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ORIGINAL ARTICLE

Copper as an antimicrobial agent in healthcare: an integrative literature review

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ABSTRACT

Object: This study is an integrative literature review aiming to identify the potential application of copper surfaces to prevent infections in healthcare assistance. **Methods:** The descriptive study was conducted by searching the electronic Medline database and the Brazilian Copper Institute website using predefined descriptors. Papers published from 1990 in English, Spanish, French, Portuguese, and Italian were searched. For each article included in the integrative literature review, previously defined variables were analyzed including the range and the level of antimicrobial action of cooper alloys, types of surfaces to be coated with the greatest potential for application in healthcare, and the potential interactions of copper with products used in healthcare. **Results:** The results showed an antimicrobial activity of copper with a significant reduction compared to other metals. **Conclusion:** Pure copper showed better results, followed by brass alloy with higher copper concentration, showing the need for studies that move further in this direction. **Keywords:** copper, antimicrobial, copper, copper surfaces, hospital infections

INTRODUCTION

Copper has been used by human civilizations for millennia, being the first metal used by man, found in its native form.[1] Its use became constant throughout the centuries, marking a presence in the technological evolution of man. Due to its physical and chemical properties, copper and its derivatives, such as bronze and brass, have shown durability and high resistance to corrosion and therefore, great utility and functionality.[2]

The sanitizing properties of copper have long been advocated, and some studies have reported the antimicrobial power of copper through different methods of analysis. Copper has been referred, along with other metals such as silver and iron ions, as a potentially useful element to control the environment associated with healthcare related infections.[3] Studies have reported the antimicrobial power of copper, claiming that the use of pure and dry metal is better than alloys.[4]

The mechanism of cell death through contact with copper is not clearly established. It has been suggested that the involvement of copper ions in the process where these ions are in contact with the cell wall or membrane, provokes structural damage in eukaryotic cells, causing rupture and subsequently fragmenting their DNA.[5]

Touch surfaces commonly found in healthcare facilities may be potentially contaminated with microorganisms that cause Healthcare-Associated Infections (HAI).[6] Such surfaces can act as ongoing sources of contamination by direct contact with the patient or indirectly through the hands of professionals. Regular cleaning combined with hand hygiene reduces the risk of microorganism transmission, but the reduction of the microbial load is always limited.[7]

Copper has been found among the potential resources applicable to the coating surface, in which the germicidal action could have a role in health service infection control. As copper refers to a resource little explored in healthcare, a review of the literature is needed in order to unveil its potential applicability and possible contraindications or side effects.

INTRODUCTION

This is a descriptive study carried out by means of an integrative literature review, the method permitting search, critical evaluation and synthesis of available evidence regarding certain topics being investigated.[8]

Papers or congress healthcare related abstracts were included, in which there were indications of copper use as an antimicrobial agent. Papers, editorials or letters without original study data and papers concerning copper application in other situations not directly linked to healthcare, were excluded.

Papers were obtained from the Medline electronic database and the Brazilian Copper Institute website. (*www.procobre.org*). The descriptors used were: copper; copper surfaces and antimicrobial copper.

The following variables were analyzed: year of publication; study financing sources; study location (city/country); study type: (non experimental or experimental; descriptive or comparative); study duration (weeks); copper alloy type; type of surface or material used; microorganisms studied; microbial isolation methods: quantitative or qualitative; type of setting where the study was carried out; interaction with cleaners, drugs and other products used regularly in healthcare; contraindications or cautions in use; study objectives and results.

RESULTS

There were a total of 4,580 papers in the databases. After applying the inclusion and exclusion criteria, with the elimination of repeats and evaluation of abstracts, 51 papers were selected for reading in full. Among them, there was a predominance of papers published in 2010; 43 (84,3%) were funded by companies linked to copper. The analysis of the papers showed that 11 countries conducted previous studies, predominantly the United Kingdom (13) and the United States (11). Only 37 papers fully met the inclusion criteria previously established and were analyzed to identify the variables previously defined.

The objectives of the analyzed studies have in common the evaluation of the effectiveness of copper against microorganisms, whether through direct contact with copper or through the surfaces of biocide products based on copper (70.2%).

The majority of research was carried out in institution labs (62.2%); studies carried out in healthcare assistance settings account for 29.7%. There was a predominance of comparative experimental studies with pre-defined inoculums (51.4%). In this type of study, a known inoculum is applied to different surfaces and the antimicrobial action is identified by counting the survivors after exposure to the surface.

Among the studies analyzed, 12 (32.4%) of them presented their duration time, an average of 24.3 weeks. Studies using copper-based biocides had longer duration due to the need of repeated sampling for several consecutive days to verify the reduction of microorganisms.

