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AN ANCIENT SOLUTION FOR NEW BIOCIDAL NONWOVEN FABRICS

Copper ions, either alone or in copper complexes, have been used for centuries to disinfect liquids, solids and human tissue¹. Introducing copper into cotton fibers, latex and other polymeric materials enables the production of clothing, bedding and other articles that possess biocidal properties². This article discusses the biocidal properties of nonwoven fabrics containing copper oxide and their possible uses. These applications include medical issues of the greatest importance, such as viral transmissions and nosocomial infections.

HISTORY OF COPPER USE

The ancient Greeks (400 BC) prescribed copper for pulmonary diseases and for purifying drinking water. The Celts produced whisky in copper vessels in Scotland around 800 AD, a practice that has continued to the present day. Copper strips were nailed to ship's hulls by the early Phoenicians to inhibit fouling, as cleaner vessels were faster and more maneuverable. Gangajal (holy water taken from the Ganges River) has been stored in copper utensils in

Hindu households for centuries due to copper's antifouling and bacteriostatic properties.

By the 18th century, copper had come into wide clinical use in the western world for the treatment of mental disorders and afflictions of the lungs. Early American pioneers moving west across the continent put silver and copper coins in large wooden water casks to provide them with safe drinking water for their long voyage. In World War II, Japanese soldiers put pieces of copper in their water bottles to help prevent dysentery. Copper sulphate is highly prized by some inhabitants of Africa and Asia for healing sores and skin diseases. NASA first designed an ionization copper-silver sterilizing system for its Apollo flights.

Today copper is used as a water purifier, algaecide, fungicide, nematocide, molluscicide, and as an antibacterial and antifouling agent³⁻⁷. It is considered safe to humans, as demonstrated by the widespread and prolonged use of copper intrauterine devices (IUDs) by women^{8,9}. In contrast to the low

sensitivity of human tissue (skin or other) to copper¹⁰, microorganisms are extremely susceptible to copper. Copper toxicity to microorganisms, including viruses, may occur through different methods: the displacement of essential metals from their native binding sites, interference with oxidative phosphorylation and osmotic balance, and through alterations in the conformational structure of nucleic acids, membranes and proteins¹¹.

IMPREGNATING COPPER OXIDE INTO POLYMERIC FIBERS

Utilizing the properties of copper, a durable platform technology has been developed in which polyester, polypropylene, polyethylene, polyurethane, polyolefin or nylon fibers are impregnated with copper oxide^{1,12}.

Basically, impregnation of copper into the various synthetic fibers mentioned above is achieved by adding a cupric oxide powder to the polymers during the masterbatch preparation stage. The masterbatch can be made in industrially accepted concentrations and added to the polymeric slurry the same way any other masterbatch

would be added, such as for pigmentation, etc. The copper oxide-doped masterbatch is designed in such a way as to allow fiber extrusion in normal production systems. The fibers can be cut into short staple or produced in filament form and texturized, if so desired. The impregnated fibers can be introduced at the blending stage of varn production or directly into nonwoven products, so that no manufacturing processes are changed. Thus, the mass production of nonwoven fabrics into which copper oxide treated fibers have been introduced may be easily achieved without any alteration of industrial procedures or machinery.

Utilizing this technology, we have produced spunbond as well as melt-blown nonwoven fabrics containing up to 3% and 5% copper oxide additive, respectively, without any production problems. Figure 1 shows scanning electronic microscope (SEM) images comparing a typical spunbond with a spunbond fabric in which the polypropylene fibers were produced from a masterbatch containing 3% (weight/weight) copper oxide.

Importantly, these copper oxideimpregnated nonwoven fabrics possess broad-spectrum biocidal properties—they are antibacterial, antifungal, and antiviral (Figure 2).

The American Association of Textile Chemists and Colorists (AATCC) Test Method 100-1993 was used to determine the biocidal properties of the fabrics against the bacteria and fungi tested. These tests were carried out by an independent laboratory (AminoLab Laboratory Services, Israel). The HIV-1 testing was done in-house. For further experimental details, see Reference 2.

Exposure of bacteria, fungi or viruses to the nonwoven fabric containing 3% (w/w) copper oxide particles for just five minutes resulted in more than a 2-log reduction (>99%) in their titers. Prolongation of the exposure of these microorganisms to the fabrics (20 minutes for HIV-1, 4 hours for the bacteria and 24 hours for the fungi) further reduced their viable titers by more than 4 logs (>99.99%).

