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# Safety of Using Diapers Containing Copper Oxide in Chronic Care Elderly Patients

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**Abstract:** Copper has very potent antibacterial, antifungal, antiviral and acaricidal properties. Recently the use of copper alloys in hospital wards has been shown to reduce bioburden and nosocomial infection rates. We hypothesized that the use of copper oxide in textiles and other products that are in close contact with the patients may significantly reduce bioburden in clinical settings and consequently reduce the risk of nosocomial infections. In order to test this hypothesis we intend to conduct a trial in which we will examine if the nosocomial infection rates in a chronic care ward will be reduced when all the textile products will include copper oxide. The risk of adverse reactions due to dermal contact with copper are considered extremely low and medical devices containing copper, such as intrauterine devices and dental amalgams, are safely used for decades. Textile products containing copper oxide are being sold worldwide for several years and not even one adverse reaction was noted. However, in spite of all the above, and in preparation to the clinical trial we intend to conduct in a chronic care ward (long-term care facility), we conducted this preliminary study in which we examined the safety of using copper oxide impregnated diapers in 16 chronic care patients that used the diapers for 6 consecutive months. Importantly, not even one adverse reaction was recorded during the whole trial, indicating the high safety of the diapers. Therefore, this study allows us to examine the efficacy of textiles containing copper oxide in reducing nosocomial infections in larger populations, including in frail chronic care patients.

**Keywords:** Vegetative state, clinical trial, copper oxide, diapers, safety, skin.

## INTRODUCTION

Copper has been used as a biocide for centuries [1]. For example, in ancient Egypt and Greece copper was used to sterilize water, treat wounds and pulmonary diseases; in Mexico the Aztecs used copper oxide and malachite for treating skin conditions; and in India, Hindu devotees drink water that is stored in copper utensils as it keeps the water sparkling clean. The fungicidal, antibacterial and antiviral properties of copper have been demonstrated in many controlled laboratory studies and are very well documented [2,3]. Copper exerts its toxicity to microorganisms through several parallel non-specific mechanisms [3], which include a) damage to the microorganisms' envelope by interacting with lipopolysaccharide patches on the outer plasma membrane, causing significant permeability changes that lead to loss of cell viability; b) eliciting marked changes in the activities of many essential membrane-dependent functions, including transport protein activity and ion permeability; c) damage of many proteins, both on the microorganism envelope or within the cell, via displacement of essential metals from their native binding sites in the proteins, or via direct interactions with the proteins, resulting in the inhibition or neutralization of the protein biological activities; d) damage of nucleic acids by cross linking within and between strands of DNA and by causing helical structure disorders and DNA denaturation; and e) redox cycling between $Cu^{2+}$ and $Cu^{1+}$, which can catalyze the production of highly hydroxyl radicals, with subsequent damage to lipids, proteins, DNA and other biomolecules. Many bacteria and fungi have different mechanisms to deal with excess copper [2]. However, over a certain threshold and time of exposure, they cannot deal with the copper overload and die. In contrast to the highly resistant microbes that have evolved to antibiotics in less than 50 years of use, tolerant microorganisms to copper are extremely rare even though copper has been a part of the earth for millions of years. This can be explained by the multisite and non-specific kill mechanisms of copper [2]. Significantly, copper displays potent biocidal activity also against antibiotic resistant bacteria and antiviral resistant viruses [4-6].

Copper and copper-based compounds are routinely used in several health-related areas. These include control of *Legionella* [7, 8] and other bacteria [9] in hospital water distribution systems; reduction of caries in dentistry [10]; reduction of food borne diseases [11-13]; and prevention of conception [14]. Copper intrauterine devices are being widely used by millions of women, are approved by the regulatory agencies (e.g. USA FDA) and has been in practice for several decades and are considered very safe [15]. Recently it has been demonstrated in hospitals, clinics and elderly homes, that substituting the existing hard surfaces

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with copper based surfaces, reduces the bioburden and the transmission of health-associated (nosocomial) pathogens [16]. The U.S. Environmental Protection Agency (EPA) in March 2008 approved the registration of copper alloys as materials with antimicrobial properties, making copper as the only metal that can be used in hospitals in order to reduce bioburden and for which public health claims can be made.

