, and animals (including humans), are of considerable concern in the food industry [22]. It has been recognised as a human pathogen since 1929, and records show that *Listeria* infections affect around 2500 people every year in the US, causing 500 deaths annually [22]. It can be critical to pregnant women, the elderly, and immunocompromised people [28]. The bacteria cause Listeriosis, whose symptoms are often septicaemia, encephalitis, spinal meningitis, and corneal ulcers, including pneumonia, which is considered the cause of miscarriage and even death [29][30]. Aisha [31] investigated copper alloys' antimicrobial effect in killing *Listeria* and found that copper ions are very effective. Wilks et al. [22] also studied copper's efficacy in killing *Listeria*, and found no viable *Listeria* on any copper alloys after 60 min (5 Log reduction), whereas viable cells were found on stainless steel even after 24 h. Furthermore, they reported that a new alloy called New Silver (65% Cu, 18% Ni, and 17% Zn) also inactivated all bacteria within 90 min of exposure. All these studies support the conclusion that copper products and surfaces can be effectively used in many locations, especially in the health industries and public places, to reduce the bacterial burden and subsequent diseases.

Even though many studies mentioned the influence of copper surfaces in reducing the microbial burden, a review by Cochrane conducted in Australia mentioned that there is only limited evidence available to support the use of environmental fittings with antimicrobial properties in preventing infections with multi-resistant bacterial organisms [32].

## 1.2. Copper as an Antiviral Agent

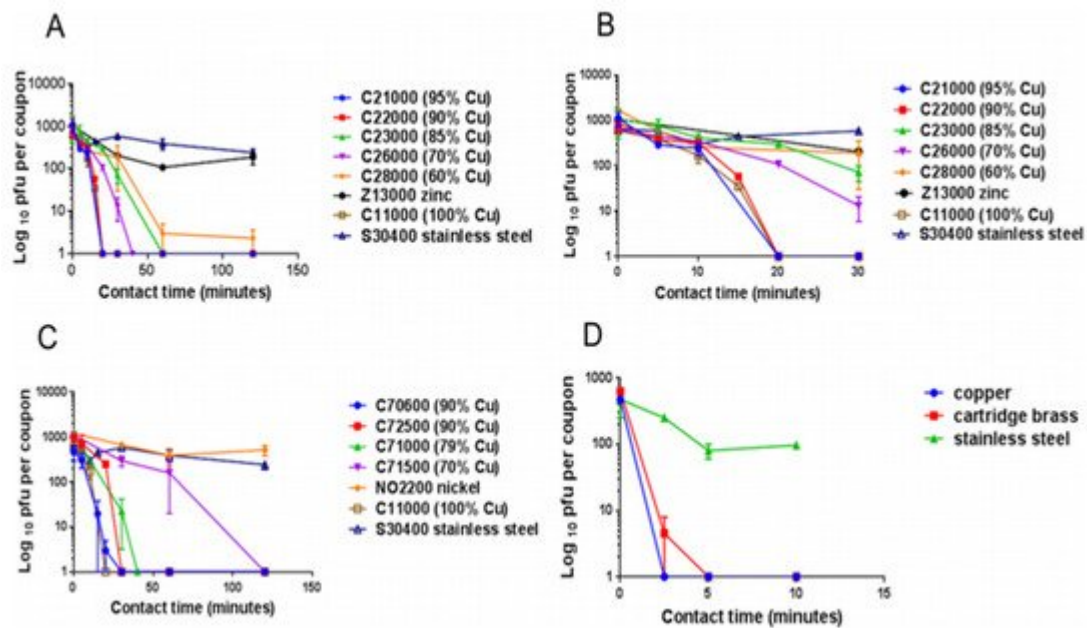
The antiviral activity of copper was studied as early as 1958 by Bauer [33], whose work was followed by many researchers who demonstrated the efficacy of copper against many viral strains [34][35][36][37]. Published studies (Table 1 and Table 2) confirmed the contact-killing property of copper surfaces against viruses such as influenza virus, norovirus, monkeypox, vaccinia virus, human immunodeficiency virus (HIV), SARS-CoV, and SARS-CoV-2 [38][35][37][33][39]. Researchers at the University of Southampton showed that they could significantly prevent the spreading of influenza using copper surfaces, and it was further revealed that the influenza virus could be eradicated within six hours of exposure to a copper surface [40]. These researchers placed two million active units of influenza A (H1N1) virus on a sheet of copper (C1100, which is pure copper under ISO standards) and stainless steel (S30400) (Figure 1). After 24 h, the virus on the steel had declined to 500,000 units, but only 500 viruses were found to be active after six hours on the copper [41][40][42].