DISCUSSION

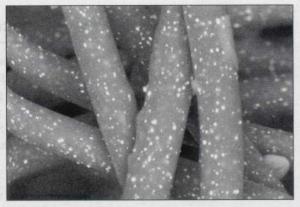
Permanent or durable binding of inorganic compounds to organic substrates is extremely difficult, especial-

SEM of Spunbond PP Nonwoven With and Without Embedded Copper Oxide



Spunbond Fibers

*Copper oxide embedded at 3% by weight



Embedded Spunbond Fibers*

Figure 1

ly for mass production processes. By utilizing the properties of copper, an inexpensive platform technology was developed which permanently binds copper to textile fibers from which nonwoven fabrics can be produced. The introduction of copper oxide at the early stages of the production cycle enables the use of the coppertreated fibers in many manufacturing processes without altering manufacturing procedures or equipment, allowing for rapid and simple production of nonwoven fabrics with potent biocidal qualities.

Animal studies demonstrated that the copper-treated fibers do not possess skin sensitizing properties². In another study, none of the 100 individuals who used socks containing copper-impregnated fibers to alleviate their athlete's foot conditions reported any

negative effects caused by the socks¹². Similarly, none of the 100 patients who slept on sheets containing copper-treated fibers reported any adverse effects¹². These findings are in accordance with the very low risk of adverse skin reactions associated with copper¹⁶.

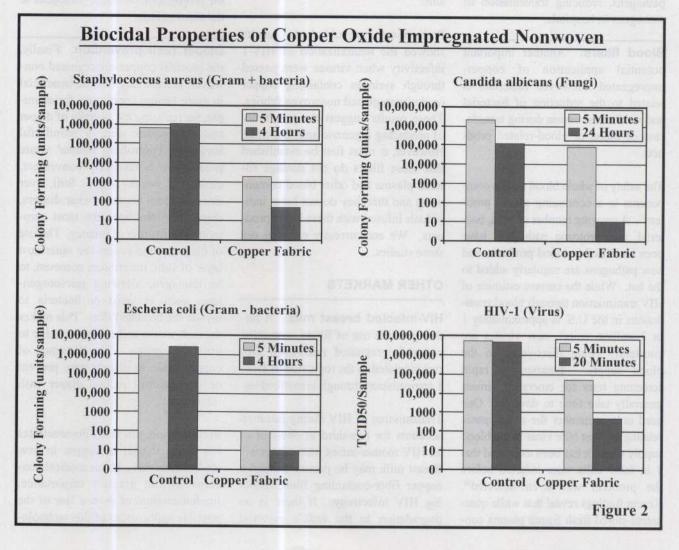
NOSOCOMIAL INFECTION

The possibility of introducing copper oxide into nonwoven fabrics may have significant ramifications. One example is the reduction of nosocomial (hospital acquired) infections in hospitals. Over 90,000 deaths in the U.S. are attributed to these infections each year, and one out of four deaths in intensive care units is caused by an infection unrelated to the initial cause of hospitalization. The main sources for contamination are the patient's

skin flora, the flora on the hands of medical and nursing staff, and contaminated infusion fluids.

AIRBORNE PATHOGENS

Although the contribution of airborne transmission of pathogens to nosocomial infections has been controversial, much data is accumulating in support of the notion that airborne transmission of bacteria significantly contributes to hospital acquired infections13. Airborne transmission is known to be the route of infection for diseases such as tuberculosis and aspergillosis. It has also been implicated in nosocomial outbreaks of MRSA (Methicillin-resistant Staphylococcus aureus14), Acinetobacter baumannii15 and Pseudomonas aeruginosa16. Furthermore, hospital ventilation systems have also been implicat-



ed in nosocomial MRSA outbreaks13.

Preliminary data indicate that addition of copper oxide-impregnated nonwoven fabrics into air filters significantly reduces the passage of viable microbes (unpublished results). Thus the use of nonwoven copper-impregnated fabrics in air filters in a hospital setting may reduce the spread of microorganisms in hospital wards, resulting in a reduction of nosocomial infections.