A durable platform technology has been developed that embeds copper oxide particles into polymeric materials [4, 5]. The introduction of copper oxide particles into polymeric materials endows them with potent broad-spectrum anti-microbial (anti-bacterial, anti-viral, anti-fungal) [4-6], anti-mite properties [4, 17], and in some applications has a direct effect on physiological processes, such as enhanced wound healing [18]. Since copper oxide is a non-soluble form of copper, the copper oxide particles do not wash out during laundry and the textile products remain active for the life of the products [4, 5].

Animal studies required by the regulatory agencies and conducted according to the International Standard ISO 10993 demonstrated that the copper oxide containing textile products do not cause skin irritation or skin sensitization or any other adverse reaction, including in intact or breached skin [4, 5, 19, 20]. The safety of the copper oxide consumer textile products containing copper oxide has also been demonstrated in several double blind clinical trials with over 200 healthy individuals [21-25] that used products containing copper oxide for up to 2 months without even one adverse reaction registered.

The innovative potential use of this technology in health-related applications include making hospital soft surfaces, like sheets, patient robes, patient pajamas, nurse clothing and diapers, from copper oxide impregnated biocidal textiles [4, 5, 19, 26]. We hypothesized that the use of copper oxide containing textiles, especially sheets, pyjamas and diapers that are in close contact with the patients may significantly reduce bioburden in clinical settings and consequently reduce the risk of nosocomial infections [26]. In order to test this hypothesis we intend to conduct a trial in which we will examine if the nosocomial infection rates in a chronic care ward will be reduced when all the textile products will include copper oxide. The safety of sheets containing copper oxide was already evaluated in a general ward with patients that slept on the sheets for a total of 300 nights and no adverse events were reported [5]. In the current study, we examined the safety of using diapers containing copper oxide in 16 elderly chronic care patients that used the diapers for a period of 6 months.

## EXPERIMENTAL

A total of 16 participants participated in the 6 month Trial carried out between August 2011 until February 2012 following informed consent obtained from each patient or each patient legal guardian, and approval by the Hospital Ethics Committee. The patients belonged to 4 different wards in the Chronic Care Reuth Medical Center. Eleven patients were females and 5 patients were males. The mean age ± SD of the patients was 67±18 years. The median age was 68 years. The youngest patient was 33 and the oldest 88. All these patients were chronic patients that were hospitalized prior to August 2010, i.e. these were well known patients for whom all clinical data was available for at least a period of one year before the commencement of the trial. Twelve patients were in a vegetative state -VS (a clinical syndrome comprising of wakefulness, unawareness, tetraplegia; patients in VS can fill pain and discomfort and show it by facial expressions) one patient was in coma and 3 patients were conscious/responsive patients. Six patients suffered from diabetes type 2, and 1 patient suffered from a pressure sore in the sacrum area at the beginning of the trial. All 16 patients had a constant feeding tube. Fourteen patients had tracheostomy (respiratory tube), 12 were receiving inhalations, all were being fed via a feeding tube, 2 had a urinary catheter, 2 received steroids at least once during the study and 6 received antibiotics at least once during the study. Each patient general and medical characteristic are detailed in Table **1**.

All patients were given the test diapers instead of the regular diapers they used. The test diapers were produced at Hugla-KC, Affula Ilit, Israel, the same manufacturer of the regular diapers used in the hospital, using standard production procedures and using the same exact materials, with the exception of the internal layer of the diaper that included copper oxide. The internal layer that comes in contact with the patient's skin in the test diapers was a non-woven polypropylene fabric containing 3% weight/weight copper oxide particles (Fig. **1**). The test diapers were used constantly every day for a 6 months period. The test diapers were changed every 2-4 hours, with the same frequency as the regular diapers are changed in the hospital, or according to necessity. No other difference what so ever in the treatment of these patients or other patients in the Wards was made during the Trial. The end points examined were the wellbeing of the skin, skin redness, and appearance of skin rashes or any other adverse reactions in the skin in contact with the diapers and elsewhere in the body. The skin of all patients was analyzed by the appointed Trial nurse (W.I.) and a wound care specialist, the Head physician and Head nurse of the particular ward in which the particular patient was hospitalized. Initially the Trial nurse, the wound care specialist and the relevant head nurse monitored the patients' skin 4 to 5 times per week for a period of 3 months, and the Head physician once a week. Till the end of the study the appearance of any skin rashes, or any other local skin adverse reactions in the treated area or elsewhere was monitored by the above mentioned individuals once a week. A 4 scale score was used to monitor the skin redness as follows: 1= no redness; 2= low redness; 3= medium redness; 4= high redness.