**Figure 1.** Effects of influenza A virus on steel surface (top) and copper surface (bottom). The influenza virus was cultured in R-mix vials that contain a monolayer of mink lung and human laryngeal carcinoma cells grown on glass coverslips. This was inoculated into sterile coupons of copper (C11000) and steel (20  $\mu$ L virus suspension with  $10^8$  virus particles per millilitre) for the experimental purpose and kept at room temperature ( $22 \pm 2$  °C) with a relative humidity of 50 to 60%. Here in the epifluorescent image, the number of green fluorescing cells are proportional to the viral inoculum. After six hours,  $10^6$  virus particles were found to be remained viable on the steel surface, and after 24 h,  $5 \times 10^5$  particles were present, capable of causing cell infection (top). In contrast to the steel surface, on copper, the virus particles reduce to  $5 \times 10^5$  after 60 min (the equivalent of 24 h of exposure on stainless steel), which reduced to  $5 \times 10^2$  after six hours (nearly 4 log reduction). After 24 h of incubation, 500,000

virus particles were present on stainless steel, but 500 only seen after six hours on the copper surface. Adapted with permission from Ref. [42]. Copyright 2007, American Society for Microbiology.

Warnes et al. [43] tested the capability of inactivating one corona group virus, (229E), that can cause common colds and pneumonia. They found that the virus became inactivated immediately after being kept on copper, but it stayed viable for five days on stainless steel and glass (**Figure 2**). Similar to bacteria, inoculation efficiency for the virus also depends on temperature, humidity, copper concentration [38][19][20][21][43][44][45], length of exposure, and microbial density [19][21][22][46].



**Figure 2.** The panels describe the rapid contact-killing efficiency of various copper alloys (varies from 60% copper concentration to 100%) on human coronavirus-229E (HuCoV-229E), which causes the common cold. Initially, around  $10^3$  PFU HuCoV-229E (20  $\mu$ L infected cell lysate) was applied on one sq. cm copper alloy coupon(s) with various copper concentrations, including stainless steel, nickel, and zinc (as control metals). (**A**) It was found that the coronavirus was inactivated less than 40 min on brass coupons and less than 120 min on copper-nickel alloy (containing less than 70% copper). Surprisingly the alloy with 70% copper showed quick antiviral activity than the alloy with 85% copper. (**B**) The observation showed an initial time lag on all alloys and metals, followed by rapid inactivation on copper coupons. The control metals stainless steel and nickel did not show any anti-coronavirus activity, except zinc, which showed little (significant only after 60 min,  $p = 0.046$ ). (**C**) When the copper concentration was reduced to 70%, it took approximately 80 min more to inactivate all the viruses compared to one with 79% copper. (**D**) When the same inoculum was applied at 1  $\mu$ L per sq. cm, the coupons inactivated the virus eight-time faster. The experiment showed that the concentration of copper and the amount of virus are significant factors in showing the antiviral activity. Adapted from Ref. [43].

Norovirus is highly infectious, causing viral gastroenteritis, and is spread through touch surfaces [47]. Warnes and Keevil [39] investigated the antiviral property of copper alloy surfaces against norovirus and found its effectiveness is proportional to the copper concentration in the alloy. Furthermore, they observed that antiviral effectiveness was



not very rapid on brass but was very effective on the copper-nickel alloy. It is also found that copper-based filters inactivate HIV-1, which can significantly reduce HIV-1 infection through breastfeeding and blood donation [48]. In addition to this, Noyce et al. [42] indicated that copper surfaces act as a barrier against the avian flu epidemic. Their experiments have shown that, after six hours of exposure on a copper surface, 99.9% of the two million active H5N1 virus particles involved in the experiment became inactive.

