Chapter 5 Biocidal Hard and Soft Surfaces Containing Copper Oxide Particles for the Reduction of Healthcare-Acquired Pathogens

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Contents

5.1	Hospital Textiles as a Source of Healthcare-Acquired Pathogens	86
5.2	Biocidal Textiles as a Tool to Fight Healthcare-Acquired Infections	88
5.3	Biocidal Textiles Containing Copper Oxide	90
5.4	Non-porous Solid Biocidal Surfaces Containing Copper Oxide	93
Refe	rences	95

Abstract Potentially overlooked and neglected sources of healthcare-acquired pathogens are non-intrusive soft and hard surfaces located in clinical settings. Microbes can survive on bedding, uniforms, trays, bed rails and other such surfaces for days to months. Furthermore, on some of these surfaces, such as patient bedding, the microorganisms proliferate as textiles are an excellent substrate for bacterial and fungal growth. Additionally the temperature and humidity conditions present between the patients and these textiles are appropriate for microorganism multiplication. Bed making in hospitals can release large quantities of microorganisms that are in direct or indirect contact with the patients can serve as a source of healthcare-acquired pathogens.

Copper oxide impregnated materials have potent intrinsic biocidal properties. This manuscript reviews the laboratory and clinical studies that demonstrate that soft and hard surfaces containing copper oxide particles reduce bioburden and healthcare-acquired infection rates.

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List of Abbreviations

AATCC	American Association of Textile Chemists and Colorists
cfu	Colony forming units
EPA	USA Environmental Protection Agency
GLP	Good laboratory practices
HAI	Healthcare-acquired infections
HD	Hospitalization days
MRSA	Methicillin-resistant Staphylococcus aureus
SEM	Scanning electronic microscope
TM	Test Method
VRE	Vancomycin-resistant enterococcus

5.1 Hospital Textiles as a Source of Healthcare-Acquired Pathogens

Textile products are widely used in the hospital environment. They range from simple cleaning wipes to advanced barrier fabrics used in operating rooms. Some of the products are in direct contact with the patients, such as blankets, sheets, pyjamas, towels, gowns, and pillowcases. Others are used by the healthcare personnel, such as uniforms, surgical gowns, face masks, and head and shoe covers. Some products are present in the patient wards, such as drapes, table covers and privacy curtains.

Textiles in general are an excellent substrate for microbial proliferation when in contact with the human body. The very large surface area, the capacity to retain oxygen, and the moisture and temperature conditions present between the skin and the textiles provide ideal environment for microbial proliferation. Humans shed bacteria directly from their skin, nasal cavities, genitalia area, and sweat onto the textiles they use [1]. Bacterial shedding is greater in patients than in healthy individuals [2, 3]. In addition, hospital textiles come in contact with spillages and body exudates, such as blood, stool, urine, nasopharyngeal secretions and vomit, all of which can contain large amounts of bacteria and serve as a bacterial nutrient source. Heavy microbial colonization of sheets, patient pajamas, healthcare worker uniforms, and privacy curtains, including by antibiotic resistant bacteria, has been reported [4–29]. Contamination of clean laundry occurs shortly after use [14]. Without washing, bacteria, fungi and viruses can remain viable on textiles, under ambient temperature and humidity, for very prolonged periods of time; even months [19, 29–36] (See also Chap. 2). The higher the bacterial titer spiked onto the fabrics, the longer the bacteria can survive [31]. Unfortunately, some microorganisms remain viable even after industrial laundry [7, 37–39], and contaminated laundry can lead to cross-contamination of clean laundry [40].

While proliferating on the textiles, some microorganisms secrete unpleasant volatile molecules creating foul odors [41]. But, more importantly, some

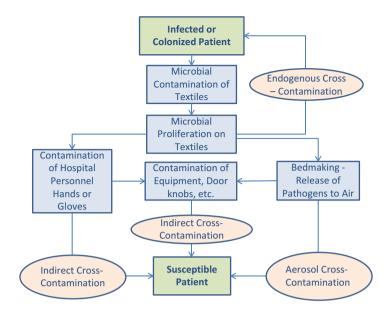


Fig. 5.1 Potential transmission routes of pathogens from a colonized or infected patient to a susceptible patient via hospital textiles

microorganisms that multiply or remain on the textiles can be a source of healthcare-acquired pathogens [7, 42] (Fig. 5.1). These pathogens can be transmitted from one part of the host's body to another [43]. They can also be the source of direct or indirect infection of patients and hospital personnel, as discussed below.