## RESULTS AND DISCUSSION

No skin rashes or any other adverse reactions on the skin in contact with the diaper or elsewhere were registered in all 16 studied patients during the whole 6 months trial. The skin redness initial condition for each patient stayed the same during the trial (Table **2**). No fever events above 38.5°C were recorded throughout the trial (Table **3**). No gastrointestinal infections were recorded in all 16 patients during the trial. One urinary tract infection and one upper respiratory infection were recorded during the trial. Three lower respiratory infection events were recorded, two in Patient 5. The 2 skin infections that occurred in Patient 10

**Table 1. Specific Patient Medical Characteristics and General Treatments**

| Pt. # | Age | Sex | Diagnosis | Background | Isolation | Mobility | Inhalation | Trache ostomy | Urinary Catheter | Feeding Tube | Steroids Given | Antibiotics Given |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 88 | F | VS[a]; Degenerative CNS[b] Disorder | Epilepsy | No | Bed | Yes | No | No | Yes | No | Yes |
| 2 | 73 | M | VS; ABD[c] | Ischemic Heart Disease | No | Bed | No | Yes | No | Yes | No | No |
| 3 | 75 | F | Respiratory Failure | Dementia; DM[g] | Yes (CRKP[j]) | Bed | Yes | Yes | No | Yes | No | No |
| 4 | 63 | F | Mechanical Ventilation; ALD[d] | Depression; DM | No | Bed | Yes | Yes | No | Yes | Yes | No |
| 5 | 84 | F | Mechanical Ventilation; COPD[e] | CVA[h]; Dementia; DM | No | Bed | Yes | Yes | No | Yes | No | Yes |
| 6 | 53 | F | VS; ABD | | No | Bed | Yes | Yes | Yes | Yes | No | Yes |
| 7 | 60 | F | VS; MS[f] | Hypertension; Anemia; Pressure sore | No | Bed | Yes | Yes | No | Yes | No | No |
| 8 | 33 | M | VS | Road Accident | No | Bed | Yes | Yes | Yes | Yes | No | Yes |
| 9 | 88 | M | VS; ABD | DM | Yes (MRSA[k]) | Bed | Yes | Yes | No | Yes | No | Yes |
| 10 | 54 | F | Muscular Dystrophy | Paranoid Schizophrenia | No | Bed | Yes | Yes | No | Yes | No | No |
| 11 | 88 | F | COPD | Chronic heart and renal failure; DM | No | Bed | Yes | Yes | No | Yes | No | No |
| 12 | 75 | M | VS; ABD | Hypothyroidism; Anemia | No | Bed | Yes | Yes | No | Yes | No | Yes |
| 13 | 45 | M | ABD; Coma | Suicide; DM | No | Bed | No | Yes | No | Yes | No | No |
| 14 | 63 | F | Traumatic brain injury | Multiple trauma; V-P Shunt; Spastic Tetraplegia | No | Bed | No | No | No | Yes | No | No |
| 15 | 42 | F | Sub-dural Hemorrhage; s/p Craniotomy | Recurrent U.T.I.[i] | No | Bed | No | Yes | No | Yes | No | No |
| 16 | 80 | F | COPD | Hypertension; Ischemic Heart Disease | Yes (CRKP) | Bed | Yes | Yes | No | Yes | Yes | No |