**Table 1.** Biocidal activity of copper on various viruses.

Types of Virus(es)	Effect(s)	Reference(s)
SARS-CoV-2	The virus was active only up to 4 h on the copper surface	[37]
SARS-CoV	The virus was active only up to 8 h on the copper surface	[37]
Influenza A virus	After incubation for six hours on copper 99% of the viral particles were inactivated	[42]
Influenza A virus	Solid-state copper oxide (Cu <sub>2</sub> O) inactivated the influenza A virus	[49]
Human coronavirus HuCoV-229E	Active only 20 min on copper surface	[43]
Hepatitis C virus (HCV)	Copper oxide-NPs significantly inhibit the infectivity of HCV, both at the entry and attachment stages	[50]
Murine norovirus-1 (MNV-1)	Copper alloy (65 to 99.9% Cu) dry surfaces inactivated the MNV-1	[39]
Vesicular Stomatitis Virus Coxsackie Virus-B4 Respiratory Syncytial Virus	Curcumin-copper synthesised compound found to effective against these viruses and could be utilised for the development of vaginal microbicidal gel	[51]
Feline Calicivirus (FCV)	CuI-NPs reduced the infectivity of FCV by order of seven magnitude	[52]
H1N1 Influenza Virus 2009 Pandemic	CuI-NPs showed antiviral activity against influenza A virus of swine-origin	[35]
Human Immunodeficiency Virus-1 (HIV-1)	When exposed to copper oxide, the HIV-1 infectivity inhibited in a dose-dependant manner	[48]
Polio Virus	Copper sulphate (20 mg/L) completely inactivated the polio virus in the presence of hydrogen peroxide	[53]
Herpes Simplex Virus (HSV)	Reducing agents such as ascorbic acid, hydrogen peroxide and cysteine enhanced the antiviral property of copper	[54]

### 1.3. Copper as an Antifungal Agent

The antifungal property of copper was first identified in 1761 when it was found that grain seeds soaked in copper sulphate solutions could inhibit the seed-borne fungi, but it took more than 100 years for the more sophisticated development of the fungicide “Bordeaux mixture” (developed by Pierre-Marie-Alexis Millardet and used in the USA) and “Burgundy mixture” (used in France) [55]. Copper sulphate and lime mixtures were sprayed onto grape vines to make them mildew-free, prevent fungal infection in other plants, and control the algal growth in water reservoirs as well on timber, and were also found useful in preserving fabric [55]. This experience again shows that even though the antimicrobial property of copper has been used in the agriculture sector for controlling fungal and bacterial infections for many years [56][57], it has come to the healthcare environment very lately.

A peer-reviewed study of the fungicidal property of copper was carried out in the 1950s, finding that copper, including copper compounds, are effective in killing several fungi and yeast, including *Candida albicans* (*C. albicans*) [58][59], *Aspergillus niger* (*A. niger*) [57], and *Aspergillus carbonarius* (*A. carbonarius*) [60]. Indeed, many thousand tons of copper-based antifungal agents, specifically copper sulphate and copper hydroxide, are annually used across the globe for agricultural purposes [61]. It is also used in wood processing to prevent roof moss formation and as an algae-resistant roofing system in the 3M industry. The biocidal efficacy of copper against *Aspergillus* and *Fusarium* species as well as *Penicillium chrysogenum* (*P. chrysogenum*) and *C. albicans* was studied by Weaver et al. [62], who found that copper surfaces were able to kill most of these fungi and were able to prevent germination of new spores. The mechanism for control with bacteria and fungi is similar as inoculation starts with membrane damage, followed by enlargement and disappearance of vacuoles and the onset of oxidative stress. *Candida* spp. can commonly survive in the healthcare environment and can cause HAIs [63]. The efficacy of copper-sputtered polyester surfaces (Cu-PES) was tested against azole-resistant *C. albicans* and *Candida glabrata* (*C. glabrata*) under dark and low-intensity visible light, with the results showing that under low-intensity visible light, the Cu-PES exhibited fungicidal activity against both strains within 30 min of exposure [63]. Of interest, it was found that, in addition to the pure copper surfaces, many copper compounds, such as the copper (II) complex of quinoline-2, could act as antifungal agents [64]. Ghasemian et al. [65] tested the antifungal efficiency of Cu-NPs against filamentous fungi (*Alternaria alternate* (*A. alternate*), *Aspergillus flavus* (*A. flavus*), *Fusarium solani* (*F. solani*), and *P. chrysogenum*) and found that Cu-NPs are very effective control agents, finding that particle size is a significant factor in antimicrobial activity. Two other studies also found that Cu-NPs are effective against *Candida* species [66][67]. The contact-killing ability of copper for various microbes, including fungi, is summarised in **Table 2**.