Barrier fabrics. Similarly, the use of copper-impregnated nonwoven fabrics in disposable hospital textiles—such as barrier fabrics—will not only confer protection to the wearer from possible pathogen exposure, for example in contaminated blood, but will also confer protection to the immediate environment from these pathogens, reducing transmission of pathogens in hospitals.

Blood filters. Another important potential application of copperimpregnated nonwoven materials is related to the reduction of bacterial and viral transmission during transfusion of blood or blood-related products.

The safety of whole blood and its components is a continuing global problem17. A growing number of viral, bacterial, and protozoa pathogens have been identified in blood products, and new pathogens are regularly added to the list. While the current estimate of HIV transmission through blood transfusions in the U.S. is approximately 1 in 2 million units18, new viruses are constantly being discovered in the Inexpensive rapid blood supply. screening tests for emerging viruses generally take time to develop. One need only remember the recent panic relating to West Nile virus in the blood supply where it has been estimated that 1 in 5000 units were infected before the problem was even detected19. Recent findings reveal that while quarantine-stored fresh frozen plasma contains physiologically active, therapeutically relevant plasma proteins, it also carries a risk of transmitting HIV and other viruses

Mortality and morbidity associated with blood transfusions that are contaminated by pathogens have been well established. In response, regulatory agencies and blood bank standards groups have called for efficient new technologies to improve the safety of blood products20. In areas of the world where screening tests are too expensive to be performed regularly, a cheap, rapid virus inactivation filter would be extremely helpful. Even in the U.S., hospitals can no longer afford to pay for expensive tests for "pathogen du jour"21. each Accordingly, a filter that can inactivate a broad spectrum of viruses in blood products would be very valuable.

Preliminary unpublished results showed the neutralization of HIV-1 infectivity when viruses were passed through syringes containing copper oxide-impregnated nonwoven fabrics. These results suggest the possibility of producing a generic antiviral filter. However, it must first be established that these filters do not damage filtered plasma and other blood components and that they do not harm individuals infused with these blood products. We are currently carrying out these studies.

OTHER MARKETS

HIV-infected breast milk. A further possible use of filters containing copper-impregnated nonwoven fabrics is related to the reduction of HIV-1 transmission through breastfeeding.

Transmission of HIV during lactation accounts for one-third to one-half of all HIV mother-infant transmissions²². Breast milk may be passed through a copper fiber-containing filter, reducing HIV infectivity. If there is no degradation to the milk's essential

nutrients as a result of filtration, the filtered milk may be fed to infants, thereby reducing the risk of HIV transmission.

Admittedly, implementing such measures may be very difficult because of sociological factors existing in developing countries. However, HIV-1, as well as other viruses, will be with us for many years, and methods to reduce their impact must be developed.

Military barrier fabrics. These non-woven copper oxide-containing fabrics may also be incorporated into army Nuclear Bacteriological Chemical (NBC) suits. Similarly to barrier fabrics used in hospitals, these suits will not only confer protection to the wearer from possible pathogens to which he may be exposed, but also will reduce the propagation of viable pathogens to the surroundings.

Diaper rash prevention. Finally, the biocidal copper-impregnated nonwoven fabrics may also be beneficial in more benign conditions, for example, for reducing the severity of diaper rash. Diapers were a wonderful invention, controlling infants' waste products in a relatively convenient, clean and healthy way. Still, ever since children began to wear diapers, diaper rash has been the most common skin disorder of infancy. The use of diapers often causes the outermost layer of skin, the stratum corneum, to be damaged, allowing microorganisms such as yeast or bacteria to invade the breached skin. This makes the rash worse and less responsive to usual treatments. The presence of copper oxide in diapers may prevent or significantly reduce diaper rash infections.

In conclusion, this study demonstrates the potential uses of copper in new applications that address medical concerns of the greatest importance. Implementation of even a few of the possible applications of this technology may have a major effect on the lives of many.