The types of alloys used in studies of the antimicrobial activity of copper are shown in Table 1. Thirty two (86.5%) studies used pure copper in the experiments and most of them used more than one type of alloy in order to assess which showed the best results.

Regarding the surfaces used in the experiments, metal coupons with predefined measures, ranging from 1cm^2 to 3cm^2 were those used most. These coupons were aseptically prepared before use in order to compare the antimicrobial effect of the metals against previously known pathogens.

Different organisms were used in the analyzed studies. The distribution frequency of micro-organisms used in studies of copper antimicrobial effectiveness can be seen in Figure 1. From the 37 studies analyzed, 22 (59.4%) inoculated more than one pathogen to test the antimicrobial action of copper. Studies that used metal coupons in research laboratories were able to quantify the bacteria before and after contact with the copper coupon or copper alloys in different time periods, allowing time to evaluate that inhibition occurs in the growth of the microorganisms studied. The evaluated studies were predominantly of the quantitative method (94.6%), which allows checking the amount of pathogens after contact with copper and copper alloys.

The results were similar to each other with respect to the reduction of microorganisms when placed in contact with copper. This reduction was significant compared to other metals, especially when compared to stainless steel. Pure copper (Cu 100%) showed the best results, followed by alloys containing a higher concentration of metal, bronze for example. Amongst the alloys tested in the studies, pure copper followed by bronze and copper-nickel (CuNi) were those used the most. Studies using solutions of copper-based biocides also had satisfactory results, exerting antimicrobial activity at the site and maintaining the bacterial growth inhibition. Table 2 presents the average time and average reduction of microorganisms in the main studies regarding the use of pure copper.

Only one study has not shown satisfactory results in relation to the significant decrease of microorganisms. The study was carried out with different fungal species tested in contact with copper and aluminium. The same method was applied to the different species, but one of them, *Aspergillus niger*, showed no significant decrease after 576 hours (24 days).

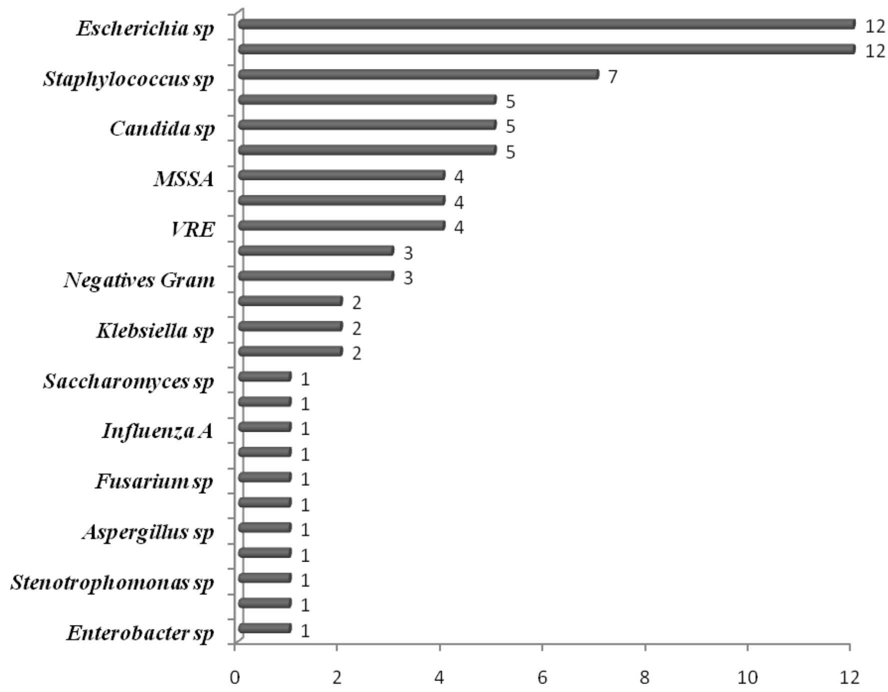
The studies analyzed in this review had no data regarding any contraindication or caution situations for copper use in health services. One of the studies analyzed showed that copper does not fix to latex items, such as gloves, thus excluding studies using this type of testing material.

Table 1. Types of alloys used in studies on the antimicrobial activity of copper. São Paulo, June 2011. Number of studies= 37.