**Table 2.** Details of contact-killing or inactivation of microbes by copper surfaces. Adapted with permission from Ref. [38]. Copyright 2007, American Society for Microbiology.

Species	Application Method (Wet (W)/Dry (D))	Time to No Viable Forms Detected	Reference(s)
SARS-CoV-2	D, 10 <sup>5.25</sup> 50% (TCID <sub>50</sub> ) per mm	4 h	[37]

Species	Application Method (Wet (W)/Dry (D))	Time to No Viable Forms Detected	Reference(s)
SARS-CoV	D, $10^{6.75-7.00}$ TCID <sub>50</sub> /mm	8 h	[37]
Human coronavirus—HCoV-229E	W, $10^3$ PFU	20 min	[43]
Influenza A virus (H1N1)	W, $5 \times 10^5$ viruses <sup>h</sup>	5 h	[42]
<i>Penicillium crysogenum</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	24 h	[62]
<i>Fusarium solani</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	24 h	[62]
<i>Fusarium oxysporum</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	24 h	[62]
<i>Fusarium culmonium</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	24 h	[62]
<i>Aspergillus niger</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	>576 h	[62]
<i>Aspergillus fumigatus</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	>120 h	[62]
<i>Aspergillus flavus</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	120 h	[62]
<i>Candida albicans</i>	W, $10^5$ CFU <sup>f</sup>	1 h	[68]
<i>Saccharomyces cerevisiae</i>	D, $10^6$ CFU <sup>k</sup>	30 s	[69]
<i>Candida albicans</i>	D, $10^6$ CFU <sup>k</sup>	5 min	[69]
<i>Candida albicans</i>	W, (2–300) $\times$ $10^5$ spores <sup>c</sup>	24 h	[70]
MRSA <sup>d</sup>	W, $10^7$ CFU <sup>f</sup>	3 h	[68]
MRSA NCTC 10442	W, $2 \times 10^7$ CFU	75 min	[18]
EMRSA-16 <sup>e</sup> (NCTC13143)	W, (1–1.9) $\times 10^5$ CFU <sup>c</sup>	90 min	[17]
EMRSA-1 <sup>e</sup> (NCTC11939)	W, (1–1.9) $\times 10^7$ CFU <sup>c</sup>	1 h	[17]
MRSA <sup>d</sup> (NCTC10442)	W, (1–1.9) $\times 10^7$ CFU <sup>c</sup>	45 min	[17]
<i>Acinetobacter baumannii</i>	W, $10^7$ CFU <sup>f</sup>	3 h	[68]