Contamination and healthcare-acquired infections (HAI) of patients and hospital personnel via contaminated towels, gowns, sheets, cleaning wipes and other hospital textiles with Methicillin-resistant *Staphylococcus aureus* (MRSA) [11, 24, 28, 44–47], Vancomycin-resistant *enterococcus* (VRE) [19, 24, 48], Carbapenem-resistant *Acinetobacter* [20], multidrug-resistant *Acinetobacter baumannii* [25, 28, 49], multidrug-resistant *Pseudomonas aeruginosa* [24, 50], *Bacillus cereus* [51–55], *Cryptosporidium* [56], *Microsporum canis* [57], *Norwalk gastroenteritis* [58], *Klebsiella pneumonia* [28], *Rhizopus* [59], *Salmonella gastroenteritis* [60], *Salmonella typhimurium* [61], *Sarcoptes scabiei* [62], or *Streptococcus pyogenes* [37, 63] have previously been reported (Table 5.1). Viruses can also survive on textiles for days and thus be a source of contamination ([33, 64–67] and Chap. 2).

When handling contaminated textiles hospital, personnel can contaminate their gloves with micro-organisms and then contaminate other surfaces, such as door knobs, and even patients directly [3, 11, 20–22, 24, 25, 49, 68, 69]. Furthermore, studies have shown that when the personnel change the bed linens or patients garments, large quantities of micro-organisms are released into the air, which then contaminate the immediate and non-immediate surroundings in the same room as well as throughout the building via the air conditioning system [3, 46, 70–72]. Healthcare workers who touch the aerosol contaminated surfaces can then

Bacteria	Textile	HAI of	Reference
Bacillus cereus	Linens, towels, sheets	Patients	[51–55]
Cryptosporidium	Uniform	Personnel relative	[56]
Hepatitis A virus	Laundry	Personnel	[66]
M. canis	laundry	Personnel	[57]
MRSA	Linens, gowns, sheets	Patients	[11, 45, 46]
N. gastroenteritis	Uniforms	Personnel	[58]
P. aeruginosa	Patients' clothes, linens	Patients	[50]
Rhizopus (fungi)	Linens, pillowcases, coats	Patients	[59]
S. gastroenteritis	Linen	Personnel	[60]
S. typhimurium	Sheets	Personnel	[61]
S. scabiei	Linens	Personnel	[62]
S. pyogenes	Babies' vests, vinyl sheet	Patients	[37, 63]
VRE	Drawsheet, seat cushions	Patients	[19, 48]

Table 5.1 Reports on textiles as a possible source of healthcare-acquired infections (HAI)

contaminate patients [3, 73]. Airborne transmission of pathogens such as *Mycobacterium tuberculosis* and *Aspergillus niger* is well documented [3]. It has also been implicated in healthcare-acquired outbreaks of *A. baumannii*, *P. aeruginosa, Scedosporium prolificans, S. aureus*, MRSA, and other *Staphylococci spp* [74–82].

5.2 Biocidal Textiles as a Tool to Fight Healthcare-Acquired Infections

Based on the above, it has been hypothesized that endowing the hospital textiles, especially those that come in contact with the patients, such as patient's sheets, pillowcases, robes, and pyjamas, with biocidal properties, would help reduce HAI by reducing an important source of microbes contributing to endogenous, indirect-contact, and aerosol transmission of healthcare-acquired pathogens [42]. Nicas and Sun [83] by using an integrated mathematical model of the infection risk in a health-care environment, also concluded that biocidal textiles have the potential to substantially reduce HAI.

Biocidal textiles should have potent broad spectrum antimicrobial, antifungal and antiviral efficacies. They should be highly effective against antibiotic resistant micro-organisms, especially those already circulating in the hospital environment causing HAI outbreaks, such as MRSA, VRE, and Carbapenem-resistant *K. pneumoniae* (CRKP). Additionally they should not enable the development of resistant micro-organisms to the biocidal compound. They should not be affected by washings and continue to be efficacious for the life of the product. Obviously, they should be safe to humans following continuous dermal exposure [42] (Table 5.2).

Wide spectrum antimicrobial, antifungal and antiviral properties
Effective against the already existent antibiotic resistant micro-organisms involved in healthcare-
acquired infections
Not allow development of resistance to the active component in the textiles by micro-organisms;
Withstand multiple industrial washings without losing biocidal potency;
Not cause skin irritation or sensitization;
Be safe to humans

 Table 5.2 Key properties that biocidal textiles should have

In the last 20 years, the development of biocidal textiles in general and specifically for the use in the hospital environment has gained momentum, and different biocidal compounds are being explored for this purpose [84–87]. Biocides can by chemically or physically attached to the natural or synthetic fibres from which the textile products are made or to the surface of the finished textile products. Surface applications usually have a lower persistence over time, as the active ingredient is lost due to friction and washing. Other biocides are introduced earlier during the production stage by impregnating them in the polymeric fibres used in the textile industry. Some of the biocidal active ingredients being studied are Cliniweave®, organofunctional silane, citric acid, copper, silver, zinc, triclosan, quaternary ammonium compounds, chitosan and zeolite. Some of the above active ingredients have been found not to be appropriate for use in hospital related applications (e.g. [88, 89]).