REFERENCES

- 1. Dollwet, H.H.A. and Sorenson, J.R.J., "Historic uses of copper compounds in medicine," *Trace Elements in Medicine*, 2: 80-87 (2001).
- 2. Borkow, G. and Gabbay, J., "Putting copper into action: copper-impregnated products with potent biocidal activities," *FASEB J.* 18(14): 1728-1730 (2004).
- 3. Cooney, T.E., "Bactericidal activity of copper and noncopper paints," *Infect. Control Hosp. Epidemiol.* 16(8): 444-450 (1995).
- 4. Cooney, J.J. and Tang, R.J., "Quantifying effects of antifouling paints on microbial biofilm formation," *Methods Enzymol.*, 310: 637-644 (1999).
- 5. Stout, J.E., Lin, Y.S., Goetz, A.M. and Muder, R.R., "Controlling Legionella in hospital water systems: experience with the superheat-and-flush method and copper-silver ionization," *Infect. Control Hosp. Epidemiol.*, 19(12): 911-914 (1998).
- 6. Weber, D.J. and Rutala, W.H., "Use of metals as microbiocides in preventing infections in healthcare," *Disinfection, Sterilization, and Preservation, Fifth Ed. Block, S.S.* (Ed.) New York: Lippincott Williams and Wilkins, pp 415-430 (2001).
- 7. Fraser, W.D., Quinlan, A., Reid, J. and Smith, R.N, "Huntingdon Res Center: Primary screening of copper compounds for herbicidal, nematocidal, fungicidal and bactericidal activity," INCRA Project no. 211: 43 (2001).
- 8. Bilian, X., "Intrauterine devices," Best. Pract. Res. Clin. Obstet. Gynaecol., 16(2): 155-168 (2002).

- 9. Hubacher, D., Lara-Ricalde, R., Taylor, D.J., Guerra-Infante, F. and Guzman-Rodriguez, R, "Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women," *N. Engl. J Med.*, 345(8): 561-567 (2001).
- 10. Hostynek, J.J. and Maibach, H.I., "Copper hypersensitivity: dermatologic aspects—an overview," *Rev. Environ. Health*, 18(3): 153-183 (2003).
- 11. Gabbay, J., et al., "Copper oxide impregnated textiles with potent biocidal activities," *Journal of Industrial Textiles*, In press (2005).
- 12. Borkow, G. and Gabbay, J., "Copper as a biocidal tool," *Current Medicinal Chemistry*, In press (2005).
- 13. Beggs, C.B., "The airborne transmission of infection in hospital buildings: fact or fiction?" *Indoor Built Environ* 12: 9–18 (2003).
- 14. Mortimer, E.A. Jr., Wolinsky, E., Gonzaga, A.J. and Rammelkamp, C.H. Jr., "Role of airborne transmission in staphylococcal infections," *Br Med J* 1: 319.; Mclean AS, Wilson, RD, Huang SJ., "Airborne methicillin-resistant Staphylococcus aureus (MRSA) in the Intensive Care Unit, http://www.aaic.net.au/default.asp?D =2002211 (1966)
- 15. Bernards, A.T., Frenay, H.M.E., Lim, B.T., Hendricks, W.D.H., Dijkshoorn, L. and van Boven, C.P.A., "Methicillin-resistant Staphylococcus aureus and Acinetobacter baumannii: An unexpected difference in epidemiologic behaviour," *Am. J. Infection Control*, 26: 544–551 (1998).
- 16. Grieble, H.G., Bird, T.J., Nidea, H.M. and Miller, C.A., "Chute-hydropulping waste disposal system: a reservoir of enteric bacilli and Pseudomonas in a modern hospital," *J. Infectious Diseases*, 130: 602 (1974).

- 17. Strong, D.M. and Katz, L., "Blood-bank testing for infectious diseases: how safe is blood transfusion?" *Trends Mol. Med.* 8: 355-358 (2002).
- 18. Goodnough, L.T., Shander, A. and Brecher, M. E., "Transfusion medicine: looking to the future," *Lancet* 361: 161-169 (2003).
- 19. Biggerstaff, B.J. and Petersen, L.R., "Estimated risk of West Nile virus transmission through blood transfusion during an epidemic in Queens, New York City," *Transfusion* 42: 1019-1026 (2002).
- 20. FDA Workshop, Minutes of "Safety and Efficacy of Methods for Reducing Pathogens in Cellular Blood Products Used in Transfusion," (Aug 8, 2003).
- 21. Snyder, E.L. and Dodd, R. Y., "Reducing the risk of blood transfusion," *Hematology* (Am. Soc. Hematol. Educ. Program), pp 433-442 (2001)
- 22. Fowler, M.G. and Newell, M.L., Breast-feeding and HIV-1 transmission in resource-limited settings," *J Acquir. Immune. Defic. Syndr.* 30: 230-239 (2002).

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