Species	Application Method (Wet (W)/Dry (D))	Time to No Viable Forms Detected	Reference(s)
<i>Pseudomonas aeruginosa</i>	W, $10^7$ CFU <sup>f</sup>	3 h	[68]
<i>Klebsiella pneumoniae</i>	W, $10^7$ CFU <sup>f</sup>	1 h	[68]
<i>Mycobacterium tuberculosis</i>	W, $2.5 \times 10^7$ CFU <sup>f</sup>	5–15 days	[68]
<i>C. difficile</i> (ATCC 9689) vc&spores	W, $2.2 \times 10^5$ CFU <sup>c</sup>	24–48 h	[15]
<i>Pseudomonas aeruginosa</i> PAO1	W, $2.2 \times 10^7$ CFU <sup>j</sup>	2 h	[17]
<i>Escherichia coli</i> O157	W, $2.7 \times 10^7$ CFU <sup>c</sup>	75 min	[18]
<i>Listeria monocytogenes</i> Scott A	W, $10^7$ CFU <sup>c</sup>	1 h	[20]
<i>Escherichia coli</i> O157	W, $(3-4) \times 10^7$ CFU <sup>c</sup>	65 min	[21]
<i>Brucella melitensis</i> NCTC 10094	D, $10^6$ CFU <sup>k</sup>	<5 min	[23]
<i>Burkholderia mallei</i> NCTC 3709	D, $10^6$ CFU <sup>k</sup>	<5 min	[23]
<i>Burkholderia pseudomallei</i> NCTC 0816-03	D, $10^6$ CFU <sup>k</sup>	<5 min	[23]
<i>Francisella tularensis</i> FSC 237	D, $10^6$ CFU <sup>k</sup>	<5 min	[23]
<i>Yersinia pestis</i> NCTC 2028	D, $10^6$ CFU <sup>k</sup>	<5 min	[23]
<i>C. difficile</i> germinating spores	W, $8 \times 10^6$ CFU <sup>i</sup>	3 h	[26]
<i>C. difficile</i> dormant spores	W, $8 \times 10^6$ CFU <sup>i</sup>	ua-3 h	[26]
<i>C. difficile</i> NCTC11204/R20291 vc	W, $(1-5) \times 10^6$ CFU <sup>i</sup>	30 min	[26]
Different <i>Enterococcus</i> spp.	W, $10^6$ CFU <sup>f</sup>	1 h	[46]
<i>Enterococcus hirae</i> ATCC 9790	W, $10^7$ CFU <sup>c</sup>	90 min	[46]
<i>Escherichia coli</i> W3110	D, $10^9$ CFU <sup>k</sup>	1 min	[71]
<i>Brachybacterium conglomeratum</i> DSM10241	D, $10^9$ CFU <sup>k</sup>	A few min	[71]
<i>Staphylococcus warneri</i> DSM 20316	D, $10^9$ CFU <sup>k</sup>	A few min	[71]
<i>Pseudomonas oleovorans</i> DSM1045	D, $10^9$ CFU <sup>k</sup>	1 min	[71]
<i>Pantoea stewartii</i> DSM30176	D, $10^9$ CFU <sup>k</sup>	1 min	[71]

Species	Application Method (Wet (W)/Dry (D))	Time to No Viable Forms Detected	Reference(s)
<i>Acinetobacter johnsoni</i> SM6963	D, 10 <sup>9</sup> CFU <sup>k</sup>	1 min	[71]
<i>Campylobacter jejuni</i>	W, 4.5 × 10 <sup>6</sup> CFU <sup>b</sup>	8 h	[72]
<i>Salmonella enterica</i>	W, 4.5 × 10 <sup>6</sup> CFU <sup>b</sup>	4 h	[72]

NB: ua—unaffected; vc—vegetative cells; TCID—tissue culture infectious dose. b—Inoculation with 1.5 mL of culture (4.5 × 10<sup>6</sup> CFU), kept under humid conditions. c—Inoculation with a 20 µL drop of culture. d—Methicillin-resistant *Staphylococcus aureus*. e—Epidemic methicillin-resistant *Staphylococcus aureus*. f—20 µL of culture spread on coupons. h—inoculation with 20 µL of virion suspension; i—100 µL of dilute culture; j—25 µL of culture spread on coupons with a glass spreader. k—Thin-film applied with a cotton swab.

## 2. Application of Copper Nanoparticles (Cu-NPs)

Nanotechnology is attracting global attention due to its enormous potential in a wide range of applications, and Cu-NPs have attracted more significance both in the health and food industries because of their antimicrobial characteristics. Various methods are used for the preparation of Cu-NPs, such as microwave irradiation, thermal reduction, vacuum vapour deposition, chemical reduction, laser ablation, and polyol [72]. Remyadevi et al. [73] synthesized Cu-NPs using the modified polyol method and carried out the antimicrobial activity against several bacteria (*S. aureus*, *E. coli*, *K. pneumonia*, and *P. aeruginosa*) and fungi (*C. albicans*, *A. niger*, and *A. flavus*). After careful study, they revealed that Cu-NPs exhibit antimicrobial activity, which is strong in bacteria than the fungi [73]. Apart from this, it is noted that Cu-NPs showed antimicrobial property against MRSA, *E. coli*, *Bacillus subtilis*, *P. aeruginosa*, *Salmonella enterica* serotype Choleraesuis (*S. Choleraesuis*) [66][74], and hepatitis C [50]. After a detailed study and data analysis, Raffi et al. [75] concluded that Cu-NPs with a large surface-to-volume ratio efficiently inactivate *E. coli* bacteria.