Only a few clinical trials have been performed to determine the efficacy of biocidal textiles in clinical settings. Most of the studies examined the capacity of the biocidal textiles to reduce microbial contamination [4, 90-94]. These studies, which included personnel uniforms, patient linens, scrubs, blankets, privacy curtains, cloths and mops, found statistically significant lower bioburden levels than those found in the matched non-biocidal controls. One study, performed with only 10 workers that used silver containing jackets and pants, did not find any significant difference in the extent of microbial contamination between the silver containing textiles and control textiles [95]. It may be that a larger sample size was required to prove the silver containing fabric's efficacy. Also, a randomized controlled study that compared the bacterial contamination of uniforms of healthcare workers when using a regular textile and two textile containing antimicrobial finishes, did not find any decrease in the bioburden levels in the antimicrobial textiles [96]. Unfortunately, the identity and nature of the antimicrobial components in the scrubs tested is not clear. Interestingly, in a recent study in which copper-coated films $(21 \times 39.7 \text{ cm})$ were attached to bed sheets used by a heavily MRSA-colonized patient found 20-130 MRSA colony forming units (cfu) in these films as opposed to 6,600–11,000 cfu on the surface of the non-film-coated control sheet areas [97].

The capacity of antimicrobial cleaning cloths to reduce bioburden and HAI was demonstrated. For example, a recent study examined the capacity of copper treated cleaning cloths in neutralizing the bacterial virus MS2. This virus serves as a non-pathogenic surrogate virus to clinically relevant viruses such as hepatitis A, enteroviruses, poliovirus or novovirus, due to its structure and environmental stability. Ninety percent of the absorbed virus in the cloths were killed, reducing significantly potential cross contamination during cleaning [98]. More dramatically, by introducing peracetic acid sporicidal wipes, the *Clostridium difficile* infections rates in an acute London trust were reduced by 72 % during the monitored 18 months as compared to the previous period [99].

In contrary to lab conditions, during *in vivo* use, continual re-inoculation with pathogens occurs. Since the killing of the microorganisms is not instant, the expectation is not to obtain a sterile fabric, but a fabric that prevents microbial proliferation and reduces the bioburden levels significantly. The concept that such textiles can reduce HAI, to the best of my knowledge, has been demonstrated in only one clinical trial (to be discussed below) and obviously more trials are needed to clearly establish the capacity of biocidal textiles to help in the fight against HAI.

Furthermore, as HAI are spreading into the community (e.g. [100]), the use of biocidal textiles and biocidal hard surfaces may not only significantly contribute to the reduction of HAI, but may also confer protection in other environments where at-risk individuals run the risk of contracting infections such as in long term care facilities.

5.3 Biocidal Textiles Containing Copper Oxide

Copper is one of the several materials that are being explored as a potent wide spectrum biocide to be used in hard and soft surfaces in clinical settings for the reduction of HAI. The biocidal mechanisms of copper are discussed in Chap. 6 of this Book. Different copper compounds that were applied to different textile fibres or polymers via different techniques, demonstrated potent *in vitro* biocidal efficacy including against antibiotic resistant bacteria [4, 101–116]. Most of these studies were conducted in the academia and the only technology that has generated textile products widely used commercially is the technology based on the impregnation of copper oxide particles into products [4, 108–110, 117–123].

Copper oxide has been chosen as the active copper form to be introduced into textiles due to two main reasons: it is a non-soluble form of copper and it is highly reactive with potent wide spectrum biocidal properties [124]. As can be seen in Fig. 5.2, the copper oxide particles are an integral part of the polymeric fibers, as they are homogenously distributed throughout the polymeric matrix. This is very important for biocidal textiles as even when some of the external polymeric fiber material disintegrates due to friction, repeated use and laundry resulting in loss of the surface copper oxide particles, there are always "new" copper oxide particles that "reach" the surface of the fiber, endowing the fiber with biocidal properties for the life of the fiber.

The biocidal efficacy is not affected by repeated use, home or industrial washings [109] (Fig. 5.3). This is in contrast to coating technologies in which the active material is only bound to the external layer of the fiber. Once this externally bound active material is removed from the surface of the fiber due to friction or laundry, the fiber losses its bioactive characteristics.