[a]Vegetative State

[b]Central Nervous System

[c]Anoxic Brain Damage

[d]Amyotrophic Lateral Disease

[e]Chronic obstructive pulmonary disease

[f] Multiple Sclerosis

[g]Diabetes Mellitus type 2

[h]Cerebrovascular accident

[i]Urinary tract infection

[j]Carbapenemresistant *Klebsiella pneumoniae*

[k]Methicillin Resistant *Staphylococcus aureus*

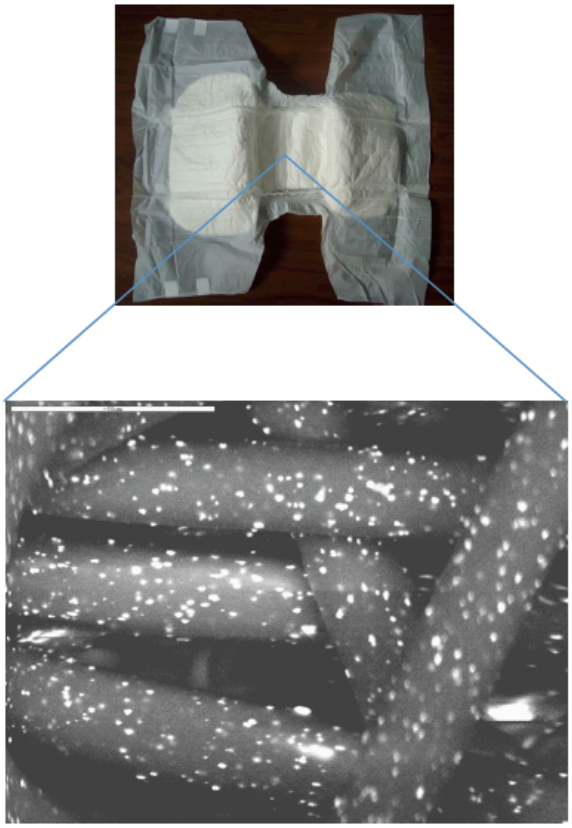

**Fig. (1).** Scanning electronic microscope image of the copper oxide containing inner layer of the diapers tested. The while dots are the copper oxide particles.

**Table 2. Skin Condition of the Patients Over the 6 Months Trial**

| Pt # | Skin Redness and or Rash[a] at | | Fluctuations in Skin Redness During Study | Number of Skin Rashes During Study | Overall Impression of the Skin Wellbeing[b] |
|---|---|---|---|---|---|
| | Beginning of Study | End of Study | | | |
| 1 | 1 | 1 | No | 0 | Improved |
| 2 | 3 | 3 | No | 0 | Improved |
| 3 | 1 | 1 | No | 0 | Improved |
| 4 | 2 | 2 | No | 0 | Improved |
| 5 | 1 | 1 | No | 0 | Improved |
| 6 | 3 | 3 | No | 0 | Improved |
| 7 | 4 | 4 | No | 0 | Improved |
| 8 | 2 | 2 | No | 0 | Improved |
| 9 | 3 | 3 | No | 0 | Improved |
| 10 | 1 | 1 | No | 0 | Improved |
| 11 | 3 | 3 | No | 0 | Improved |
| 12 | 4 | 4 | No | 0 | Improved |
| 13 | 2 | 2 | No | 0 | Improved |
| 14 | 3 | 3 | No | 1[c] | Improved |
| 15 | 3 | 3 | No | 0 | Improved |
| 16 | 2 | 2 | No | 0 | Improved |

[a]A 4 scale score was used to monitor the skin redness as follows: 1= no redness; 2= low redness; 3= medium redness; 4= high redness.[b]The impression of the wellbeing of the skin was based on the impression of the treating stuff of the improvement in the texture/softness/appearance of the patients skin following the switch to the use of the diapers containing copper oxide. [c]A trial non-related local rash and redness event was registered following shaving (the shaving was done for reasons not related to the trial).