The Cu-NPs can be immobilized and coated onto various surfaces to generate or improve antimicrobial activity. In this respect, Cu-NPs- and nanoparticle-impregnated materials, including cloths and plastic, have been shown to exhibit antimicrobial properties, which can be used in various fields, specifically in the health industry [76]. For example, some researchers found that Cu-NP-impregnated face masks showed biocidal activity against human and avian influenza A virus [48].

As mentioned above, the antimicrobial properties of Cu-NP fabrics have been incorporated in textile technology to develop materials suited for use in the health industry, and a specific platform technology has been developed to introduce copper into cotton fibres, latex, and other polymeric materials. The copper oxide NPs (CuO-NPs) (3%–10%) (prepared by a wet chemical method) were microencapsulated by ionic gelation and applied to plain weave cotton fabric, following a pad-dry-cure technique, and it was found that the fabric demonstrated a high level of antimicrobial activity, which could be used in the healthcare environment to reduce the bioburden [77]. In this respect, the studies of Niiyama et al. [78] and Palza et al. [79] are very encouraging. Niiyama et al. [78] determined

whether a copper film bedsheet would reduce MRSA infection in a dermatology ward and found that the MRSA count on the sheet coated with Cu-NPs was significantly lower (20–30 colony-forming units, or CFUs) when compared to the non-copper coated bed sheet (6600–11,000 CFUs). Palza et al. [79] tested the antimicrobial behaviour of materials with copper-based additives (copper NPs on plastic matrices) in a hospital environment. As a part of this study, the researchers replaced the normal plastic waiting room chairs with Cu-NPs-embedded chairs, and IV poles made of metals were coated with organic paint impregnated with nanostructured zeolite/copper. They continued sampling once a week for ten weeks and analysed the levels of viable microorganisms. It was found that the copper substrates reduced 73% of the viable microbes in the waiting room chairs and found only low levels of microbes remaining in the IV poles. Apart from this, Harikumar and Aravind [77] investigated the antimicrobial characteristics of Cu-NPs and Cu-nanocomposites against *E. coli* using the well diffusion method and found that the antimicrobial activity increases with an increase in particle dose and contact time.

Research indicates that the antibacterial activity of copper-based NPs is far superior to that of a normal copper surface, mainly because of the small size (high surface area compared to the volume) and higher cell penetration [80]. Several studies indicated that both Cu-NPs and copper oxide ( $\text{Cu}_2\text{O}$ ) induced DNA degradation occurs in Gram-positive and negative bacteria even though the concentration of released ions was far below the normal level for inhibiting bacterial growth [80][81]. This highlighted that with Cu-NPs, the concentration of released ions is less significant than the effect of NP size [81]. Other studies support this finding and have suggested that the size of the Cu-NPs is the major contributing factor for its antimicrobial activity [66][82]. To support this, Padil and Cernik [83] found that small (4.8  $\pm$  1.6 nm) CuO-NPs have significantly higher antimicrobial activity than the larger particles (7.8  $\pm$  2.3 nm), whilst Applerot et al. [80] surmised that the advantage of small particles would be their higher penetration capacity into the microbial covering. In addition to their antibacterial activity, normal copper and Cu-NPs were shown to have antifungal property against several fungi, including *C. albicans* and *Saccharomyces cerevisiae* (*S. cerevisiae*) [65][69], and found that the control mechanism in fungi was similar to that in the case of bacteria [69].

Currently, Cu-NPs are used in various industries and production sectors, but this increased use comes with a cost. Copper NPs have several adverse effects regarding environmental health since, in many regions, these copper NPs have been released into the environment. This is of special concern in the aqueous environment, where it generates health risks to aqueous organisms. It has been observed that copper NPs are not only toxic to bacteria but act on some species of fish and also on mice [84][85][86]. In general, copper, which is released from various industries, normally emerges in two forms, either as dissolved copper or particulate-bound copper, and the toxicity and the mobility of the copper depend on the form [87].