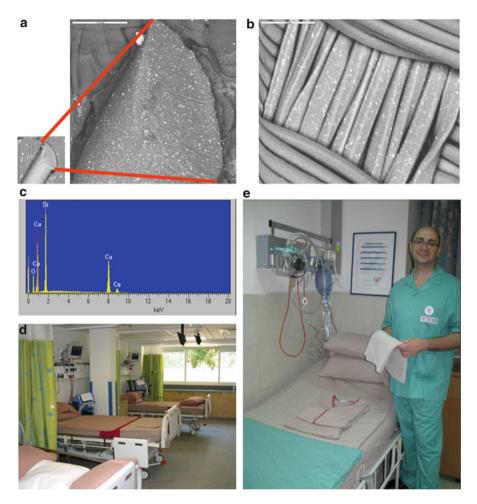


Fig. 5.2 Copper oxide impregnated textiles. (a) Scanning electronic microscope (SEM) picture of a cross section of a synthetic fiber impregnated with copper oxide particles (*white dots*). (b) SEM picture of a woven fabric in which the copper oxide impregnated polyester yarn is found only in the weft of the textile. (c) An X-ray photoelectron spectrum analysis of a *white dot* shown in (b), demonstrating that it is copper. (d and e) Pictures showing hospital textiles containing copper oxide in use in clinical settings (e.g. the beige and *brown linens* and the *green* uniform and blanket)

The biocidal potency of a hospital linen containing 1 % copper oxide particles (w/w) was tested by an independent laboratory (AminoLabs, Rehovot, Israel) by using the American Association of Textile Chemists and Colorists (AATCC) test method (TM) 100. The linen was washed following the AATCC TM 150. *Candida albicans* and *Trichophyton mentagrophytes* were exposed to the fabric for 24 h. *Staphylococcus aureus* and *Escherichia coli* were exposed to the fabric for 4 h. The results shown are the mean of duplicate samples. The titers of each microorganism before being exposed to the fabric samples are shown by the arrow.

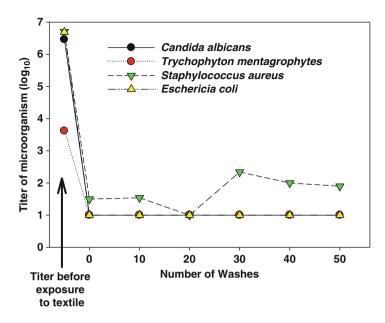


Fig. 5.3 No loss of biocidal efficacy with laundry

The copper oxide impregnated products possess broad-spectrum antimicrobial properties, including against antibiotic resistant bacteria [4, 108–110, 117, 119, 125, 126]. These products include biocidal fabrics [4, 108, 109, 117], anti-fungal socks [108, 118, 121, 123, 127], anti-viral masks and filters [119, 125, 126, 128], anti-dust mite mattress-covers [108, 129], and non-porous biocidal countertops (see next section).

A preliminary pilot study with 30 patients, who slept overnight on regular sheets and then overnight on sheets containing copper-oxide, demonstrated a statistically significant lower (~50 %) bacterial colonization on the copper-oxide containing sheets than on regular-sheets [4]. Similar statistically significant lower titers of gram positive and gram negative bacteria were recovered from copper oxide containing sheets than regular sheets (n = 40), immediately after 7 h of patient's use [130].

Importantly, in a clinical trial in the Reuth Medical Center (Tel Aviv, Israel), in which the regular non-biocidal linens in a chronic care head injury ward were replaced with the biocidal copper oxide impregnated linens, the rates of HAI per 1,000 hospitalization days (HD) were reduced by 24 % (P < 0.05). Accordingly there was a 32.8 % reduction in total number of days of antibiotics administration per 1,000 HD (P < 0.0001) and there was a 47 % reduction in the number of fever days (>38.5 °C) per 1,000 HD (P < 0.01) [130]. The study was conducted in a chronic care head injury ward as most of the patients hospitalized in this ward are high risk patients typically immunocompromised. Unfortunately the most common medical complication which afflicts them is a HAI [131–133]. Based on

the successful result of this trial, the Reuth Medical Center has now changed all their linens in all wards to the copper oxide impregnated linens.

There is no reason to believe that reducing bioburden in other wards or clinical settings by using biocidal linens would not reduce bioburden and HAI. The use of biocidal textiles should be a complementary approach to fight HAI in medical institutions as well as long term care facilities, where the risks of acquiring an infection are high. However, additional studies with other patient populations and different wards should further test this notion. Currently, a study is being conducted at Sentara Norfolk General Hospital (Norfolk, Va.), where a critical care unit that shares the same nursing staff will test the biocidal fabrics in one side of the unit for 6 months before switching them to the other unit for another 6 months.