**Table 3. Number of Concomitant Infectionand Fever Events that Occurred During the 6 Months Trial**

| Pt Number | Upper Respiratory Infections | Lower Respiratory Infections | Urinary Tract Infections | Skin Infections | Gastrointestinal Infections | Eye Infections | Fever Events (>38.5°C) |
|---|---|---|---|---|---|---|---|
| 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 5 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 8 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 9 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| 10 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| 11 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 14 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 16 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

(Table **3**) were not in the area of contact with the diaper. Four eye infections occurred. Overall the frequency of infections and type of infections that occurred are typical to the population studied and were very similar and even somewhat lower than those that occurred in these patients during the same period a year earlier. No statistical differences between both periods were found (data not shown).

In all patients, without exception, the skin in contact with the diaper looked healthier as earlier as one month of the test diapers usage. The skin continued to look healthy throughout the 6 month trial and several personnel mentioned that the skin seemed to look like "baby skin". Based on the experience of the hospital personnel, all 12 patients with VS responded positively to the diapers, i.e. they did not express any discomfort and did not have any skin irritation due to using the diapers. The 3 conscious patients verbally mentioned their satisfaction of the diapers. Obviously no feedback could be obtained from the patient in coma, as the patient was not responsive at all.

The improved skin appearance could not be explained by better absorbency of the test diapers, as both the test and the regularly used diapers have the same exact absorbency capacity (data not shown). The skin well-being effect of the diapers may be explained by the positive effect that copper has on the skin. Copper ions are liberated into the moisture found between the skin and the diapers. It has been shown that copper ions can be absorbed through skin [27, 28]. Once absorbed they induce fibroblast proliferation, and stabilization and stimulation of formation of extracellular matrix proteins, such as collagen, fibronectin and integrin [29-32]. Collagen, a component of the extracellular matrix (ECM), provides together with other proteins (e.g. fibronectin) structure and strength to skin, whereas elastin provides firmness and resiliency/elasticity characteristics. Several proteins, such as lysyl oxidase, needed for efficient ECM protein cross-linking, including of collagen, elastin and fibronectin, require copper as a cofactor [33]. Human peptide Gly-(L-His)-(L-Lys) or GHK, when it interacts with copper ions, increases protein synthesis of collagen and elastin [34]. Copper is also required by the enzyme superoxide dismutase present in the skin, which is important in protection against free radicals [35]. Accordingly, double blind placebo controlled studies demonstrated improvement of the facial skin condition when in contact with pillowcases containing copper oxide particles [21, 22].

No new sores occurred in all 15 patients without sores at the commencement of the Trial, and the size of the pressure sore in the sacrum in one patient (60 years female suffering from VS, multiple sclerosis and in need of mechanical ventilation) diminished from 7.2 $cm^3$ to 1.75 $cm^3$ within 2 months, i.e. by ~75% during the first 2 months of the trial and then stayed the same. Thus, not only the diaper did not interfere with the wound healing process, but it may have even helped this process, based on our previous observations of enhanced wound healing by copper oxide containing wound dressings [18, 20, 36].

The use of copper in medical devices is considered safe, as demonstrated by the wide and prolonged use of copper intrauterine devices and dental amalgams [15, 37]. Biocidal textiles may be important in the reduction of nosocomial infections [16, 26, 38, 39]. It is important to make sure that

these textiles are extremely safe for use in medical facilities and in elderly homes. While the high safety of biocidal textile products containing copper oxide has been demonstrated in healthy individuals and in patients in an acute care general ward [5, 23], it was important to examine their safety with weak and difficult to treat patients and following continuous exposure of the patients, including the patients' openings to the copper oxide containing products. Indeed, the special importance of this study is that a) the test patients were all very weak, immune-compromised individuals, with many chronic life threatening diseases and conditions (e.g. constantly intubated, etc.); and b) the urinary/sex and gastrointestinal patient openings were constantly exposed to the test diaper. Even under such relative extreme conditions, the lack of any adverse effects demonstrates the high safety not only of diapers containing copper oxide, but in general of textile containing copper oxide in a hospital environment. This study allows for larger trials to be conducted including in a long-term care facility, in order to test the safety and efficacy of using textiles containing copper oxide in the fight against nosocomial infections.

## CONFLICT OF INTEREST

GB is the Chief Medical Scientist of Cupron, the company that developed the technology of incorporating copper into textile products. All other authors have no conflicts of interests.

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Declared none.

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