### 3. The Various Applications of Copper in the Built Environment

Cooling towers and potable water distribution systems have recently been determined as the source of hospital outbreaks of several Legionnaires' diseases [88][89]. However, after several studies, it has been confirmed that the use of a copper-silver ionisation system is the most successful long-term water disinfection system that can be

used in the hospital environment [90][91][92][93][94]. In similar investigations, it has been established that in the dental industry, dental cement having copper shows potential antimicrobial properties [95], and in the food industry environment, shifting to copper surfaces and copper-made food carrying, and transportation surfaces produce a significant reduction in foodborne diseases [20][21][72][73][85][96][97]. In addition, thin-film copper oxide (CuO)-coated glass [98], CuO-impregnated degradable phosphate glass fibres [99], and copper alloys also have shown potential biocidal properties against string bacteria spores [15][98]. Drinking glasses made of copper or copper-impregnated glasses were found to reduce the biofilm formation, thereby reducing the risk of several potential infections [96]. Copper and copper alloys can also be used to produce sanitary installation tubes, fittings, door handles, knobs, hand-rails, and vehicle door handles to reduce the microbial burden.

Apart from the above, silver-zinc (Ag-Zn) and silver-copper (Ag-Cu) incorporated soda-lime glass prepared by ion exchange has shown significant antimicrobial properties [100], which could be useful for several daily applications, specifically in the health industry and public places. Copper metal and CuO-NPs embedded in a polypropylene matrix is also an evidence of antimicrobial property. After careful preparation, Delgado et al. [101] found that the composite has a strong antimicrobial activity against *E. coli* and could kill 95% of the colony within four hours, acting through the release of the Cu<sup>2+</sup> ions.

Although many water purification methods exist, potable water is still beyond the reach of millions of people around the globe. Sudha et al. [102] conducted a study to investigate the microbial efficacy of copper pots in killing the bacteria (*V. cholera* O1, *Shigella flexneri* (*S. flexneri*) 2a, *E. coli*, *Salmonella enterica* Typhi (*S. Typhi*), and *Salmonella enterica* serovar Paratyphi (*S. Paratyphi*) in the water. When drinking water was contaminated with 500 CFU/mL of those bacteria stored in copper pots for 16 h at room temperature, no bacteria were recovered in the culture medium. They observed a slight alteration in the water pH from 7.83 to 7.93, but no other changes were observed. Copper pots are consequently considered an interim microbial purification solution for drinking water in under-developed and many developing country areas [102]. It is also found that a copper-coiled device put into a glass bottle overnight can also inactivate the bacteria, including *E. coli*, *S. typhi*, and *V. cholera* [103]. This observation still needs to be investigated for the possibility of viable but non-culturable microbial inactivation. It is recalled that the use of copper or copper alloy pots were common in Indian, Chinese, and Egyptian households, but they were displaced by the arrival of cheaper aluminium, steel, and plastic wares. The major advantage of copper's biocidal activity is that there is no need for any kind of energy, fuel, including electricity. It is also found that similar to dry copper metal efficacy, the biocidal effectiveness of copper in water also follows a temperature pattern, with the fastest biocidal effects occurring at higher temperatures [104]. The presence of chloride salts (NaCl) resulted in faster inactivation (of *E. coli*) compared with pure water, but the presence of complex organic mixtures such as humic acids, proteins, and amino acids reduced the inactivation [104]. It gives an indication that natural organic constituents and salts in the water influence the antibacterial efficacy of copper when used to treat water.

In addition to the above, the antimicrobial efficacy of copper-impregnated textiles and latex were mentioned in many studies [105][106]. For example, research from Israel highlighted the antimicrobial properties of copper-impregnated textiles [105], and the researchers developed copper-impregnated textile products such as cotton and

latex and tested them against various bacteria (*E. coli*, *S. aureus*, MRSA, and VRE), viruses (HIV-1 and West Nile virus), and fungi (*C. albicans*). They demonstrated that >2 log reduction of all tested bacteria occurred within two hours, and the materials inactivated the fungi within an hour. They also observed that latex gloves were able to reduce the infectivity of both viruses (HIV-1 and West Nile virus). Later studies also found that copper oxide-impregnated fabrics could reduce >98.7% of microbes within 20 to 240 min of exposure [\[106\]](#).

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