5.4 Non-porous Solid Biocidal Surfaces Containing Copper Oxide

Elemental copper and copper alloys have been registered by the USA Environmental Protection Agency (EPA) as antimicrobial substances with approval to make public health claims that the copper-oxide impregnated surfaces kill greater than 99.9 % of gram negative and gram positive bacteria within 2 h of exposure. The approvals were obtained after demonstrating in independent laboratories potent biocidal efficacy following Good Laboratory Practices (GLP) testing. The significant contribution of metallic copper surfaces to the reduction of bioburden in clinical settings [134–140] and to reduction of HAI [141] has recently been demonstrated and is discussed in Chap. 4.

Recently, similarly to the elemental copper and copper alloys, also non-porous hard surfaces containing copper oxide particles (Fig. 5.4) have been registered by the EPA as antimicrobial surfaces and allowed to make public health claims (EPA Registration number 84542–7). The approval is based on GLP testing demonstrating the ability to kill specific disease-causing bacteria: MRSA, *Staphylococcus aureus, Enterobacter aerogenes, P. aeruginosa and Escherichia coli* (O157:H7). The product is approved for use in a wide range of applications, including health care. The samples were tested in various environmental conditions, cleaning protocols, and for efficacy after repeated exposure. The non-porous copper infused surfaces also underwent extensive American Society for Testing and Materials (ASTM) standard testing to support mechanical performance claims, allowing making efficacy claims that the copper-oxide impregnated surfaces kill greater than 99.9 % of gram negative and gram positive bacteria within 2 h of exposure between routine cleaning and sanitizing steps and even after repeated exposure [142].

Currently seven hospitals have already installed the non-porous copper infused surfaces – six in the USA and one in Israel, with the aim of further reducing the rates of HAI. The Sentara Leigh Hospital, which is one of the 11 acute care Sentara

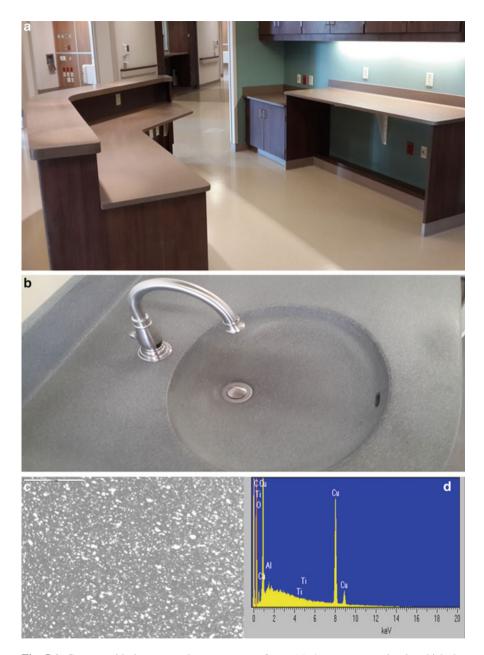


Fig. 5.4 Copper oxide impregnated non-porous surfaces. (a) A nurse top station in which the non-porous countertops are impregnated with copper oxide particles. (b) A sink made with non-porous copper oxide impregnated material. (c) SEM picture of the non-porous material shown in (b), demonstrating the homogenous distribution of the copper oxide particles on the material surface. (d) An X-ray photoelectron spectrum analysis of a *white dot* particle shown in (c), demonstrating the presence of copper

Hospitals in Virginia, has outfitted the copper-infused countertops, bed rails, and over the bed tables in their new 129 bed-tower in all patient care areas, including nursing units, visitor lounges, and patient rooms. In early 2014, the hospital also introduced copper-infused hospital gowns, pillowcases, and towels in the new tower. They will compare the rates of HAI, such as urinary catheter-associated and central line blood stream infections, with the infection rates in a similar existing 129-bed tower, in which no copper containing products will be utilized.

In conclusion, the introduction of soft and hard surfaces containing biocidal copper oxide particles in clinical settings may be an important adjunct for the reduction of bioburden and HAI. Furthermore, as HAI are now spreading out from the hospital environment into the community, the use of biocidal textiles, such as those impregnated with copper oxide, and hard surfaces containing a high percentage of copper, may not only significantly contribute to the reduction of HAI, but may also confer protection when used in homes for the elderly and in other environments where immune compromised individuals are at high risk of contracting infections.

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