Type of alloy	Frequency	%
Copper	32	86.5
Bronze	14	37.8
Cupronickel	13	35.1
CuNiZn (Cupronickel Zinc)	5	13.5
Other copper alloys (*)	9	24.3
Other alloys without copper (**)	8	21.6
Stainless steel	16	43.2
Uninformed	1	2.7

(*) Other copper alloys: CuFe, CuCr, CuAg, CuAl and copper-based solutions.
(**) Other alloys without copper: Tin, Silver, Aluminum, Nickel, Titanium, Cobalt, Zinc, Chromium, Lead, Molybdenum, Zirconium, Plastic.

Figure 1. Frequency distribution of micro-organisms used in studies of antimicrobial efficacy of copper, São Paulo, June 2011. Number of studies = 37 (#).



MRSA (Methicillin Resistant Staphylococcus aureus*), VRE (Vancomycin resistant* Enterococci*), HIV1 (Human Immunodeficiency Virus 1). (#) Some papers assessed more than one species of microorganism.*

Table 2. Average time and amount of reduction of microorganisms in studies evaluating pure copper (Cu 100%). Number of studies = 32. São Paulo, June 2011.

Main microorganism	Average time (minutes)	Average reduction (Log)
Acinetobacter baumannii	60 – 180	5
Candida albicans	24 – 60	7
Clostridium difficile	80 – 220	6
Enterococcus sp	60 – 90	6
Escherichia coli	45 – 100	6
MRSA	60 – 120	6
Pseudomonas aeruginosa	60 – 72	NI*
Staphylococcus aureus	60 – 120	NI*
VRE	60 – 90	NI*

MRSA (Methicillin Resistant Staphylococcus aureus), VRE (Vancomycin resistant Enterococci), NI Not Informed.*

DISCUSSION

The present literature review identified a high frequency of comparative experimental studies in order to find a copper alloy which is more effective against microorganisms. Experimental study with pre-defined inoculums is the best method to find appropriate responses to the antimicrobial action of previously known pathogens commonly found in hospitals.

A metal used in comparison with copper alloys is stainless steel, a metal found predominantly in hospital settings, due to its appearance of cleanliness and corrosion resistance, but there are no advantages in using this antimicrobial metal. Recent studies have concluded that important microorganisms were found alive on stainless steel surfaces for an extended period.[5] These surfaces can act as reservoirs for the transfer of microorganisms between healthcare workers and patients; this method of transmission is one of the most frequent found in hospitals.[9] Therefore it is reasonable that the majority of studies found in the present review favour research on pathogens most frequently found in hospital settings, MRSA, *Escherichia coli*, *Candida albicans*, and *Staphylococcus* sp., for instance.

The present literature revision concludes that there is evidence that surfaces of copper and copper alloys reduce some living cells of bacteria when in contact with the metal. The results showed that pure copper has good efficacy when exposed to pathogens and its alloys containing high concentrations of copper also showed good results.

The mode of action exerted by copper against microbial agents has not been determined in the studies evaluated. The mechanism of death by contact with the copper surface has not yet been clearly explained. It was found that bacteria placed in contact with the dry antimicrobial copper surface suffered the greatest impact, suggesting the involvement of dissolution of copper ions in the process.[10] One of the alternatives suggested in the studies is that cell membrane can be subjected to stress caused by the copper surface, where membrane damage occurring in contact with the copper surface leads to physical disruption of cells and consequently cell lysis. Another suggestion proposes a model of DNA damage as a subjacent mechanism.[4]

The Centres for Disease Control and Prevention (CDC) guideline for preventing infections associated with the environment included copper among other elements to be evaluated in future research to prevent contamination of water systems by *Legionella* spp. The same guide cites the possible incorporation of copper in building materials with a view to a fungicide effect, targeting the prevention of *Aspergillus* sp infections.[11]

Assessment developed by Wexford Labs, DKI and Hill-Rom, on behalf of the Copper Development Association to identify the effect of disinfectants on copper alloy surfaces, indicate the possible use of the most frequently used germicidal agents in healthcare institutions.[12] However, this use in clinical practices has not been sufficiently explored.

Despite the knowledge of very ancient civilizations in the use of copper, this review identified a major gap in information regarding the toxicity and potential interactions with substances used in healthcare, pointing out the need for studies that go further in this direction.

In conclusion, the present study demonstrated that there is evidence of an antimicrobial action of copper, although the mechanism is still not well understood. Surfaces with pure copper showed the best effects on microorganisms, followed by alloys containing high concentrations of copper. The antimicrobial effect of copper showed variations in time and degree, related to the reduction of microorganisms according to different species.

Studies to recognize aspects of toxicity and interactions with products used in healthcare can contribute to the evaluation of the potential use of copper as an agent for preventing healthcare-associated infections.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest related to the present study.

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